Official Title: LCI-NOS-PAIN-001: A Prospective, Pharmacogenomic-Driven Pilot Study of Pain Management in Oncology Outpatients
NCT02542397
IRB-Approved Date: 12/16/2015

CAROLINAS HEALTHCARE SYSTEM
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Sponsor / Study Title:	**Levine Cancer Institute/LCI-NOS-PAIN-001: A Prospective, Pharmacogenomic-driven Pilot Study of Pain Management in Oncology Outpatients**
Protocol Number:	**LCI-NOS-PAIN-001**
Principal Investigator:	**Jai N. Patel, PharmD**
Telephone:	[redacted] **(24 Hours)** [redacted] **(24 Hours)**
Palliative Clinic:	[redacted] **(8AM-4PM)**
Address:	**Levine Cancer Institute** [redacted]

INTRODUCTION

Dr. Patel and his associates (the investigators) are asking you to participate in a research study at Levine Cancer Institute (LCI) and Carolinas HealthCare System (CHS) testing the application of a pharmacogenomic panel (a form of genetic test) to make decisions about pain medications and dosages. The purpose of this study is to better understand how genetic test results from a pharmacogenomic panel can be used to guide pain management, including selection and amount of drug(s) to prescribe. You are being asked to take part in this study because you have pain caused by your cancer.

Cells in your body contain DNA. DNA is the substance that makes up all genes. Genes are passed on from your parents and help guide the growth, development, and function of your body. For example, some genes control the color of your hair or eyes. There are many natural differences or variations in DNA from one person to another. These variations may affect the way a person responds to a particular drug. Pharmacogenomics is the study of how one's DNA influences his or her response to drugs. A pharmacogenomic panel tests for these variations in DNA.

Understanding if a person has these variations may help the clinician select the most appropriate drug and/or dose for that person. The potential benefit of using this test to guide your pain therapy will be assessed by recording your pain scores. The results of this test may also help to guide the management of other medications related to these genes.

This is a clinical trial, a type of research study. Taking part in this research study is entirely voluntary. Your study investigator will explain the clinical trial to you. Clinical trials only include

people who choose to take part. Please take your time to make your decision about participating. You have also been told that you have the option not to participate. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study investigator for more explanation.

This study is being carried out under the sponsorship of Levine Cancer Institute (LCI). XGene Diagnostics is the company that will process the pharmacogenomic results.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine if a pharmacogenomic panel can be used to help improve pain management by guiding medication decisions, including the type and amount of medicine to prescribe.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

You may be one of approximately 78 subjects participating in this study at Levine Cancer Institute.

HOW THE STUDY WORKS

Baseline (one visit):

First, you will be asked to fully read and sign this consent form. If you are willing to take part in the study, and you meet all other study eligibility criteria, we will obtain a swab from the inside of your cheek. This is non-invasive and there is no expectation that this will cause any pain or suffering. You will be asked questions about your medical history, your current disease, your current pain level, any treatments you have received, and any medications you are currently taking. You will be prescribed a pain medication based on your level of pain, medical history, and other clinical factors. We will also provide you with a Bothersome Symptom Log that you can use to record any symptoms you may experience and a tool to record information such as your daily pain medication use, daily pain score, caffeine intake, and other pain medications each day. Instructions will be provided on how to complete both forms.

Assessment #1 (Day 7 + or - 1 day or before):

When you return home, you should fill out the Bothersome Symptom Log in the event you experience any symptoms you think are related to your pain or the treatment of your pain, starting on the first day you take your prescribed drug(s). You will be asked questions at Assessment #1 about your daily pain medication use, daily pain score, caffeine intake, and other pain medications.

If your pain does not improve during this time (allowing at least 48 hours for the drug to start working), you should call the LCI Palliative Clinic at the number on the first page of this form. Let them know that you are participating on this study, that your pain remains uncontrolled and that you need a follow up assessment. This assessment will be considered Assessment #1.

You do not need to call the LCI Palliative Clinic if your pain is controlled and you are not experiencing any bothersome symptoms. If you do not call the LCI Palliative Clinic before day 7 +/- 1, you will receive a phone call from study personnel to speak about your pain since your Baseline visit with your clinician. You can use your Bothersome Symptom Log and the recording tool during this phone call.

If your pain has not improved at Assessment #1 and a medication adjustment is needed, the team may use the pharmacogenomic test results from your cheek swab, your pain score, and/or information about how you feel, to determine the most appropriate medication change(s). If a new prescription is required, you may be asked to return to the clinic to pick up the new prescription as the majority of pain medications are not allowed to be called or faxed into a pharmacy. In some cases, the clinician may just recommend a change in the number of pills you are taking. You should start the new prescription and/or dose change immediately.

At Assessment #1, if your pain is controlled and you are experiencing no other symptoms related to your pain medications after the first week of treatment, you will continue taking the medication(s) as prescribed and return to clinic on day 30 +/- 5 for a final study visit. If your pain is controlled at Assessment #1, you will not have an Assessment #2; however, you should continue to complete the Bothersome Symptom Log, as needed.

If your pain worsens after Assessment #1, you should call the LCI Palliative Clinic immediately at the number on the first page of this form. Let them know that you are participating on this study, that your pain is uncontrolled, and that you need a follow-up assessment.

<u>Assessment #2 (7 days +/- 1 after Assessment #1 or before):</u>

Assessment #2 will only occur if you received a new prescription and/or dose at Assessment #1. If your pain does not improve after beginning the new drug/dose (allowing at least 48 hours for the drug to start working), you should call the LCI Palliative Clinic at the number on the first page of this form. Let them know that you are participating on this study, that your pain remains uncontrolled, and that you need a follow up assessment. This assessment will be considered Assessment #2.

If you do not call the LCI Palliative Clinic before 7 days +/- 1 after Assessment #1, you will receive a phone call from study personnel to speak about your pain since Assessment #1. You can use your Bothersome Symptom Log and the recording tool during this phone call. If your pain still has not improved, we will re-evaluate your medication and/or dose. Again, you may be asked to return to clinic to pick up a new prescription, if needed. You should start the new prescription and/or dose change immediately. **After beginning the new regimen, if you continue to experience pain, or your pain worsens, you should call the LCI Palliative Clinic at the number on the first page of this form. Let them know that you are participating on this study and that your pain is uncontrolled.**

If your pain is controlled at Assessment #2, you should continue taking the medication(s) as prescribed and return to clinic on day 30 +/- 5 for a final study visit.

Unscheduled Visits

Should you experience symptoms related to your pain medications or if your pain worsens outside of scheduled study assessments, you should call the LCI Palliative Clinic at the number on the first page of this form. Let them know that you are participating on this study, that your pain is either uncontrolled or you are experiencing symptoms from your pain medication and you need to speak with a Palliative clinic staff member.

Final Assessment (Day 30 + or - 5 days)

At this visit, you will be assessed by your clinician in person in the clinic. This is your last study assessment. After this visit, you will be considered "off study" but will continue to see your clinician to manage your pain as needed according to standard of care.

At this visit, you will have another pain assessment and review any other bothersome symptoms with your clinician. At your request, you will be provided a copy of your pharmacogenomic test results. You may share this information with your other physicians, at your discretion. Because the pharmacogenomic test results may provide additional information about how your other medications (not relating to pain) should be managed, the clinician may suggest a drug and/or dose change for other drugs for conditions from which you are not experiencing relief.

RISKS

All pain medications used in this study are FDA approved. Our clinicians have extensive experience with using these medications to treat subjects' pain. The side effects and effectiveness of these drugs have been extensively studied and additional information about the drug will be available in the pamphlet provided by the pharmacy at the time the prescription is filled. However, while you are on this study, you are at risk for the side effects outlined below, and may be at risk for other unexpected side effects. Most people do not experience all of the side effects and some experience no side effects. Your study clinician will closely monitor and treat/prevent the side effects you might have throughout the study period.

Common side effects of opioids are:

- Drowsiness
- Constipation
- Fatigue
- Nausea
- Vomiting
- Shortness of breath

You should call the LCI Palliative Clinic immediately at the number on the first page of this form if you experience any of these side effects. Let them know that you are participating on this study.

Less common side effects of opioids are:

- Cognitive dysfunction (difficulty thinking)
- Respiratory depression (severe difficulty breathing)
- Allergic reaction (severe shortness of breath, itching, rash, hives)

You should call 911 immediately if you experience any of these severe side effects.

By taking part in this study, we do not expect for the risks of these side effects to increase any more than if you were taking them as part of standard of care.

Privacy Risks

If your genetic research data are shared with unauthorized users, you may be at risk of loss of the privacy of your health data. This risk is minimized by protections described in the Confidentiality section below.

EXCLUSION CRITERIA

You may not be eligible to participate in this study if any of the following criteria are true:

- Inability to swallow medicine by mouth.
- Active or recent (within one year) illicit/illegal drug and/or alcohol abuse.
- Known allergic reaction to any opioid.
- Significant mouth sores that would prevent obtaining the swab of your inner cheek.
- Receiving treatment for epilepsy (seizure disorder).
- Unable or unwilling to sign the study consent form.

Please let your clinician know if any of the above are true.

BENEFITS OF STUDY TREATMENT

You may or may not benefit from participating in this study. There is a possibility that the use of genetics to guide your pain management may help your pain control. The results of this study may help us determine whether or not genetic information can be used to guide pain medication management, which may help other patients with cancer pain in the future.

ALTERNATIVE TO BEING IN THE STUDY

You may choose not to participate in this study and instead receive routine care as recommended by your clinician. Your clinician can discuss the alternatives and the risks and benefits of these alternatives with you. Please ask any questions you may have and take as much time as you need to make your decision. If you choose not to participate in the study, this will in no way harm your relationship with your doctors or with Carolinas HealthCare System.

COSTS AND COMPENSATION FOR PARTICIPATION IN THIS STUDY

There will be no out of pocket costs to you for the pharmacogenomic testing. Your clinic visits and prescriptions will be billed to your insurance in the usual manner.

You will not receive payment for taking part in this study. For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

If you become ill or are hurt while you are in the study, get the medical care that you need right away.

In the event that you are harmed as a result of your participation in this study, inform your study investigator immediately so you can access medical treatment. You and/or your insurance/Medicare will be charged for this treatment in the usual manner. The study will not pay for standard medical treatment.

In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

BEING A STUDY VOLUNTEER AND WITHDRAWING FROM THE STUDY

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, that will not in any way harm your relations with your doctors or with Carolinas HealthCare System. You are free to stop being in the study if you change your mind after entering it. This would not harm your relations with your doctors or Carolinas HealthCare System.

- You may always say no. You do not have to take part in the study.
- If you start a study, you may stop at any time. You do not need to give a reason.
- If you do not want to be in a study or you stop the study at a later time, you will not be penalized or lose any benefits.
- If you stop, you should tell the study staff and follow the instructions they may give you.

Your part in the research may stop at any time for any reason, such as:

- The sponsor or the study doctor decides to stop the study.
- The sponsor or the study doctor decides to stop your part in the study for your safety.
- You need additional medicine.
- You do not follow the study rules.
- You have a new injury or illness.
- You decide to stop.

You may be asked to stop the study even if you do not want to stop.

Information contributed to the study will remain in the study even if you choose to withdraw. If you choose to withdraw from the study, please notify the study investigator in writing at the address on page one of this consent.

The study investigator may choose to involuntarily withdraw you from the study for any reason.

NEW INFORMATION

We will tell you about any new medical findings that may affect your willingness to continue in the study.

CONFIDENTIALITY

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your record for this study may, however, be reviewed and/or photocopied by XGene Diagnostics, by Levine Cancer Institute, by Carolinas HealthCare System, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

To ensure that your information collected for this study will be kept private, your name will not be used whenever possible. A code will be used instead of your name. All of your study data will be kept in a secure location.

A description of this clinical trial will be available on 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.

Privacy risks of genetic testing

Results of your pharmacogenomic panel will be provided to you, at your request. It is up to you whether or not you would like to share this information with your other healthcare providers.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that the sponsor will get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

If you wish to take part in this clinical study, you will be asked to sign this consent form. It allows the study sponsor and the study investigator (Dr. Patel) to collect, process and pass on to the sponsor organizations any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- the study investigator, Dr. Patel, and study staff,
- the study sponsor and/or its associated companies, XGene Diagnostics,
- Levine Cancer Institute,
- regulatory or other governmental authorities of the United States and other countries,
- other persons authorized by the study sponsor,
- Carolinas HealthCare System employees,
- other persons or agencies as required by law or allowed by federal regulations.

You have been told that your personal data are being collected and processed to:

- check your suitability to take part in the study,
- monitor activity with the pain medications under study,
- compare results with those of other subjects in the study,
- support the development of other study protocols.

You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing, and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing, and/or storage. Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, the groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Carolinas HealthCare System.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study investigator if you desire to access your record.

You have been told whenever your personal information is processed, it will be kept confidential and secure, to the best of our ability. It will be used only for the purpose for which it was collected.

This Authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study investigator in writing at the address and telephone number listed on the first page of this form.

Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.

STUDY STAFF PAYMENT/FINANCIAL DISCLOSURE

None of the doctors asking you to participate in this study has received or will receive money or other benefits for personal use from XGene Diagnostics, the company that developed the pharmacogenomic panel used in this study. However, the sponsor will give money or other benefits to a research fund, foundation, educational institution, or other organization with which the doctor or study staff is associated.

GETTING ANSWERS TO YOUR QUESTIONS OR CONCERNS ABOUT THE STUDY

You can ask questions about this consent form or the study (before you decide to start the study, at any time during the study, or after completion of the study). Questions may include:

- Who to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a study subject;
- Eligibility to participate in the research;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;
- Other questions, concerns, or complaints.

Contact the study doctor or study staff at Carolinas Healthcare, listed on the first page of this form, with any questions, concerns or complaints.

GETTING ANSWERS TO YOUR QUESTIONS ABOUT YOUR RIGHTS AS A RESEARCH SUBJECT

This study has been reviewed by an Institutional Review Board (IRB). This Committee reviewed this study to help ensure that your rights and welfare are protected and that this study is carried out in an ethical manner.

For questions about your rights as a research subject, contact:

- By mail:
  Study Subject Adviser
  [redacted]
- or call **toll free**: [redacted]
- or by **email**: [redacted]

PLEASE REFERENCE THE FOLLOWING NUMBER WHEN CONTACTING THE STUDY SUBJECT ADVISER: PRO00012942.

Optional Use of Pharmacogenomic Results by LCI Palliative Care Physicians to Modify Non-Pain related Drugs

You have been told that, at your request, you will be provided a copy of your pharmacogenomic test results. You may share this information with your other physicians, at your discretion. We also want to provide you with the option, if you indicate below, to allow the use of your pharmacogenomic results to modify and manage other non-pain related medications you may be taking. Because the pharmacogenomic test results may provide additional information as to how your other medications (not relating to pain) work, your clinician may want to speak to you about how other prescriptions should be managed. Based on your results, your clinician may suggest a drug and/or dose change for drugs treating conditions other than pain. If you consent to this, your clinician will speak with you about any suggested change(s) to prescriptions, directly.

Whether you agree or do not agree to this section, you may still take part in the study if you chose to.

If you have any other questions, please talk to your doctor or healthcare team member. Please read the following statement and mark your choice:

I agree to having my pharmacogenomics test results used to determine if non-pain related medications I am receiving should be considered for a dose or drug change.

Yes ☐ No ☐ Please initial here: _____ Date: _____

CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form. Dr. Patel, one of his associates, or their designee, will give me a copy of this signed and dated form.

_____ ____/____/____ _____

Signature of Research Subject Date Time

_____

Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

_____ ____/____/____ _____

Signature of Person Explaining Consent Date Time

_____

Printed Name of Person Explaining Consent