

Kansas City Clinical Oncology Program

N08CB, A Phase III Randomized, Placebo-Controlled, Double-Blind Study of Intravenous Calcium/Magnesium in Two Different Versions to Prevent Oxaliplatin-Induced Sensory Neurotoxicity

This is an important form. Please read it carefully. It tells you what you need to know about this research study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. 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 doctor for more explanation.

You are being asked to take part in this research study because you have been diagnosed with colon or rectal cancer, which will be treated with a type of chemotherapy, called oxaliplatin (which is standard treatment, not research).

Why is this research study being done?

It is well known that this type of chemotherapy can cause side effects on nerves that result in symptoms such as sensitivity to cold or touch, pain, tingling or numbness of fingers and toes which can interfere with activities of daily living. In some patients, the chemotherapy has to be stopped because of these symptoms.

The purpose of this study is to compare the effects, good and/or bad, of calcium gluconate and magnesium sulfate with a placebo (an inactive agent) on possible nerve damage that could be caused by oxaliplatin chemotherapy treatment. In this study, you will get the calcium gluconate and magnesium sulfate together right before and after each dose of chemotherapy or a placebo right before and after each dose of chemotherapy, or the calcium gluconate and magnesium sulfate before each dose of chemotherapy and a placebo after each dose of chemotherapy. This is to see if 1 dose will be as effective as 2 doses.

How many people will take part in the research study?

About 354 people will take part in this study.

What will happen if I take part in this research study?

Before you begin the study ...

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You will be starting chemotherapy treatment with oxaliplatin chemotherapy for your cancer. To start this study, you will need to have a port or catheter so that study medications can be administered into a large vein in your chest.

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history and physical exam, including height and weight and rating of how well you perform activities of daily living.
- Routine blood tests (blood counts, liver tests, a kidney test, and other tests your doctor thinks should be done). About 2 teaspoons of blood will be drawn from a vein in your arm for the blood tests.
- An electrocardiogram of your heart (also known as ECG or EKG) may be obtained if your doctor thinks it should be done.
- Pregnancy test if you are a woman of childbearing potential.

You will need to get the following test to participate in this study:

- Complete pre-chemotherapy questionnaires (about 10 minutes). These questionnaires will contain questions about your feeling of well-being, and about any pain, numbness or tingling you may be feeling.

During the study

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. The following are part of regular cancer care and are not being done more often because of this study.

- Medical history and physical exam, including height and weight and rating of how well you perform activities of daily living, prior to each dose of chemotherapy.
- Routine blood tests. About 2 teaspoons of blood will be drawn from a vein in your arm for the blood tests. These will be obtained one time prior to each planned chemotherapy cycle.

The following is not part of regular cancer care but is being done because of this study.

- Research blood tests. This can be done at the same time as your routine blood tests. An additional 2 teaspoons of blood will be drawn at the same time, for research purposes. This research blood test will only be obtained one time and is required. You will have the option of allowing a portion of this blood sample to be used in future research. Your options are described

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later in this form. This research test will look at genetic material to see if certain genes are involved in oxaliplatin's effect on nerves. Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test. The test results will not be put in your medical record either.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance (as in a roll of the dice). 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 one in three chance of being placed in any group.

If you are in group 1 You will get the study drugs, calcium gluconate and magnesium sulfate, through a vein (IV) over a time period of 30 minutes. You will get the study drugs immediately before you get chemotherapy, and immediately after you get chemotherapy. When your chemotherapy ends, your treatment with the calcium gluconate and magnesium sulfate will end too.

If you are in group 2 You will get the placebo (inactive agent), through a vein (IV) over a time period of 30 minutes. You will get the placebo immediately before and immediately after you get chemotherapy. When your chemotherapy ends, your treatment with the placebo will end too.

If you are in group 3 You will get the study drugs, calcium gluconate and magnesium sulfate, through a vein (IV) over a time period of 30 minutes. You will get the study drugs immediately before you get chemotherapy. You will get the placebo (inactive agent) immediately after you get chemotherapy. When your chemotherapy ends, your treatment with calcium gluconate and magnesium sulfate/placebo will end too.

We want to find out if the calcium gluconate and magnesium sulfate will help to lessen nerve damage from chemotherapy and make the quality of your life better. Questionnaires will be used to assess changes in your daily life and your feeling of well-being, and about any pain, numbness or tingling you may be feeling. You will be given a booklet that has the questionnaires in them. You will be given a new booklet at each cycle of treatment. It should take you less than 5 minutes each day to complete. You will be asked to continue filling out these booklet questionnaires for as long as you continue receiving chemotherapy. These questionnaires will be for the days of chemotherapy and for 5 days after each dose of chemotherapy. At the end of your chemotherapy treatment, we will ask you to continue filling out a booklet questionnaire at 1 month, 3 months, 6 months, 12 months, and 18 months from your last chemotherapy dose. The booklet questionnaires will be mailed to you, if do not have an appointment with your doctor. If you would like to see these questionnaires before signing the consent form, please ask your study nurse or coordinator for a copy to review.

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When I am finished taking the calcium gluconate and magnesium sulfate/placebo and chemotherapy

After you are done with chemotherapy, you will have a physical exam, including weight, a rating of how well you perform activities of daily living, and routine blood tests. Further visits will be coordinated by your oncologist as part of the routine follow-up for your cancer.

How long will I be in the research study?

You will be asked to take the study drugs (calcium gluconate and magnesium sulfate, placebo, or calcium and magnesium together and placebo) during your chemotherapy treatment.

After you are finished taking the calcium gluconate and magnesium sulfate or placebo and chemotherapy treatment, the study doctor will ask you to visit the office for follow-up exams at 1 month, 3 months, and 6 months. You will be asked to fill out a monthly questionnaire booklets during these visits. You will also be asked to complete booklets 12 months and 18 months after your last chemotherapy dose. The booklet questionnaires will be mailed to you, if do not have an appointment with your doctor.

Can I stop being in the research study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the calcium and magnesium can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what followup care and testing could be most helpful for you.

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

What side effects or risks can I expect from being in the research study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the calcium and magnesium. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to the **calcium gluconate** include those which are:

Likely

- Tingling sensations
- A sense of heaviness or heat waves
- A chalky taste right after getting the drug

Less Likely

- Irritation at the IV site
- Fainting
- Low blood pressure
- Abnormal heartbeat
- Slowed heart rate

Rare but serious

- Cardiac arrest (heart stopping)

You should not get this drug if you have an irregular heartbeat or high levels of calcium in your blood. Your study doctor will check these levels before you start oxaliplatin chemotherapy treatment.

Risks and side effects related to the **magnesium sulfate** include those which are:

Likely

- Rash, itchiness
- Flushing or redness
- Sweating

Less Likely

- Trouble breathing or shortness of breath
- Low blood pressure
- Rapid beating of your heart
- Chest pain
- Diarrhea
- Widening or opening (dilation) of blood vessels
- Lowered activity of the nervous system possibly causing sluggishness/sleepiness

Risks and side effects related to the neurologic testing:

You should have very little, if any, discomfort during the neurologic testing. If you are uncomfortable, tell the person doing the test. During the neurologic testing you may experience a pin-prick sensation and/or hot and cold sensations. The heat test may cause a brief (1-2 second) burning sensation. At any time you may tell the person doing the test

to stop. It is recommended that you not take anything for pain or sleep 12 hours prior to your testing.

As with any medication, allergic reactions are a possibility.

The risks of drawing blood include pain, bruising or rarely infection at the needle site.

Reproductive risks: You should not become pregnant or father a baby while on this study because the chemotherapy you are getting to treat your cancer can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your health care provider about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the research study?

Taking part in this study may or may not make your health better. While doctors hope that calcium gluconate and magnesium sulfate will help protect you against the side effects to your nerves from the chemotherapy, there is no proof of this yet. We do know that the information from this study will help doctors learn more about calcium gluconate and magnesium sulfate as a prevention from chemotherapy side effects to the nerves. This information could help future cancer patients.

What other choices do I have if I do not take part in this research study?

You do not have to be in this study to receive treatment for your nerve damage. Your other choices may include:

- Getting treatment or care for your nerve damage without being in a study
- Taking part in another study
- Getting no treatment

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

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Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- North Central Cancer Treatment Group (NCCTG)
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.

What are the costs of taking part in this research study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking

part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

The study is supplying the calcium gluconate and magnesium sulfate at no cost to you. However, you or your health plan may need to pay for costs of the supplies and personnel who give you the study drugs.

The study agent, calcium gluconate and magnesium sulfate will be provided free of charge while you are taking part in this study. However, if you should need to take the study agents much longer than usual, the stock of free study agent that has been supplied could run out. If the free supply runs out, your study doctor will discuss with you how to get more study drugs. You may be asked to pay for it.

You will not be paid 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 research study?

It is important that you tell your study doctor, _____ [investigator's name(s)], if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ [telephone number].

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You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this research study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the research study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number].

For questions about your rights while taking part in this study, call the Kansas City Clinical Oncology Program Institutional Review Board (a group of people who review the research to protect your rights) at 913-948-5588

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study. You may take part in these additional studies if you want to. You can still be a part of the main study even if you say 'no' to taking part in any of these additional studies.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

About Using Biological Samples for Research

This study also has laboratory tests that will be performed to study small samples of blood.

A blood sample will be done by drawing some blood from a vein. The blood will be taken before the first of second cycle of chemotherapy treatment starts.

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The blood will be sent to laboratories associated with NCCTG, where the tests will be done. These tests will be done in order to understand how your cancer responds to treatment. It is hoped that this will help investigators better understand your type of cancer. The results of these tests will not be sent to you or your study doctor and will not be used in planning your care. These tests are for research purposes only and you will not have to pay for them.

We would like to keep some of the blood that is/are left over for future research. If you agree, this blood will be kept and may be used in research to learn more about cancer and other diseases.

The research that may be done with your blood is not designed specifically to help you. It might help people who have cancer and other diseases in the future.

Reports about research done with your blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the blood for future research is up to you. No matter what you decide to do, it will not affect your care.

If you decide now that your extra blood can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your blood. Then any blood that remains will no longer be used for research.

In the future, people who do research may need to know more about your health. While NCCTG may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes blood is used for genetic research (about diseases that are passed on in families). Even if your blood is used for this kind of research, the results will not be put in your health records.

Your blood will be used only for research and will not be sold. The research done with your blood may help to develop new products in the future.

Benefits

The benefits of research using blood include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

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The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our research review board at the IRB's phone number.

No matter what you decide to do, it will not affect your care.

1. My blood sample(s) may be kept for use in research to learn about, prevent, or treat cancer.

Yes No Please initial here: _____ Date: _____

2. My blood sample(s) may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Please initial here: _____ Date: _____

If you want your sample(s) destroyed at any time, write to the Secretary of the _____ Institutional Review Board

NCCTG has the right to end storage of the sample(s) without telling you.

The sample(s) will be the property of NCCTG. Outside researchers may one day ask for a part of your sample(s) for studies now or future studies.

How do outside researchers get the sample?

Researchers from universities, hospitals, and other health organizations do research using blood and tissue. They may call NCCTG and ask for samples for their studies. NCCTG looks at the way that these studies will be done, and decides if any of the samples can be used. NCCTG sends the samples and some information about you to the researcher. NCCTG will not send your name, address, phone number, social security number, or any other identifying information to the researcher. If you allow your sample(s) to be given to outside researchers, it will be given to them with a code number. If researchers outside NCCTG use the sample(s) for future research, they will decide if you will be contacted and, if so, they would have to contact the researchers at NCCTG. Then NCCTG will contact the clinic where you registered for this study, who will contact you.

Please read the following statements and mark your choice:

I permit NCCTG to give my sample(s) to outside researchers:

Yes No Please initial here: _____ Date: _____

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Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>
- For NCI's general information about cancer in Spanish, go to <http://www.cancer.gov/espanol>

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

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.

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Signature

I have been given a copy of all 12 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Printed Participant Name: _____

Participant Signature: _____

Date: _____

Printed name of person obtaining informed consent:

Signature of person obtaining informed consent:

Date _____

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