

Kansas City Clinical Oncology Program

A Randomized Comparison of Oral Methadone as a “First-Switch” Opioid versus Opioid Switching Between Sustained-Release Morphine and Oxycodone for Oncology-Hematology Outpatients with Pain Management Problems: The “Simply Rotate” Study

You are being asked to take part in this clinical research study. This research study is strictly voluntary. This consent form explains why we are performing this research study and what your role will be if you choose to participate. This form also describes the possible risks connected with being in this study. After reviewing this information with the person responsible for your enrollment, you should know enough to be able to make an informed decision on whether you want to participate in the study. This is an investigational study. This study complies with all laws and regulations that apply.

WHY IS THIS STUDY BEING DONE?

You are being asked to take part in this study because you are taking pain medication that is not completely stopping your pain.

The goal of this clinical research study is to compare the effects, good and/or bad, of methadone to sustained-release morphine or oxycodone on you and your cancer pain. In this study, you will get either methadone or sustained-release morphine or sustained-release oxycodone. You will not get both.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 300 patients will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

In order to participate in this study you must be taking either oxycodone or morphine for your cancer pain.

If you decide to take part in this study, before treatment starts you will have the following procedures done:

- A complete physical exam by your physician, including your vital signs, height, weight, a history of your current and past medical conditions, and an evaluation of your pain level
- You will be asked to complete a questionnaire called the M. D. Anderson Symptom Inventory (MDASI), this form collects information about symptoms people with cancer have that is either related to their disease itself or to the treatment they are receiving for the disease

You will be randomly assigned (as in the toss of a coin) to one of two groups. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you

will be in. You will have a 50% chance of being placed in one of the groups. You will either be assigned to Group 1 that will be switched from your current pain medication (oxycodone or morphine) to Methadone, or Group 2, that will be switched from your current pain medication (oxycodone or morphine) to morphine or oxycodone. For example, if you are currently taking morphine, you will be switched to oxycodone. If you are currently taking oxycodone, you will be switched to morphine.

Treatment will last for 4 weeks (about 28 days). Evaluations for this study will be on Day 1, 8, 15, 22, and 28. Your first evaluation will be conducted by your doctor in person before you begin the study. You will have another face to face visit with your doctor or his/her assistant on either day 8 or 15 to see how the new medication is working for your pain and answer any questions you may have. Remaining evaluations for Day 8, 15, or 22 can be conducted in person or over the phone. You will be contacted either in person or by telephone on these days while you are on treatment to ask you how you are doing and to answer any questions you may have. During each visit, in person or on the phone, you will be asked to complete the MDASI questionnaire and you will be asked about any side effects you are having. Once you have completed 4 weeks of treatment, you will have a final evaluation on Day 28 by your healthcare provider, including a physical exam and completion of the M.D. Anderson Symptom Inventory questionnaire (MDASI), and the study will end. Your doctor will decide what pain medication you will be on after the study is over.

HOW LONG WILL I BE IN THE STUDY?

Depending on how you respond to the treatment, how well the medication works, and any side effects that you may have, you will most likely take the study medication for 4 weeks (28 days). You will stay on this treatment until one of the following happens:

- You complete the protocol required treatments and assessments
- You develop an illness that prevents more treatment
- You have a side effect that is not tolerable
- You decide to stop the study
- Your doctor has you stop because of general or specific changes in your condition that no longer qualify you for the treatment

CAN I STOP BEING IN THE STUDY?

You may stop participating in this study at any time you want. However, if you decide to stop participating in the study, we encourage you to talk to the study doctor and your regular doctor first.

You should not stop taking the study medication without talking to your doctor about how to safely stop taking the medicine.

The study doctor may stop you from taking part in the this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or of the study is stopped.

After all treatment is completed, you will have a final evaluation and the study will end.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for these side effects. There also may be other side effects that we cannot predict. Other drugs may be given to make side effects less serious and/or less uncomfortable. Many side effects go away shortly after the medication is stopped, but in some cases side effects can be serious, long-lasting or permanent. Some may be life-threatening. You should discuss these with the study doctor and/or your regular doctor.

Instructions for all three medications:

Do not drive an automobile or operate heavy machinery while taking morphine, methadone or oxycodone until you know how you react to it.

Constipation: This side effect can be decreased or prevented by taking a non-prescription stimulant laxative with a stool softener, on a regular basis. Do not use suppositories or enemas if your white blood cell count or platelet count is low because they may cause an infection or bleeding.

Nausea/Vomiting or Loss of Appetite: Taking methadone, morphine or oxycodone with food or milk may help to decrease the nausea.

Tell your doctor or nurse if constipation continues to be a problem or if you have not had a bowel movement in 3 days. Tell your doctor or nurse right away if you have an irregular heartbeat, shortness of breath, slowed breathing, trouble breathing, hives, skin rash, twitching or trembling, confusion, or hallucinations, or yellowing of eyes and/or skin. Tell your doctor or nurse right away if you have nausea or vomiting and cannot keep food or water in your stomach.

MORPHINE

Likely

Morphine may cause constipation, nausea, feeling tired, sleepiness/drowsiness, dizziness, itching, rash, or dry mouth.

Less Likely

It may cause mental changes such as confusion, restlessness, and/or the inability to think clearly. It may cause vomiting, and/or appetite loss. It may cause blurred vision, sweating, difficulty urinating, headache, low blood pressure, difficulty sleeping, lightheadedness, mood changes/depression, muscle twitching or trembling, and/or decreased sexual desire.

Rare but Serious

Rarely, morphine may cause shallow and/or trouble breathing, bowel obstruction, slow heartbeat, allergic reaction, or seizure

METHADONE

Likely

Methadone may cause constipation, feeling tired, sleepiness/ drowsiness, and/or dry mouth.

Less Likely

It may cause mood changes, depression, confusion, inability to think clearly, nervousness, dizziness, unsteadiness, or restlessness. It may cause a decrease in sex drive. It may cause nausea, vomiting, and/or appetite loss. It may cause twitching, difficulty urinating, sweating, fainting, low blood pressure, itching, skin rash, difficulty sleeping, or headache.

Rare but Serious

Methadone may also cause irregular heartbeat, slow heartbeat, shortness of breath, slowed breathing, and/or trouble breathing. It may cause bowel obstruction, hives, allergic reaction, and/or yellowing of the eyes and/or skin.

OXYCODONE

Likely

Oxycodone may cause constipation, nausea, dry mouth, sleepiness/drowsiness, or feeling tired

Less Likely

Oxycodone may cause vomiting, loss of appetite, dizziness, confusion, light-headedness, fainting, headache, low blood pressure, sweating, itching, difficulty urinating, twitching, nervousness/restlessness, difficulty sleeping, hives, skin rash, or mood changes/depression.

Rare but Serious

Oxycodone may cause shallow breathing, slow heartbeat, or seizure (convulsions). It may also cause bowel obstruction, hives or allergic reaction.

If any doctor other than the study doctor prescribes other drugs, you must tell the study nurse right away.

This research study may involve unpredictable risks to the participants.

Reproductive Risks: Because the treatment used in this study may affect an unborn baby, you should not become pregnant or father a baby while on this study. You must practice birth control during the study if you are sexually active. If you are pregnant, you should not be enrolled on this study. Mothers should not breast-feed during the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information gained on side effects and effectiveness of the study treatment will benefit other patients in the future with pain management.

The potential benefit of taking part in the study is the improvement of your pain or side effects from drugs for pain, but it is possible that your condition may worsen despite treatment.

There may be no benefits for you in this study.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

- You may choose not to take part in the study.
- You may choose to receive other investigational research therapy, if available.
- You may choose to remain on your current pain medication.

In all cases, you will receive care for symptoms and pain. Please talk to your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

Organizations or their representatives that may inspect and/or copy your research records for quality assurance and data analysis include groups such as: The National Cancer Institute (NCI), the Food and Drug Administration (FDA), and M. D. Anderson Community Clinical Oncology Program.

WHAT ARE THE COSTS?

This protocol is partially funded by a research grant from the National Cancer Institute (NCI). Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance problems. In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of a physical or psychological injury. You or your insurance company will be charged for continuing medical care and/or hospitalization. You will receive no payment for taking part in this study.

All drugs are approved by the FDA and commercially available. You will be financially responsible for the cost of the study drugs and treatments.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Refusing to participate, or leaving the study will not result in any penalty or loss of benefits to which you are entitled. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

A Data Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

Authorization for Use and Disclosure of Protected Health Information:

During the course of this study, the research team at _____ will be collecting information about you that they may share with the FDA and/or the NCI. This information may include, but is not limited to your treatment schedule and the results of any tests, therapies, or procedures that you undergo for this study. The purpose of collecting and

sharing this information is to learn about how the treatment affects your disease and any side effects you experience as a result of your treatment.

Your doctor and the research team may share study information with certain individuals. These individuals may include, but are not limited to, representatives of the FDA, the NCI and/or any above mentioned sponsor, clinical study monitors who verify the accuracy of the information, individuals with medical backgrounds who determine the effect that the treatment has on your disease, and/or individuals who put all the study information together in report form. The research team may provide this information to the FDA, the NCI and/or the above listed sponsor at any time. There is no expiration date for the use of this information as stated in this authorization.

You may withdraw your authorization to share this information at any time in writing. You may contact the Kansas City Clinical Oncology Program IRB at 816-823-0560 with questions about how to find information about the Notice of Privacy Practices (NPP).

If you refuse to provide your authorization to disclose this protected health information, you will not be able to participate in the research project.

You understand that your personal health information will be protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and may be re-disclosed at some point.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher _____ at _____ (TELEPHONE NUMBER).

For questions about your rights as a research participant, contact the _____ (NAME OF CENTER) Institutional Review Board (which is a group of people who review the research to protect your rights) at _____ (TELEPHONE NUMBER).

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's **Cancer Information Service** at: **1 800 4 CANCER (1 800 422 6237)** or **TTY: 1 800 332 8615**

Visit the NCI Web site:

- <http://www.cancer.gov/>

You will get a copy of this form. You may also request a copy of the protocol (full study plan).

RELEASE

By signing this form you authorize KCCOP to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

SIGNATURE

I agree to take part in this study.

Participant _____

Date _____

Person Obtaining Consent _____

Date _____