ID: UMCC 2019.173

Olanzapine for the Prevention of Chemotherapy Induced Nausea and Vomiting in Gynecologic Oncology Patients

NCT04503668

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Phase III randomized controlled trial investigating olanzapine for the prevention of chemotherapy induced nausea and vomiting in patients with gynecologic malignancies receiving every 3-week carboplatin and paclitaxel chemotherapy (UMCC Number 2019.173)

Company or agency sponsoring the study: None

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator:
Aimee Rolston, MD MS
Michigan Medicine, Department of Obstetrics and Gynecology

Study Coordinator:
Daniela Martin
Michigan Medicine, Department of Obstetrics and Gynecology

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find childcare, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying a drug, Olanzapine, in a large group of people to learn how well it works to prevent nausea and vomiting related to chemotherapy. This research will find out if Olanzapine, when given with other standard medications, will improve our ability to prevent nausea and vomiting in

patients with gynecologic cancers receiving carboplatin and paclitaxel chemotherapy. Olanzapine will be compared to the current standard of care drug, a neurokinin-1 receptor antagonist. Your health-related information will be collected for this research study.

This study involves a process called randomization. This means that the drug you receive in the study (Olanzapine versus neurokinin-1 receptor antagonist) is not chosen by you or the researcher. The study design divides study participants into separate groups, based on chance (like the flip of a coin), to compare different treatments or procedures. If you decide to be in the study, you need to be comfortable not being able to decide which treatment you will receive. You will know the treatment you are receiving once assigned to a certain group.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include increased sedation and increased appetite. More detailed information will be provided later in this document.

This study may offer some benefit to you now or others in the future by decreasing the amount of nausea and vomiting you experience with chemotherapy. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be approximately 5 months.

You can decide not to be in this study. Alternatives to joining this study include standard of care management for nausea and vomiting related to chemotherapy or choosing not to take medications for this reason during chemotherapy.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to find more effective medications for the prevention of nausea and vomiting caused by chemotherapy. This study is being performed to find out whether Olanzapine, when given with other standard anti-nausea medications, improves our ability to control nausea and vomiting related to chemotherapy in patients receiving carboplatin and paclitaxel for a gynecologic cancer.

Current standard of care involves the use of a neurokinin-1 receptor antagonist (NK1-RA), along with other anti-nausea medications, to prevent nausea and vomiting related to chemotherapy. Olanzapine is an alternative drug that has been shown to prevent nausea and vomiting related to chemotherapy in other patient populations. It's use in patients with gynecologic cancers receiving carboplatin and paclitaxel chemotherapy is not well studied.

Our objective is to compare the use of Olanzapine to NK1-RAs in patients with gynecologic cancers receiving standard chemotherapy. The results of our proposed work have the potential to significantly improve patients' experiences related to chemotherapy.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You are invited to take part in this study because you have a gynecologic cancer for which you are receiving carboplatin and paclitaxel chemotherapy at The University of Michigan and are between the ages of 18 and 89. You also are not receiving any radiation treatments, have not been treated with any chemotherapy in the last 12 months, have no history of adverse reactions to Olanzapine, have no history of significant heart disease, are not on any medications for diabetes, ls, and have not had 5 or more episodes of vomiting within 1 week prior to initiation of chemotherapy.

Every study has strict guidelines for determining which people may participate. These are called eligibility criteria. You will need to meet all of these criteria before you can participate in this study. If you agree to consider participating in this study, you will undergo evaluations to see if you meet the eligibility criteria for this study. Even though you may meet all the criteria for participation, it is possible that you may not be enrolled in this study for other reasons.

3.2 How many people are expected to take part in this study?

The research study is planned to include approximately 170 patients receiving carboplatin and paclitaxel chemotherapy for a gynecologic cancer. We expect to enroll all of these patients at the University of Michigan.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

The study team will explain the research study and answer any questions you may have about the study. If you are interested in participating in the study, the study team will look through your medical chart

and ask you questions to determine whether you are eligible for the study. Any labs/studies required to evaluate your eligibility for this study are already collected as part of standard of care for receiving chemotherapy. No additional labs or studies need to be performed solely for the purpose of this study.

Once eligibility is confirmed and you decide to participate, you will be asked to sign the informed consent form at the end of this document.

If you are currently participating in any other study, you should let the study team know and they will determine if it is safe for you to also take part in this study. If you do not meet the requirements for participation, the study doctor will explain why and will discuss with you other options.

Participation in the study will start with your first standard of care cycle of chemotherapy. In addition to coming to the hospital for your standard of care visits, lab work, and chemotherapy infusion, as part of the study, we will ask that you complete short (less than 10 question) surveys regarding your symptoms on days 1-6 of chemotherapy. More details regarding these surveys can be found below.

As a subject participating in this research study, you have certain responsibilities that may apply to this study, such as ensuring that you arrive at all of your scheduled appointments, take your medications as directed, and report any adverse reactions you may have during the study.

Screening Period

Screening for this study will take place prior to your first cycle of chemotherapy / during your chemotherapy education visit. Your labs and medical history will be reviewed to determine eligibility. If you are able to have children, a pregnancy test will also be required.

Study Intervention Period

If you meet all criteria to participate in the study, you will enter the intervention period.

As for this study, you will be randomly assigned to receive either Olanzapine (taken at night by mouth on days 1-4 of chemotherapy) or a neurokinin 1 receptor antagonist (given by IV on day of chemotherapy). You have an equal chance of receiving either medication. Which treatment you receive is decided at random by a computer (purely by chance, like tossing of a coin).

We will ask that you complete short (less than 10 question) surveys regarding your symptoms on days 1-6 of chemotherapy. You will be given a booklet with these questionnaires to complete. You will be sent text reminders to complete the questionnaires. In addition, for cycle 1, a study team member will be calling you to remind you to complete the questionnaires. We ask that you bring the booklet with you to your next doctor's visit prior to your next cycle of chemotherapy. We ask that you complete these questionnaires for all planned cycles of chemotherapy.

The schedule for study procedures is as follows:

- Pre study/consent visit: consent, history and physical, baseline questionnaires, standard of care labs, contraceptive counseling
- Before chemo treatments: pre-chemo study questionnaire and standard of care labs. The labs can be completed the day of chemo or before.

- On chemo days: standard of care labs if not completed prior, study drug administration
- Post Chemo Treatment: patient diary filled out for days 1-6, study drug administration if randomized to Olanzapine arm.

If your nausea and vomiting is not well controlled by the medications you are assigned to receive, it is possible your doctor may change or add to the prescriptions for your next cycle of chemotherapy. This will be determined based on your symptoms.

Study Completion and Follow Up Period

After completion of the study, a final assessment of side effects will be performed during your routine post chemotherapy office visit by a member of our study team. There will be no additional follow up.

4.2 How much of my time will be needed to take part in this study?

Your study visits will all coincide with standard of care clinic visits prior to scheduled chemotherapy. We anticipate additional time for study purposes as follows:

- Screening/Enrollment Period: additional 30 minutes to allow for consent process, randomization and education
- Study Intervention Period: additional 10 minutes each visit to allow study team member to retrieve prior questionnaires, answer questions, and discuss any side effects/concerns
- Study Completion and Follow up Period: additional 10 minutes at final follow up visit to allow study team member to retrieve complete questionnaires, answer questions, and discuss any side effects/concerns

In addition to the above, you will be asked to complete a short questionnaire on days 1-6 of chemotherapy. We expect that this will take you ~5 minutes each day.

4.3 When will my participation in the study be over?

The expected duration for your participation depends on the study treatment and your health condition. All patients will continue participation in the study until the end of chemotherapy, cancer progression necessitating a different therapy, or if you, the study team, or your provider decides that you should not continue to be in the study.

4.4 What will happen with my information and/or biospecimens used in this study?

Your collected information may be shared with other researchers:

- With appropriate permissions, your identifiable collected information may be shared, and/or,
- Without your additional consent, your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

Your provider and the study team will monitor you closely for side effects. Even with frequent monitoring, enrolling in this study involves risks, and some side effects of the medications cannot be

predicted. Side effects can range from mild to severe to life threatening. Most side effects will get better when you stop taking the study drug, but some may be long lasting or may never go away. Side effects may even cause death. You should tell your provider or the study team immediately about any side effects that you have or any change in how you feel while on this study. If you have side effects, your dose may have to be reduced, or you may have to stop taking the drugs and wait until you feel better before you start again. Your study team may give you medicines or lower your dose of drugs to help lessen side effects. If any side effect is intolerable, you may have to permanently stop taking the drugs.

The known or expected risks are:

Risks associated with Olanzapine:

Common side effects:

- Sedation
- Increased appetite

Less common side effects

- Dizziness
- Headache
- Hypotension
- Constipation
- Fatigue
- Increased prolactin
- Increased liver enzymes
- Weakness
- Increased risk of diabetes mellitus

Risks or other discomforts associated with study procedures

Questionnaires

As part of the study, you will be asked to complete questionnaires about your symptoms during chemotherapy. Some of the questions may seem very personal or embarrassing. They may make you uncomfortable. You may refuse to answer any of the questions that you do not wish to answer. If the questions make you uncomfortable, we can help you to find a counselor.

The researchers will try to minimize these risks by monitoring you closely. The study will give the lowest effective dose of Olanzapine. Additionally, the study design is one where Olanzapine is used intermittently for short periods which minimizes side effects when compared to chronic, daily use. If you have side effects, we will make appropriate adjustments as defined by the study protocol. You may need to discontinue Olanzapine if side effects are too serious. Your risks are further minimized by using the results of blood tests you are already having for your clinical care. There are no additional tests or studies required specifically for this research study.

Additionally, there may be a risk of loss to confidentiality or privacy. For example, if your identity as a participant in this research or your identifiable genetic or health information were disclosed to unauthorized persons, there is the possible risk of discrimination by employers or insurance providers. The researchers believe that the risks of such improper disclosure are very small because strict privacy and confidentiality procedures for this research have been adopted. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

There could be risks to a fetus in this study. If you are pregnant or become pregnant during the study, these risks could affect you or your fetus. Women must agree to either abstain from sexual activities that could result in pregnancy or use at least one acceptable method of birth control (i.e. condom, IUD, pill) while taking part in this study.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. Some of the possible benefits to you as a participant in this study are reduction in the nausea and vomiting you experience with chemotherapy, or elimination of those symptoms all together. Less nausea and vomiting with chemotherapy improves your ability to get your treatments on time. Others may also benefit from the knowledge gained from this study.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?
If you decide not to take part in this study, you will be provided with current standard of care medications for the prevention of nausea and vomiting related to chemotherapy.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

If you withdraw full consent from the study, your data will be destroyed at that time. If you withdraw from study treatment, the data that has been collected up until that point in the study will be used.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
Tell the study doctor if you are thinking about stopping or decide to stop. It is important to tell the study doctor if you are thinking about stopping so any risks can be evaluated by your doctor. If you decide to leave the study before it is finished, please tell your study doctor or one of the researchers listed in Section 10 "Contact Information" (below).

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
No, you will not be paid for taking part in this study.

8.3 Who could profit or financially benefit from the study results?
No person or organization has a financial interest in the outcome of this study.
Even so, research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?
Your participatin will occur at the University of Michigan. Your data will be kept confidential, to the extent permitted by applicable laws, in the following manner:

- Your name will not be used in any reports about the study
- Your will be identified only by a study code (subject ID number)
- Your identifying information will be kept secure

The study team will assign a code number to your study data. Some study data may contain information that could be used (perhaps in combination with other information) to identify you (e.g. date of birth). The study team will use the study data for research purposes to support the scientific objectives of the study. Study data (that does not directly identify you) may be published in medical journals or shared with others as part of scientific discussions.

Your research information will be stored entered into a secure database and stored in a locked cabinet. It will not be made part of your regular medical record. Your stored research information will be labeled with your study code and will not include any identifying information. Only the study team will have access to the document linking your study code with your name/other identifiyng information. This document will be locked with restricted access.

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.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Health plan/health insurance records
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Aimee Rolston, MD MS
Mailing Address: University of Michigan

1500 East Medical Center Drive
Telephone: 734-647-8906
734-936-4000 Hospital Operator – 24-hr paging

Study Coordinator: Daniela Martin
Mailing Address: 1500 East Medical Center Drive
Telephone: 734-232-1846

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document (you will receive a copy of the signed and dated informed consent) (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*
- Questionnaire packet

12. SIGNATURES

Sig-A

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with [NAME OF STUDY TEAM MEMBER OBTAINING CONSENT] _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-D

Consent/Assent to Collect for Unspecified Future Research

This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow future use of my specimens. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep my specimens for future research.

_____ No, I do not agree to let the study team keep my specimens for future research.

Print Legal Name: _____

Signature: _____

Sig-G

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____