Version Date: 08 June 2023

CONSENT FOR RESEARCH
Penn State College of Medicine
Penn State Health

Title of Project:	Neuro-pharmacological properties of repurposed posaconazole in glioblastoma: A Phase 0 clinical trial
Principal Investigator:	Alireza Mansouri, MD
Address:	30 Hope Drive, Hershey, PA 17033
Telephone Numbers:	Weekdays: 8:00 a.m. to 5:00 p.m., (717) 531-3828. After hours call (717) 531-8521. Ask for the Neurosurgery doctor on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

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, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

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

We are asking you to take part in this voluntary research study because your recent magnetic resonance imaging (MRI) scan suggests that you have a high grade glioma (HGG), a rapidly growing brain tumor and will be having a biopsy or surgery. A biopsy just collects some of the tumor to make a diagnosis. Surgery (resection) involves removal of as much of the tumor as possible. You may have just been diagnosed with HGG or is may be a recurrence of a previous tumor.

What is the purpose of this research study?

The purpose of this voluntary research study is not to treat a patient's brain tumor, but rather to see if the study drug (posaconazole), which doctors already use for some infections, can enter brain tumors at a high enough amount to stop the tumor cells from dividing. Findings from this study can form the basis of future trials with therapeutic intent.

How long will the research study last?

It will take a maximum of 31 days to complete the study.

Version Date: 08 June 2023

What will I need to do?
If you agree to participate in the study, you will have blood drawn to check your count blood cell (CBC) and Comprehensive Metabolic Panel (which includes electrolytes, renal function and liver function) , and if they are acceptable, be given the study drug to begin taking. If you haven't had your biopsy or surgery within 3 day of starting the study drug, you would come in for a research only visit. The day of your surgery or biopsy, you will take the study drug, have a piece of tissue removed during surgery saved for research, and have some very tiny tubes called microdialysis catheters placed in your brain. After your surgery or biopsy, you will take study drug as directed. Fluid from the catheters in your brain will be collected on post –surgical Days 1 and 2. The catheters will be removed on Day 2 and your hospital visit will continue as normal. You will have a 2 weeks follow-up appointment with your surgeon as normal.

The control group will follow the same processes above, but without taking the study drug.

What are the main risks of taking part in the study?
For this study, the main risks to know about are: side effects from the study drug (common examples: headache, dizziness, numbness or tingling, diarrhea, nausea); infrequent: liver problems; uncommon: very slow, fast or irregular heartbeat), and those related to the insertion of the microdialysis tubes. For example, there is a chance that the catheter may break or get stuck in the brain that would require surgical intervention to remove it. There is also a very small possibility of bleeding along the catheter tip.

What are the possible benefits to me that may reasonably be expected from being in the research?
There are no benefits to you from taking part in this research. Results of the study may benefit other people in the future by helping us learn more about how the study drug (posaconazole) this drug is tolerated by people with HGGs and how it may affect brain tumor cells.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You can decide to participate or not to participate.

Instead of being in this research study, your choices may include:

- Receive commercially available treatments, including radiotherapy and other chemotherapy drugs.
- Be part of a different research study, if one is available.
- Choose not to be treated for your medical condition and only receive care to make you more comfortable).

DETAILED INFORMATION
The following is more detailed information about this study in addition to the information listed above.

1. Why is this research study being done?

This research is being done to find out if the study drug (posaconazole) can enter brain tumors at a high enough amount to stop the tumor cells from dividing. Posaconazole is a drug which doctors already use for fungal infections and is thought to be able to effect tumor cells. As treatments for this type of brain tumor are limited, it is hoped that the results of this study will help to determine if the study drug should be studied further as a possible treatment.

Approximately 10 people will take part in this research study at Penn State Health.

2. What will happen in this research study?

No study procedures will be performed until the informed consent process has been completed and you have signed the consent form.

Visit 1 (Screening and baseline)

Once informed consent has been obtained, the following are performed as **routine (standard)** or data collected from the electronic medical record (EMR) if they were performed within 31 days of consent:

- Demographics.
- CBC and Comprehensive Metabolic Panel (which includes electrolytes, renal function and liver function) (approximately 2 teaspoons of blood).
- Medical history.
- Neurological examination.
- Your baseline MRI scan will be reviewed.
- Concomitant (those you are already taking) medications are reviewed.
- A 12-lead electrocardiogram (ECG; tracing of your heart).
- If you are a female of childbearing age, a pregnancy test will be performed.

You will have additional blood (about 2 teaspoon) drawn for Comprehensive Metabolic Panel (CMP) **for the study drug group only**. You will then wait at the clinic or emergency department if no urgent surgery or biopsy indicated until these results are available (usually within 4 hours).

If your routine tests show that you are eligible and your liver function tests are acceptable, you will be able to continue in the study.

For female and childbearing potential patients, if you are pregnant, confirmed by the pregnancy test, the medical team can take appropriate steps to ensure the safety of both you and the fetus, and you will not be able to continue in the study.

Control group

If you are not eligible to participate in the posaconazole study or if the study drug group has been fully enrolled, you may be enrolled in the ketoconazole study, which has a separate consent form. If the ketoconazole study is fully enrolled or you are not eligible for the ketoconazole study, you will be enrolled in the control group.

Study drug group

You will be given 12 days' worth of the study drug (pills) and verbally instructed how and when to take them. The prescription bottle will have a label with this information on it as well.

You will be taking 300 mg of the study drug (three 100 mg tablets) by mouth twice a day the first day and then 300 mg once a day until the day of your biopsy or surgery. On the day of your biopsy or surgery, you will take your medication the morning of your biopsy or surgery (before the operation). You will then take the last dose of the medication in the morning of the day after your biopsy or surgery.

A medication diary will be provided to you if you are taking study medication as an outpatient.

If any of your routine tests or liver function tests are outside the acceptable ranges for the study, you will not be able to continue in the study. Your doctor will follow-up with you regarding any abnormal results.

Visit 2 (3 days +/-2 days days after starting the study drug)

This visit is ONLY for the study drug arm and ONLY if the participant doesn't have biopsy or surgery within 7-10 days. Participants will return to the clinic for a **research-only visit**. At this visit, the following will be performed:

- .
- Collection of adverse events.
- Concomitant medications reviewed.
- A 12-lead ECG to rule out QTc prolongation
- Comprehensive Metabolic Panel (which includes electrolytes, renal function and liver function)(approximately 1 teaspoon of blood).

Visit 3 (Day of your biopsy or surgery)

Control group

The following will be performed for the **research only**:

- Collection of adverse events.

Study drug group

You will bring your study drug prescription bottle and your medication diary with you to the hospital.

-

The following will be performed for **research only**:

- You will take your study drug 8 (+/- 4 hours) am, before your biopsy or surgery.
- Concomitant (those you are already taking) medications are reviewed.
- Collection of adverse events.

For both the study and control groups, the following will be performed for **research-only**:

- During your biopsy or surgery, a small piece of the tissue you are having removed would be set aside for the research.
    - If you are having a resection, two samples, with no individual sample greater than 1cm x 1cm, will be taken from your tumor.
    - If you are having biopsy, a small sample called a "core needle sample" will be taken.
- A blood sample will be taken during your surgery or biopsy (about 1 teaspoon).
- If your tumor is diagnosed as a HGG, microdialysis catheters (very tiny tubes) will be placed in your brain.
- **If your tumor is NOT diagnosed as a HGG, your biopsy or surgery and hospital stay will continue without Visits 4-7**. You will still attend a post-operative visit approximately 14 days after your biopsy or surgery, but no research-only procedures will be performed. Safety data collected to this point will still be used.

Visit 4 (Post-operative, Day 0)

Control group

After your biopsy or surgery is completed, you will have the following as **routine (standard care)**:

- Computed tomography (CT) of the head.
- Neurological examination.

The following will be performed for **research only**:

- Any adverse effects you may have experienced during your biopsy or surgery will be collected.

Study drug group

After your biopsy or surgery is completed, you will have the following as **routine (standard care)**:

- Computed tomography (CT) of the head.
- Neurological examination.

The following will be performed for **research only**:

- Any adverse effects you may have experienced during your biopsy or surgery will be collected.

For both groups:

If the CT of the head shows that the catheter is not where we want it or if there are complications such as a bleed in the brain, we will remove the catheter and the study will end. However, we will still collect safety data and information from the tumor that we removed as it will be important.

Visit 5 (Post-operative, Day 1)

Control group

- You will have the following as **routine (standard care)**:Neurological examination.

The following will be performed for **research only**:

- Any adverse effects you may have experienced since the previous day will be collected.
- Fluid that is similar to spinal fluid will circulate in the Microdialysis system, which allows the exchange of drug and other small molecules that are present in the brain (filtered by the Microdialysis catheter membrane). Each time, fluid from the Microdialysis system will be collected (about ½ a teaspoon). Please note that no fluid is being removed from your brain or your own spinal fluid. Any amount removed is from fluid that is already circulating in the pump system. Samples will be collected at various time points (0, 15, 30 minutes, and 1, 2, 4, 6, 8, 24 hours), over 24 hours, for a total of 9 sample collections. You will not have to do anything for this part of the sample collection.

Study drug group

You will have the following as **routine (standard care)**:

- Neurological examination.

The following will be performed for **research only**:

- You will take your study medication at 8am +/- 4 hours. This will be the last time you take the study medication.
- Comprehensive Metabolic Panel (which includes electrolytes, renal function and liver function) (approximately 1 teaspoon of blood).
- Any adverse effects you may have experienced since the previous day will be collected.

- Fluid that is similar to spinal fluid will circulate in the Microdialysis system, which allows the exchange of drug and other small molecules that are present in the brain (filtered by the Microdialysis catheter membrane). Each time, fluid from the Microdialysis system will be collected (about ½ a teaspoon). Please note that no fluid is being removed from your brain or your own spinal fluid. Any amount removed is from fluid that is already circulating in the pump system. Samples will be collected at various time points (0, 15, 30 minutes, and 1, 2, 4, 6, 8, 24 hours), over 24 hours, for a total of 9 sample collections. You will not have to do anything for this part of the sample collection.
- Blood for research-only liver function tests will be collected (about 1 teaspoon). Samples will be collected at various time points (0, 15, 30 minutes, and 1, 2, 4, 6, 8, 24 hours), over 24 hours, for a total of 9 sample collections. You will not have to do anything for this part of the sample collection.

Visit 6 (Post-operative, Day 2)

Control group

-

The following will be performed for **research only**:

- Collection of adverse events: Any adverse effects you may have experienced since the previous day will be collected.
- Fluid from the microcatheters will be collected (about ½ a teaspoon) – 24h time-set collection.
- Blood for research-only will be collected (about 1 teaspoon) – 24h time-set collection.
- The microcatheters will be removed by a study physician at the bedside. The entry site of the catheter will be closed with a small bandage or possibly a suture (stitch).

Study drug group

The following will be performed for **research only**:

- Collection of adverse events: Any adverse effects you may have experienced since the previous day will be collected.
- Fluid from the microcatheters will be collected (about ½ a teaspoon) – 24h time-set collection.
- Blood for research-only will be collected (about 1 teaspoon) – 24h time-set collection.
- The microcatheters will be removed by a study physician at the bedside. The entry site of the catheter will be closed with a small bandage or possibly a suture (stitch).

Visit 7 (Post-operative follow-up 14+/-7 days)

Control group

You will have the following as **routine (standard care)**:

- Neurological examination.

The following will be performed for **research only**:

- Collection of adverse events: Any adverse effects you may have experienced since Visit 6 will be collected

Study drug group

You will have the following as **routine (standard care)**:

- Neurological examination.

The following will be performed for **research only**:

- Any adverse effects you may have experienced since Visit 6 will be collected

What are my responsibilities if I take part in this research?

If you take part in this research, your major responsibilities will include:

- Tell your study doctor about your current medical conditions.
- Tell your study doctor if you miss 3 doses of study drug. In the outpatient setting, participants will be provided with a medication diary.
- Tell your study doctor if you are thinking about participating on another research study.
- Tell your study doctor if you become pregnant or father a child while participating on this study.

For your safety, you must tell the study doctor or nurse about all the prescription drugs, herbal products, over-the-counter drugs (OTC), vitamins and other supplements you are taking. Check with the study doctor before starting any new medicines (including prescription, OTC drugs, vitamins and herbal supplements) or changing doses of medications that you are already taking.

3. What are the risks and possible discomforts from being in this research study?

Risk of drug

While this drug has never been tested specifically in the HGG population, it is an FDA-approved drug. The potential side effects are:

Common side effects (occurring in at least 1 in 100 patients) are:

- Headache
- Dizziness
- numbness or tingling;
- sleepiness
- feeling or being sick
- loss of appetite
- stomach pain
- diarrhea
- upset stomach
- nausea
- vomiting
- flatulence (excessive gas in the digestive tract)
- dry mouth
- abnormal liver function tests
- rash
- weakness
- tiredness
- a decrease in white blood cells (that can increase the risk of infections)
- fever
- abnormal amounts of salts in the blood

Infrequent

- Liver problems, including liver failure, with symptoms such as:

- dark colored urine
- pale stools
- yellowing of the skin and eyes
- abdominal pain
- nausea
- vomiting

Uncommon

- Heart problems such as very slow, fast or irregular heartbeat

Rare

- Severe allergic reaction with symptoms such as:
  - severe skin blistering
  - peeling rash
  - swollen lips, mouth and throat
  - difficulty in breathing

Risks of microdialysis
Microdialysis is an invasive surgical procedure with a small risk of bleeding at the site of insertion and discomfort for the patient. Removal of the catheter can result in minor discomfort as well. There is a chance that the catheter may break or get stuck in the brain that would require surgical intervention to remove it. There is also a small risk of infection (1%), but pre-operative antibiotics are used to reduce the risk. However, this is a small device and it is removed early postoperatively, similar to other surgical drains placed postoperatively. There is also a very small possibility of bleeding along the catheter tip.

Risks of venipuncture
The discomfort associated with removing blood by venipuncture (by a needle from a vein) is a slight pinch or pin prick when the sterile needle enters the skin. The risks include mild discomfort and/or a black and blue mark at the site of puncture. Less common risks include a small blood clot, infection or bleeding at the puncture site, and on rare occasions fainting during the procedure.

Risks of electrocardiogram (ECG):
The patches that the study staff will stick to your chest and other areas of your body to monitor your heart may irritate your skin and cause itching and redness. The study staff might need to shave your body hair so that they can stick the pads to your skin. The shaving may cause some irritation (depending on the tools and soap used); also, a local allergic reaction could occur. When the sticky patches are removed, it might sting for a few seconds. The test itself is painless.

Reproductive risks
The class of drugs, azoles, which the study drug is part of, can cause birth defects. There is only limited information regarding their effect on infants of breastfeeding mothers. For this reason, all women of childbearing potential MUST have a negative pregnancy test.

The study doctor will discuss methods with participants to ensure that they do not become pregnant or father a baby during the study. Women should not breastfeed a baby while taking study treatment and for 30 days after the last dose because the drug used in this study might be present in breast milk and could be harmful to a baby.

Pregnancy statement and use in nursing women
Azoles can be teratogenic.[57] Information regarding adverse effects on infants of breastfeeding mothers taking azoles is limited. All women of childbearing potential MUST have a negative pregnancy test. If the pregnancy test is positive, the patient must not receive any investigational product and must not be enrolled in the study.

We will request that female participants wait 30 days after the last dose of drug before considering becoming pregnant or starting breastfeeding.

Definition of childbearing potential: For the purposes of this study, a female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time during the preceding 24 consecutive months).

Study participants must be willing to comply with fertility requirements as described below:

- Male participants must agree to use an adequate method of contraception for the duration of the study and for 30 days afterwards.
- Female participants must be either postmenopausal, free from menses ≥ 2 years, surgically sterilized, willing to use two adequate barrier methods of contraception to prevent pregnancy, or agree to abstain from heterosexual activity starting with screening and for 30 days afterwards.
- Participants must agree not to donate blood, sperm/ova during study participation and for at least 30 days after stopping treatment.

During the course of the trial, if a participant suspects that they may have conceived a child, they will be instructed to contact the study doctor named at the top of this form immediately. In addition, a missed or late menstrual period during the course of the trial should be also reported to the study doctor

If a male patient is suspected of having fathered a child while on study drug, the pregnant female partner must be notified and counseled regarding the risk to the fetus. In addition, the treating physician must follow the course of the pregnancy, including prenatal and neonatal outcome. Infants should be followed for a minimum of 30 days.

Upon live-birth delivery, the minimum information that should be collected includes date of birth, length of pregnancy, sex of infant, major and minor anomalies identified at birth. Outcomes can be obtained via mailed questionnaires, maternal interviews, medical record abstraction, or a combination of these methods.

Risk of loss of confidentiality
There is a risk of loss of confidentiality if participant information or identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of participant electronic data created by the participant or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

Version Date: 08 June 2023

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

You will not benefit from this research study.

4b. What are the possible benefits to others?

No one has even looked at the use of posaconazole against HGGs so this is a one-of-kind chance to study whether it can have an effect against this aggressive cancer. If we can show that posaconazole gets in the brain and stays there long enough to have the same effects we have seen in the laboratory, it would be very important as we may be able to improve survival for patients with these tumors.

5. What other options are available instead of being in this research study?

You do not have to take part in this study to be treated for your condition. Instead of participating in this research, you could:

- Receive commercially available treatments, including radiation and chemotherapy.
- Be part of a different research study, if one is available.
- Choose not to be treated for your medical condition and only receive care to make you more comfortable.

Before you decide if you want to be in this research, we will discuss the other choices that are available to you. We will tell you about the possible benefits and risks of these choices.

Because it is investigational, the therapy offered in this research is only available to you if you take part in the research study.

6. How long will I take part in this research study?

If you agree to take part, it will take you about 31 days to complete this research study. There are maximum of 7 study visits. You will be asked to attend the research site a maximum of 4 separate times (Visit 1, Visit 2 (only if required), Visits 3-6 will take place during your stay in the hospital, and Visit 7).

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed, and there may be situations where disclosure is required by law.

In our research files at Penn State Health (PSH) and Penn State College of Medicine (PSU) we will include these identifiers: your name/initials, address, phone number, date of birth, medical record number, pathology number, and a code number.

- A list that matches your name with your code number will be kept in a locked file in Dr. Mansouri's office.
- Your research records will be labeled with your code number and will be kept in a safe area in Dr Mansouri's research office.
- Your research samples will be labeled with your name/initials, date of birth, and medical record number and will be stored in the clinical laboratory.

- A copy of this signed consent form will be included in your PSH medical record. This means that other PSH healthcare providers will know you are in this study.
- Results of some of the research-related clinical tests (including, but not limited to liver function tests, research-only ECG) will be kept in your PSH medical record.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot disclose information that identifies you to anyone not connected with the research. This protection also prevents this information from being used or disclosed for legal proceedings, such as being accessed through a court order. The Certificate of Confidentiality however does not prevent disclosures required by law, such as information about child abuse or neglect and harm to yourself or others. Also, your information may be disclosed in accordance with any consent you provide, including for your medical treatment or use in other research. Additionally, the Certificate of Confidentiality does not prevent your information from being disclosed to the NIH in order for it to evaluate or audit the research, or prevent disclosures required to meet FDA requirements. For additional information ask the principal investigator or a member of the study team or contact the Human Research Protection Program at (814) 865-1775.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. What will happen to my research information and/or samples after the study is completed?

We may use your research information and your biological samples in future studies or may share your information or biological samples with other investigators for future research without your additional informed consent. Before we use or share your information or samples we will remove any information that shows your identity.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

7c. How will my identifiable health information be used?

In general, under federal law (including the Health Insurance Portability and Accountability Act – HIPAA or privacy laws) your health information is private. By signing this form, you are authorizing us to collect, use, and disclose your identifiable health information, sometimes referred to as "Protected Health Information" or "PHI" under HIPAA, for the purposes of this research study. We will use and disclose your information only as described in this form, in the PSH Privacy Notice, and as may be required or allowed under the applicable privacy laws.

The research team may use the following health information:

- Past, present, and future medical records, including identifiable information
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- PSH/PSU research staff involved in this study
- The PSH/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare

- The PSH/PSU Human Subjects Protection Office
- The PSH/PSU Research Quality Assurance Office
- Non-research staff within PSH/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- The PSH/PSU pharmacy
- The sponsor of this study, the National Institutes of Health, monitors and auditors, and other people or groups it hires to help perform this research
- A group that oversees the data (study information) and safety of this research

These groups may also review and/or copy your original PSH/PSU records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your identifiable health information and samples may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

We may remove identifying information from your protected health information. Once we do this, the remaining information will not be subject to the privacy laws. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have

if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.

- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:

- The study drug, posaconazole, will be provided by at no cost to you while you take part in this study.
- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- The research-related tests and procedures that will be provided at no cost to you include:
    - CBC at Visit 1
    - CMP at Visitis 1, 2, and 5, including blood draws
    - 12-lead ECG at Visit 1 and 2
    - Microdialysis catheter and related reagents, and catheter monitoring at visits 3 through 6.
    - Removal of the micro-dialysis catheter, performed at bedside

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

PSH/PSU compensation for injury

- There are no plans for PSH/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?

You will receive a $50.00 gift card for completing Visit 2 in this research study, if the visit is required, as compensation for the extra travel/time. No compensation will be available for any other study visits. The payment will be provided by Greenphire Clincard.

This reimbursement will be issued by an external company called Greenphire, which will issue your reimbursement. You will be issued a ClinCard, which is a debit card that your funds are loaded onto and can be used at your discretion. The research team will give Greenphire some personal information about you, as described below. Greenphire will only use your personal information to process this reimbursement and will not share it with anyone for any other purpose. Details of the debit card system are explained on an additional sheet. If you lose the card, you may be responsible for the replacement fee.

When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 2-3 business days. In order to assign a ClinCard to you and load funds onto the ClinCard, Greenphire will need your Study/Subject ID, Name, Address, date of birth and Social Security Number.

You will have the option to receive updates related to payment alerts via text message and/or email message. Standard text messaging rates will apply. In order to send you messages Greenphire will need your Mobile Phone Number and/or E-mail Address.

It is possible that your research information and/or specimens (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

10. Who is paying for this research study?

This research is being supported by an Institutional Research Grant from a grant from the National Institutes of Health.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

If you decide to leave the research, contact the investigator so that the investigator can document the reason for withdrawal and have a final study visit.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Your research doctor may take you out of the research study without your permission.

- Some possible reasons for this are: continuing the research would be harmful, your condition has become worse, you become pregnant, you did not follow the instructions of the study doctor, or you experience serious side effects.
- Also, the sponsor of the research may end the research study early.
- If your participation ends early, you may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study (principal investigator), Dr. Mansouri at (717) 531-3828 or the Neurosurgery doctor on 24-hour call at (717) 531-8521 if you:

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the PSH Human Subjects Protection Office (HSPO) at (717) 531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, 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 Web site at any time.

Version Date: 08 June 2023

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name

Witness to Consent of Subjects Who Cannot Read or Write

Witness Statement: Your signature indicates that you were present during the informed consent discussion of this research for the above named subject, that the information in the consent form and any other written information was presented orally to the subject or subject representative, that the subject or subject representative was given the opportunity to ask questions, that the informed consent decision was freely made by the subject or subject representative who indicated consent and authorization for participation by (check the box as applicable):

☐ Making a mark
☐ Other means: _____
(fill in above)

_____	_____	_____	_____
Witness Signature	Date	Time	Printed Name