NCI Community Oncology Research Program – Kansas City (NCORP-KC)

Study Title for Study Participants: Testing Low-Dose Ibuprofen for Cognitive Problems in Colorectal Cancer Patients

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

NCT 03186638: Phase II Study of Low-Dose Ibuprofen for Cognitive Impairment in Colorectal Cancer Patients Receiving Chemotherapy

This consent form describes a research study, what you may expect if you decide to take part, and important information to help you make your decision. Please read this form carefully.

The study staff will explain this study to you. Please ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about this study and discuss with family or friends.

- Being in this study is voluntary – it is your choice.
- If you join this study, you can change your mind and stop at any time.
- There are risks from participating and you should understand what these mean for you.

The study is being conducted by the University of Rochester Cancer Center (URCC) and its affiliates throughout the United States in the National Cancer Institute Community Oncology Research Program (NCORP).

WHAT IS THE USUAL APPROACH TO MY CHEMOTHERAPY-RELATED COGNITIVE PROBLEMS?

You are being asked to participate in this study because you have been diagnosed with colorectal cancer and have begun chemotherapy. One side effect of treatment may be cognitive problems (such as problems with remembering things, multi-tasking, or concentrating). There is no standard of care treatment for helping people with cognitive problems related to chemotherapy.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to receive usual care by your doctor
- you may choose to take part in a different study, if one is available

WHY IS THIS STUDY BEING DONE?

Many cancer patients report mild to moderate cancer-related cognitive difficulties (such as problems remembering things, multi-tasking, or concentrating) during and following treatment of their cancer. Currently, the medical community does not have standard of care treatments for these difficulties. We also do not know what may be causing these difficulties. The purpose of this study is to help doctors and researchers better understand the cognitive problems related to cancer and chemotherapy and to evaluate the effects of ibuprofen (e.g. Advil®, Motrin®) for alleviating cognitive difficulties during chemotherapy. Ibuprofen is an FDA approved over the

counter anti-inflammatory medication commonly used to treat pain, fever, and inflammation and is not currently approved to treat cognitive difficulties.

The anti-inflammatory agent being used in this research study is a low-dose ibuprofen (an over-the-counter anti-inflammatory medication). Research suggests that anti-inflammatory agents may slow the decline of cognitive processes and diseases involving the brain, such as Alzheimer's disease, although results of these studies have been inconsistent.

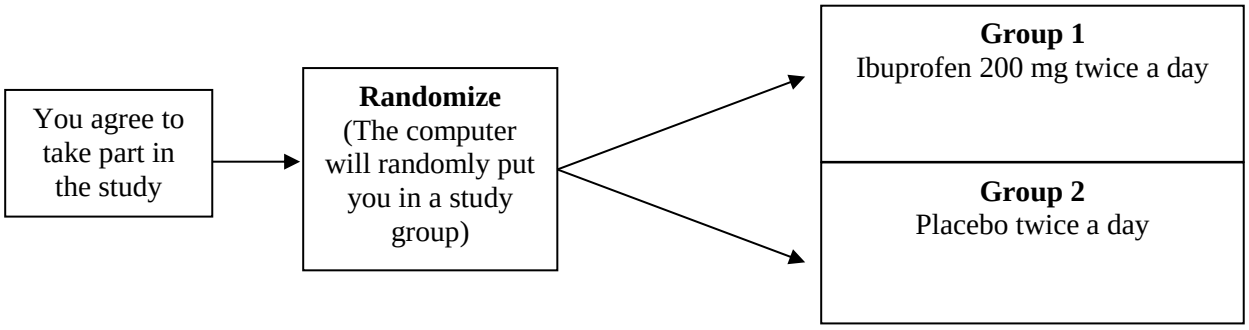
Cognitive difficulties related to cancer and chemotherapy may be related to inflammation; increased levels of small proteins secreted by immune system cells, called cytokines, are associated with cognitive difficulties in other diseases. Researchers will investigate how ibuprofen influences cytokines during chemotherapy.

The researchers leading this study are also interested in how cognitive difficulties may relate to other symptoms you may or may not develop such as fatigue, depression, sleep problems and anxiety, and how ibuprofen may affect these symptoms.

There will be about 86 people taking part in this study nationwide.

WHAT ARE THE STUDY GROUPS?
This study has 2 study groups.

- Group 1 will take a 200 mg capsule of ibuprofen twice a day, once in the morning and once in the evening (8 hours apart) for 6 weeks.
- Group 2 will take a placebo capsule that looks like the study drug but contains no medication twice daily, once in the morning and once in the evening (8 hours apart) for 6 weeks. The placebo capsule contains trace amounts of lactose (approximately 0.32 grams).



We will use a computer to assign you to one of the study groups for the six week period. This is called randomization. This means that you will be put into a group by chance. We assign patients this way because no one knows if one treatment is better or worse than the others.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in the study will last approximately 7-8 weeks, depending on scheduling of your first and last study visits.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures to make sure it is safe for you to take part. If you join the study, your doctor will continue to monitor your safety and health. Neither you nor your insurance carrier will be billed for any assessments that will be completed for this study. You will be asked to complete the following during the study:

Start of Study Assessment (Pre-Intervention Visit; i.e., Baseline Visit)

- **Questionnaires:** Complete questionnaires that ask basic information about your medical history, current medication usage, cognitive functioning, fatigue, quality of life, depression, anxiety, sleep, and physical activity. These forms will take approximately 15 minutes to complete.
- **Pregnancy Status:** If you are female, we will confirm that you are not pregnant prior to going on the study by reviewing your medical record.
- **Cognitive Tests:** Complete computerized cognitive tests on a touch screen computer that assess your memory, your ability to plan, and your attention. You will first become familiar with using the touch screen computer prior to beginning tests. The study coordinator will guide you through each of the four tasks. These tasks will take approximately 35 minutes of your time to complete. Following the computerized tasks, you will take 4 brief tests using paper and pencil or verbally to evaluate reading, attention, organization, and memory. These will take approximately 25 minutes of your time to complete. In total, the cognitive testing could take up to 60 minutes of your time with breaks.
- **Blood Draw:** Have a fasting blood draw (about 2 tablespoons) taken after you have not eaten for approximately 6-8 hours in order to measure the levels of proteins secreted as part of the body's immune responses (inflammatory cytokines). This measurement will be within 5 days of your cognitive or can be done the day of, but prior to, your next cycle of chemotherapy while on this study.

We estimate that your Pre-Intervention assessment visit will take about 1 hour to complete. The in-person visit is scheduled sometime within 8 days of the first cycle of chemotherapy you receive while on this study.

We will review your medical record to identify information about your cancer and treatments, as well as other medical conditions and laboratory data obtained by your doctors.

You will need a telephone and be willing to provide the number to study staff. Within the week following your first visit, someone from the URCC Research Base will call you to complete a brief phone-based evaluation of your cognitive functioning. These tests will be similar to those

done on the computer and the ones done verbally with the study coordinator, but will be done via the phone. We will need a phone number to reach you for this part of the study. The phone call assessment will take approximately 15 minutes of your time.

During the study, you will be asked to complete a daily diary every night before bed that asks about your symptoms, and your use of the study medication.

We will contact you once per week to see how you are doing and to ask if you have any questions about the study intervention, to remind you to complete study procedures (i.e. study medication, questionnaires) and to schedule study visits.

Mid-Study Assessment (Mid-Intervention Visit)

- Complete a questionnaire that will ask about your cognitive functioning.
- Have a fasting blood draw (approximately 2 tablespoons) taken after you have not eaten for approximately 6-8 hours.

End of Study Visit (Post-Intervention Visit)

At the end of the study, there will be a third assessment that will likely occur the day before (or within a few days of) your last cycle of chemotherapy while on this study. The assessments will be exactly like those at the first study visit, which involve completing questionnaires and computer cognitive tests, a fasting blood draw (about 2 tablespoons; blood draw will be taken the morning prior to scheduled chemotherapy if possible), and a phone-based assessment of your cognitive functioning. As in the baseline assessment visit, your in-person visit will take approximately 1 hour.

You must return the study medication bottle, whether empty or still containing capsules, and we will record how many capsules are left, if any.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

There is a risk that you could have side effects from participating in this study. Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may be serious and may even result in death.
- You may lose time at work or home and spend more time in the hospital or doctor's office than usual.
- You may be asked sensitive or private questions which you normally do not discuss.
- The study drug may not be better, and could possibly be worse, than the usual approach for your cancer-related cognitive problems.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.

- The study doctor may be able to treat some side effects.

The paragraphs below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Ibuprofen:

The risks of taking ibuprofen include headaches, dizziness, drowsiness, rash, abdominal pain, nausea, diarrhea, constipation, renal insufficiency, and heartburn. Since ibuprofen reduces the ability of blood to clot, bleeding may be increased after injury. Studies of high doses of ibuprofen (800 mg 3 times per day; not used in this study) have been associated with low incidence of stomach ulcers.

Possible side effects include:

COMMON, SOME MAY BE SERIOUS
• Nausea • Swelling of body, fluid retention

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ibuprofen, from 1 to 20 may have:
• Anemia, which may cause tiredness, or may require blood transfusions • Reduction in number of white blood cells which makes infection more likely

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving ibuprofen, from 1 to 10 may have:	
• Pain in belly • Constipation, vomiting, diarrhea • Indigestion, heartburn, passing gas • Dizziness • Ringing in ears	• Vomiting • Headache • Rash • Prolonged Bleeding Time • Lab results that show problems with the liver

RARE, AND SERIOUS In 100 people receiving ibuprofen, 1 or fewer may have:	
• Serious allergic reactions which cause rash, low blood pressure, wheezing, shortness of breath, difficulty in breathing, swelling of the face or throat or loss of consciousness • Reduction in red blood cells which can cause weakness, bruising or make infections more likely • Abnormal or worsening of abnormal heartbeat • Swelling of the protective membranes covering the brain and spinal cord • Sores in stomach • Kidney damage which may cause swelling, require dialysis • Hypersensitivity reaction similar to an allergy with possible symptoms of fever, rash, itching, possible blisters, arthritis • Severe skin rash with blistering and peeling which can involve skin and other parts of the body • Vision loss	• Internal Bleeding which may cause belly pain, black tarry stool, blood in vomit • A tear or a hole in the stomach which may cause belly pain or require surgery • Hearing Loss • Heart Failure which may cause shortness of breath, swelling of ankles and tiredness • Reduction in red blood cells which can make the skin yellow and cause weakness or breathlessness • Blurred vision with chance of blindness

POSSIBLE, SOME MAY BE SERIOUS In 100 people receiving ibuprofen, an unknown number may have:	
• Swelling of the face and/or blockage of the airway which may cause shortness of breath, cough, wheezing • Anxiety, worry • Brief interruptions of breathing during sleep • Lack of energy or feeling of weakness • Difficulty breathing or wheezing • Coma • Sweating • Difficulty swallowing or painful swallowing • Shortness of breath • Painful urination • Bruising • Burping • Narrowing or sores of the esophagus (tube that goes from the mouth to the stomach through which food passes) • Redness and scaling of the skin • Fever • Inflammation, (swelling and redness) of the stomach lining • Tongue inflammation • Vomiting of blood • Damage to the liver which may cause belly pain, bleeding, yellowing of eyes and skin, swelling • Too much sugar in the blood • Too much potassium in the blood • Increased blood level of uric acid, a waste material from food digestion • Not enough sodium in the blood • High blood pressure	• Swollen or painful glands • General feeling of discomfort, uneasiness, or pain • Heart Attack • Decreased urine output • Infection • Infertility • Irritation or sores in lining of mouth or nose • Reduction in blood cells which can cause weakness, bruising, or make infections more likely • Overly sensitive to light • Decreased number of a type of blood cell that helps to clot blood • More protein leaking into the urine than usual, often a sign of kidney disease • Bleeding underneath the skin • Slow breathing rate • Seizures • Stroke, which may cause paralysis, weakness • Fainting • Tremor (abnormal body movement) • Inflammation of blood vessels • A feeling of dizziness or “spinning” • Weight Gain or Loss • Wheezing • Withdrawal

Questionnaires:

Although very unlikely, it is possible that answering some of the questions may cause you to feel upset or worried. If this happens, please let the study doctor or research staff know. You do not have to answer any questions that make you uncomfortable.

Computerized and Paper-Based Cognitive Testing:

There is no known risk associated with participating in the computerized or paper-based cognitive tests. You may feel slightly frustrated, uncomfortable or upset during some points of the cognitive testing; however, these tests are meant to increase in difficulty throughout the tests for everyone.

Blood Draw:

Blood drawing may cause pain and bruising at the site where the blood is taken, and sometimes, may cause people to feel light-headed or even to faint. Rarely, you might get an infection at the site of the needle stick.

Every effort will be made to minimize the risks through 1) obtaining approval of your physician to enter the study for either intervention and 2) using trained study coordinators.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?
It is not possible to know at this time if the ibuprofen is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

CAN I STOP TAKING PART IN THIS STUDY?
Yes, you can decide to stop any part of the study at any time. If you decide to stop the study medication or want to stop the entire study for any reason, it is important to notify the research staff as soon as possible, so you can stop safely. If you stop, you can decide whether or not to let the research team continue to provide your medical information to the organization running the study.

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights. For questions about your rights while in this study, call the Central Institutional Review Board at 888-657-3711.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
Neither you nor your insurance carrier will be billed for any assessments that will be completed for this study. The ibuprofen/placebo will be supplied at no charge while you take part in this study. Blood draws for study lab tests are provided at no charge.

In the case that you are directly injured by the study intervention or procedure that are part of this study, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. No funds have been set aside to compensate you in the event of injury.

You will be paid for taking part in this study. If you complete all assessments, you will receive a total reimbursement of $100.00. You will receive $25.00 after completing the Pre-Intervention assessment, $30.00 after completing the Mid-Intervention assessments ($5/wk x 6 weeks), and $45.00 after completing the Post-Intervention assessment. You will only be reimbursed for the study assessments that you actually complete.

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance coverage, you would be responsible for any costs. If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The University of Rochester and its affiliates in the NCI Community Oncology Research Program
- The NCI Central Institutional Review Board, which is a group of people who review the research with the goal of protecting the people who take part in the study
- James P. Wilmot Cancer Center Data Safety Monitoring Committee
- The Department of Health and Human Services
- The Food and Drug Administration and the National Cancer Institute

Your study records also will be stored for future use. However, your name and other personal information will not be used. Some types of future research may include looking at your records and those of other patients to see who had side effects across many studies or comparing new study data with older study data. However, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.

- You will not get reports or other information about any research that is done using your information.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research study is over.

How long will this permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
Yes, you may withdraw from the study. If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
No. There is a risk that your information will be given to others without your permission.

WHERE CAN I GET MORE INFORMATION?
You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?
You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDY SECTION:
This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results. You will not be billed for these optional studies. You can still take part in the main study even if you say "no" to this study. If you sign up for but cannot complete the study for any reason, you can still take part in the main study.

OPTIONAL SAMPLE COLLECTIONS FOR FUTURE LABORATORY STUDIES

Researchers are trying to learn more about chemotherapy-related cognitive difficulties, and other cancer-related health problems. Much of this research is done using samples of tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems. Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

The researchers ask your permission to store and use your leftover blood samples for medical research to learn about, prevent and treat chemotherapy-related cognitive difficulties, and to learn about other health problems. Your blood samples will be stored temporarily with a blood requisition form containing related health information until final processing. Your health information will not be stored indefinitely. These blood samples will not be made available for use by investigators outside of the URCC Research Base unless there is a collaborative agreement with the study's lead investigator. We will not be able to diagnose you with any disease. The DNA analyses are only for information-gathering purposes and are not known to put you at risk for any disease. These are not clinical laboratory tests, only research tests and results will not be given to you or your doctor and will not be put in your medical record. The research that may be done is unknown at this time.

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) About one and a half tablespoons of blood will be collected from a vein in your arm and will be collected at same time as the blood draw at the beginning of the study and the blood draw at the end of the study. Your sample and some related health information will be stored in a storage facility at the Cancer Control and Psychoneuroimmunology Laboratory at the University of Rochester and supported by the National Cancer Institute.
2) Your sample will be stored with samples and information from other people who take part. The samples will be kept until they are used up.
3) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The

researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your samples are sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any staff with access to the list must sign an agreement to keep your identity confidential.
3) Information that identifies you will not be given to anyone, unless required by law.
4) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor who will let the researchers know. Then, any sample that remains in storage at the University of Rochester will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor _____ (insert name of study doctor[s]) at _____ (insert telephone number).

Please circle your answer to show whether or not you would like to take part in each option:
My samples and related information may be kept for use in future health research.

YES NO

This is the end of the section about optional studies.

Release

By signing this form you authorize NCORP-KC 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.

My signature agreeing to take part in the main study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes.'

Participant Name_____

Participant Signature _____

Date _____

Person Obtaining Consent_____

Signature of Person Obtaining Consent_____

Date _____