THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

Levorphanol as a Second Line Opioid in Cancer Patients Undergoing Opioid Rotation: An Open Label Study
2017-0925

Study Chair: Akhila S. Reddy

_____ _____
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 learn about how well levorphanol can control cancer pain.

This is an investigational study. Levorphanol is FDA approved and commercially available for the treatment of pain. It is investigational to learn about how helpful it is in treating pain in cancer patients.

The study drug may help control 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. You may choose not to take part in this study because the use of Levorphanol may cause addiction, abuse, misuse, and may lead to overdose and death.

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

Your participation in this study will be complete once all study activities are concluded, if you are rotated off the study drug, or if differences of 10 or more pills are found in the remaining tablets compared to the daily log on 2 different visits.

Levorphanol will be provided at no cost to you while you are taking part in this study. If the study doctor thinks it is in your best interest, the sponsor of the study (Sentynl Therapeutics Inc.) will continue to provide levorphanol for up to 6 months at no cost to you while you are on study.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive the drug outside of the study or take another opioid pain drug. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Baseline Tests

If you agree to take part in this study, you will complete 5 questionnaires. These questionnaires ask basic questions (such as your age, sex, and so on), about any side effects or symptoms you may be having, your drug and alcohol history, and about any pain you may be having.

It should take about 20 minutes total to complete the questionnaires.

Up to 86 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration

Levorphanol is a strong opioid pain drug, much like the one you are currently taking. You will take levorphanol by mouth. You should take the study drug with a full (8 ounce) glass of water. It can be taken with or without food. Your study drug dose or schedule may be changed during the first 10 days of the study depending upon how your pain is managed. Changes to your breakthrough pain medication will also be made.

After Day 10 +/-2 days, you will pick up a supply of levorphanol from the MD Anderson Pharmacy to last for the next 30 days.

Study Calls/Visits

On **Days 1-10** (+/- 1 day), you will be called every day and asked about any symptoms including pain and any side effects you may be having. These calls will last about 5-10 minutes each time.

On or about **Days 10 and 30**, you will be called or return to the clinic. You will be asked about any symptoms and side effects you may be having, the level of pain you are having, and if you think the study drug is working. This visit or call will last about 10-15 minutes.

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 drug.

These side effects are similar to those caused by all opioids, including the current opioid pain drug that you are taking.

Levorphanol Side Effects

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

• slow/irregular/fast heartbeat • sudden stopping of the heart • low blood pressure (possible dizziness/fainting) • flushing • shock • memory loss • loss of consciousness and slowing of the heart and breathing rate • coma • confusion • seizures • depression • dizziness • fatigue • hallucinations (seeing or hearing things that are not there) • headache • difficulty sleeping	• increased pressure between the skull and brain (possible vision changes and/or headaches) • nervousness • mental status change • restlessness • itching • skin rash • hives • abnormal salts, minerals, and/or acids in the blood (possible weakness, swelling, fatigue, low blood pressure, organ failure, heart problems, changes in mental status, and/or seizure) • abdominal pain • loss of appetite • bile duct spasm (possible pain)	• constipation • upset stomach • nausea • paralysis of the intestines • stomach cramps • vomiting • dry mouth • decreased urine output • inability to urinate • low sex hormone levels (possible abnormal sexual characteristics and/or function) • weakness • double vision • eye pupils getting smaller • interrupted breathing • blue skin • difficulty breathing (may be serious and/or life-threatening) • allergic reaction

Levorphanol may cause addiction, abuse, and misuse, and may lead to overdose and death.

Other Risks

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.

If you are feeling distressed and the study staff or doctor thinks it is needed, you will be referred to another doctor or therapist for additional help.

Although every effort will be made to keep **study data** safe, there is a chance that your personal health information could be lost or stolen. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

This study may involve unpredictable risks to the participants.

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 or Sentynl Therapeutics Inc. 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.

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

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Akhila S. Reddy, at 713-745-2668) 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, Sentynl Therapeutics Inc., 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.

9. This study is sponsored and/or supported by: Sentynl Therapeutics Inc..

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

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

Before being shared for future research, every effort will be made to remove your identifying information from any data. 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 are used for future research. If this research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data 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.

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

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
- Sentynl Therapeutics Inc., who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2017-0925**.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

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

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION