

MARQUETTE GENERAL HEALTH SYSTEM

Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

**NSABP FC-4/CP13-0708 CONSENT FORM FOR
PRE-ENTRY K-RAS TESTING**

TITLE: NSABP PROTOCOL FC-4/CP13-0708: A Randomized Phase II Clinical Trial Investigating Irinotecan Plus Cetuximab With or Without Anti-Insulin-Like Growth Factor-I Receptor Monoclonal Antibody (IMC-A12) for the Treatment of Patients with Metastatic K-RAS Wild-Type Carcinoma of the Colon or Rectum that has Progressed on Oxaliplatin and Bevacizumab Given as First-Line Therapy.

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Consent Form for

K-RAS Testing to Determine Eligibility for NSABP FRP FC-4/CP13-0708: A Randomized Phase II Clinical Trial Investigating Irinotecan Plus Cetuximab With or Without Anti-Insulin-Like Growth Factor-I Receptor Monoclonal Antibody (IMC-A12) for the Treatment of Patients with Metastatic K-RAS Wild-Type Carcinoma of the Colon or Rectum that has Progressed on Oxaliplatin and Bevacizumab Given as First-Line Therapy

You are being asked to allow a test to be done on a sample of your tumor that has already been removed. This test is called a K-RAS test because it will look at a gene in your tumor cells known as K-RAS.

The results of the K-RAS test will help determine if you can take part in a clinical trial (a research study called FC-4/CP13-0708). The FC-4/CP13-0708 study is enrolling patients who have colon or rectal cancer that has spread to other parts of their body and has not responded to therapy. The information contained in this consent form is only for the K-RAS testing at the central laboratory. You will be given a separate consent form that will describe the FC-4/CP13-0708 study.

Your study doctor will explain the testing to you. This testing only includes 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.

Who is conducting the K-RAS testing?

The K-RAS testing will be done by Esoterix Clinical Trial Services (Esoterix) on behalf of the National Surgical Adjuvant Breast and Bowel Project (NSABP) Foundation Research Program (FRP). The NSABP FRP is conducting the treatment study. Marquette General Hospital is conducting the trial locally.

Why is this K-RAS testing being done?

You are being asked to allow a test to find out if your tumor cells have a mutation in the K-RAS gene. This means that a change has occurred in the K-RAS gene that makes it function differently in your tumor than it does in normal cells. The results of the K-RAS test will be used to see if you can take part in a treatment study to treat your metastatic colon or rectal cancer.

In some patients with colon or rectal cancer, there is a mutation in the K-RAS gene of the tumor cells. It has been found that one of the drugs that will be used in the FC-4/CP13-0708 study is not effective in treating people whose tumors have a mutation in the K-RAS gene. If there is no mutation, this is known as K-RAS wild-type. If the central testing shows that you do not have a mutation, which means your tumor is K-RAS wild-type, you may be eligible to take part in the FC-4/CP13-0708 treatment study. You will be asked to sign another consent form to take part in the treatment study. If your tumor has the mutation, you will not be able to take part in the treatment study.

The main purpose of the treatment study is to compare the effectiveness of the combination of a standard chemotherapy drug called irinotecan and a drug called cetuximab (also called Erbitux®) with or without a third drug called IMC-A12. Irinotecan is a chemotherapy drug commonly used to treat colon and rectal cancer. Chemotherapy drugs like irinotecan work by killing cancer cells directly. Cetuximab and IMC-A12 are each a type of drug called "targeted therapy." Targeted therapy works by blocking or interfering with a specific part of the cancer cell to slow down or stop the tumor from growing. Cetuximab is considered by the Food and Drug Administration (FDA) to be an "investigational" drug in the FC-4/CP13-0708 study because it is still being researched for use in patients with your stage of cancer who have not yet received the chemotherapy drug irinotecan.

IMC-A12 is also an investigational drug. IMC-A12 targets a different area on the cancer cell. IMC-A12 targets Insulin-like Growth Factor-I Receptor (IGF-IR) to interfere with the growth and survival of the cancer cell.

How many people will have the K-RAS testing done?

About 100 people from different cancer treatment centers will take part in the FC-4/CP13-0708 treatment study. More patients will have the test described here, which is required for all patients who would like to take part in the FC-4/CP13-0708 treatment study.

What will happen if I have the K-RAS testing done?

By signing this consent form, you are agreeing to allow your local hospital to send Esoterix a sample of your tumor that was already removed. Every patient who is considering joining the FC-4/CP13-0708 study will have a tumor sample tested at Esoterix because the K-RAS test is not yet part of regular cancer care for patients with colon or rectal cancer. Testing all of the samples at Esoterix also will make sure that the K-RAS testing was done in the same way for everyone. At Esoterix, the staff will test your tumor sample to find out if your tumor cells have one of several possible mutations in the K-RAS gene. If any tumor sample remains after the K-RAS testing, it will not be used for any other testing and will be destroyed by Esoterix.

Your doctor will be given the results of your K-RAS testing approximately 1 week after Esoterix receives your tumor sample. Your doctor will tell you the results. If the test shows that your tumor cells have a K-RAS mutation, you will not be able to take part in the treatment study. This is because some of the drugs used in the study are not expected to be effective in treating tumors that have a K-RAS mutation.

If the test shows that your tumor is K-RAS wild-type, which means it does not have a mutation in the K-RAS gene, and you meet all other study requirements, you can join the treatment study. You will need to sign another consent form that explains the treatment study.

Can I stop K-RAS testing from being done on my tumor sample?

Yes. You can withdraw permission for testing on your tumor sample. Tell the study doctor immediately if you are thinking about withdrawing permission for K-RAS testing. If you withdraw your permission, you will not be able to join the FC-4/CP13-0708 study. Because the K-RAS testing is being done quickly, depending on when you withdraw permission, testing may have already been done on your tumor sample. It is possible that there may be no remaining tumor to return. Even if the K-RAS testing has been done, and the test showed your tumor cells do not have the mutation in the K-RAS gene, you can choose to not take part in the FC-4/CP13-0708 study.

What risks can I expect from allowing the K-RAS testing?

The only risk from allowing the K-RAS testing is the accidental release of private information about you. Every effort will be made to ensure this does not happen.

Are there benefits to having the K-RAS testing done?

Taking part in the K-RAS testing will not make your health better. Taking part in the treatment study may or may not make your health better. While doctors hope these drugs will be effective in treating metastatic colon and rectal cancer, there is no proof of this yet. We do know that the information from this study will help doctors learn more about these drugs as a treatment for cancer. This information could help future cancer patients.

What other choices do I have if I do not have the K-RAS testing done?

You can proceed with getting treatment that is recommended by your doctor for your metastatic colon or rectal cancer without having the K-RAS testing.

Talk to your doctor about your choices before you decide if you will allow the K-RAS testing to be done as part of this study. If you decide not to have the K-RAS testing as part of this study, you will not be eligible to participate in the FC-4/CP13-0708 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 testing is published or presented at scientific meetings, your name and other personal information will not be used.

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

- the National Surgical Adjuvant Breast and Bowel Project (NSABP) Foundation Research Program (FRP);
- Esoterix Clinical Trial Services, which is the laboratory that will be conducting the K-RAS testing;
- ImClone Systems Incorporated, which is the company providing support for the FC-4/CP13-0708 study;
- International Drug Development Institute (IDDI), which is the company that will analyze the data for the treatment study;
- Chesapeake Research Review, Inc., which is a Research Ethics Review Board that reviews this study;
- the Marquette General Hospital Institutional Review Board (IRB), a local group of people who reviewed and approved the research study to protect your rights.
- government agencies including the U.S. Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP). These agencies may review the research to see that it is being done safely and correctly.

What are the costs of the K-RAS testing?

There will be no charge to you or your insurance company for the collection, shipping, and K-RAS testing of your tumor sample at Esoterix to determine if your tumor cells have the mutation in the K-RAS gene.

You will not be paid for taking part in this testing.

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 are my rights if I allow the K-RAS testing?

Having the K-RAS testing done to determine if you can take part in the treatment study is your choice. You may choose either to have it done or not. If you decide to have the testing done, you do not have to join the treatment study. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Choosing to not have the K-RAS testing done will not affect your medical care. You can still get your medical care from our institution.

Who can answer my questions about the K-RAS testing?

You can talk to your study doctor about any questions or concerns you have about this testing. Contact your study doctor _____ at _____.

For questions about your rights while taking part in this testing, call the Patient Advocate at Marquette General Hospital at 906-225-3183.

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

Signatures

I have been given a copy of all six pages of this form. I have read the consent form or it has been read to me. This information was explained to me and my questions were answered. I agree to have the K-RAS testing.

Date

Patient's signature

Print name of patient

Date

Signature of person
conducting the informed consent discussion

Print name of person
conducting the informed consent discussion