THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Effect of Opioid Infusion Rate on Abuse Liability Potential and Analgesic Efficacy of Intravenous Hydromorphone among Inpatients with Cancer Pain: A Randomized Crossover Trial
2019-0678

Study Chair: Joseph A. Arthur

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to compare the effects of slow intravenous (by vein) hydromorphone and fast intravenous hydromorphone in patients with breakthrough cancer pain. Breakthrough cancer pain is a temporary flare of severe pain.

In this study, participants will receive the study drug at 2 different infusion rates. A matching placebo will be given each time you receive the study drug. A placebo is not a drug. It looks like the study drug but is not designed to treat any disease or illness. It is designed to be compared with a study drug to learn if the study drug has any real effect.

This is an investigational study. Hydromorphone is FDA approved and commercially available to help treat breakthrough cancer pain. It is considered investigational to compare a slow infusion rate with a fast infusion rate of hydromorphone.

The study doctor can explain how the study drug is designed to work.

Taking the study drug may help decrease your pain. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment. If you take part in this study, you may experience side effects such as drowsiness, nausea, or dry mouth.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You will be able to receive 2 infusions of hydromorphone as part of this study.

Hydromorphone and placebo will be provided at no cost to you during this study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard drugs, including hydromorphone, for breakthrough cancer pain outside this study. You may choose other investigational therapy, if available. You may choose not to have treatment for breakthrough pain. In all cases, you will receive appropriate medical care.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- Information about your demographics (age, gender, race) and medical history (cancer diagnosis, current cancer stage, medication history) will be collected from you or your medical record.
- You will be asked to complete a questionnaire about your symptoms. It should take about 5 minutes to complete.
- The study staff will measure your vital signs.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discuss with you.

Up to 84 participants will be enrolled in this study. All will take part at MD Anderson.

Baseline Tests

If you agree to take part in this study, the following tests will be performed after the screening tests ensure that you are still eligible:

- You will be asked to rate your pain on a scale of 1 to 10.
- You will complete 5 questionnaires about your symptoms and side effects, your use of alcohol, opioids, and illicit (illegal) drugs, and how you feel about the study drug. It should take about 15 minutes total to complete these questionnaires. You will complete the questionnaires either on a paper copy or electronically on an iPad.

- Blood (about 1½ teaspoons) will be drawn for pharmacokinetic (PK) and pharmacogenetic (PGx) testing. PK testing measures the amount of study drug in the body at different time points. PGx testing looks at how someone's genes may influence the study drug's effects.

Study Groups and Study Drug Administration

You will be randomly assigned (as in the flip of a coin) to 1 of 2 groups: Group A or Group B. This is done because no one knows if one study group is better, the same, or worse than the other group.

You will be asked to tell the study staff or nurse when you experience a pain intensity of 4 or more on a scale of 1 to 10. The first time you rate your pain at 4 or more, you will receive the study drug in the 1st treatment period. The 2nd treatment period will happen at least 6 hours after the 1st treatment period, when you again rate your pain at 4 or more on a scale of 1 to 10. You may still ask the study staff for pain medication at any point during the 1st treatment period if you do not think your pain is controlled.

If you are in **Group A:**

- During the 1st treatment period, you will receive hydromorphone by vein over 2 minutes and placebo by vein over 15 minutes.
- During the 2nd treatment period, you will receive hydromorphone by vein over 15 minutes and placebo by vein over 2 minutes.

If you are in **Group B:**

- During the 1st treatment period, you will receive hydromorphone by vein over 15 minutes and placebo by vein over 2 minutes.
- During the 2nd treatment period, you will receive hydromorphone by vein over 2 minutes and placebo by vein over 15 minutes.

You have an equal chance of being placed in Group A or Group B. Neither you nor the study staff will know which group you are in. However, if needed for your safety, the study staff will be able to find out what you are receiving.

For both groups**,** at **15, 30, 60, and 120 minutes** after the start of your infusion in the 1st and 2nd treatment periods**:**

- You will be asked to rate your pain on a scale of 1 to 10.
- You will complete 2 questionnaires about how you feel about the study drug and any side effects you may be experiencing. It should take about 2 minutes to complete these questionnaires each time. You will complete the questionnaires either on a paper copy or electronically on an iPad.
- Blood (about 1½ teaspoons) will be drawn for PK and PGx testing during the **1st treatment period only**.

At the end of the 2nd treatment period, you will complete a questionnaire about your preference between the 1st and 2nd treatment periods. It should take about 1 minute to complete this questionnaire.

Your participation in this study will be over after you complete the last questionnaire.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. Tell the study staff about any side effects you may have, even if you do not think they are related to the study drugs/procedures.

Hydromorphone Side Effects

It is not well known how often the side effects of hydromorphone may occur.

• slow/extra/fast/irregular heartbeats • high blood pressure • low blood pressure • flushing • swelling (arm/leg) • fainting • abnormal dreams • difficulty walking • difficulty thinking • drowsiness • seizure • chills • confusion • dizziness • difficulty forming or speaking words • emotional distress (possible mood swings, depression, panic attack, paranoia, suicidal thoughts, crying, nervousness, restlessness, agitation,	• loss of consciousness and slowing of the heart and breathing rate • abnormal sensation (such as pins and needles) • skin rash/itching/hives/ redness/burning/swelling • sweating • low blood levels of potassium (possible weakness and/or muscle cramps) • dehydration • weight loss • anal sores • abdominal swelling • increased or loss of appetite • bile duct spasm (possible pain) • constipation	• vomiting • dry mouth • urinary tract spasm • difficult/painful/frequent urination • decreased/inability to urinate • painful defecation • impotence • low sex hormone levels (possible abnormal sexual characteristics and/or function) • decreased sex drive • sexual disorder • low levels of testosterone • abnormal liver tests (possible liver damage) • uncontrolled movements • muscle twitching/tremor

and/or aggressive behavior) • euphoria (unusual feelings of great happiness or well-being) • fatigue • hallucinations • headache • increased sensitivity of the senses • numbness • low body temperature • difficulty maintaining body temperature • increased pressure in the brain • difficulty sleeping • difficulty concentrating • trouble with balance • memory loss	• slow emptying of food from the stomach into the intestines • diarrhea • nausea • paralysis of the intestines • stomach cramps • stomach or intestinal blockage • abnormal taste • burping • heartburn • gas • inflammation of the stomach and/or intestines • hole in the intestines (possible leaking contents into the abdomen) • difficulty swallowing • bright red blood in the stool	• overactive reflexes • pain (muscle/joint) • weakness • blurry/double vision • dry eyes • eye pupils getting smaller • eye twitching • ringing in the ears • high blood levels of uric acid (possible painful joints and/or kidney failure) • fast breathing • interrupted breathing • difficulty breathing due to narrowing of the airways • low oxygen level in blood (possible lightheadedness) • runny nose • flu-like symptoms • allergic reaction • drug dependence • injection site • pain/swelling • closing of the throat

Hydromorphone may be habit-forming.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create need for blood transfusions.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby. Patients who take the study drug at high doses or for long periods of time may be at risk for pregnancy-related risks. The study staff does not expect this to occur in this study because of the relatively low amount and short length of time you will be receiving the study drug. However, in order to be cautious, the study staff recommends that you not become pregnant or breastfeed a baby if you take part in this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

A $50 gift card will be given to participants who receive any of the study drugs.

Additional Information

4. You may ask the study chair (Dr. Joseph A. Arthur, at 713-792-6085) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the

Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

You may choose to not allow your samples to be used for future research at any point by telling the study team.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research
Research samples collected from you as part of this study will be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

This research study involves genetic testing. The Genetic Information Nondiscrimination Act (GINA) prohibits health insurers or health plan administrators from requesting or requiring genetic information of you or your family members, or using such information for decisions regarding your eligibility for insurance or your premiums. However, this law does not provide the same protection for disability, life insurance, or long-term care insurance. GINA also prohibits most employers (with 15 employees or more) from using genetic information when making decisions on your employment, including decisions related to hiring, firing, promotion, pay, and job assignments. Information obtained through genetic testing may be susceptible to re-identification. Please contact your study doctor if you would like more information about GINA and how it protects you from genetic discrimination.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Some of your de-identified data from your blood samples will be sent to Dr. Alan L. Myers at the UT Health Science Center. Dr. Myers will study the data and will

provide reports to Dr. Arthur (Study Chair). He will also take part in any future research. However, any identifying information (such as your name, medical record number and/or health information) will be removed from the data before it is sent to Dr. Myers.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT