

MARQUETTE GENERAL HEALTH SYSTEM

Regional Medical Center

CONSENT TO PARTICIPATE IN AN INVESTIGATIONAL STUDY

NSABP P-5 Statin Polyp Prevention Trial in Patients with Resected Colon Cancer

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This is a clinical trial, which is a type of research study. You are being asked to take part in this study because you have colon cancer that has been removed by surgery.

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.

Who is conducting the study?

The National Surgical Adjuvant Breast and Bowel Project (NSABP) is conducting this study.

Marquette General Health Systems is conducting this study locally.

Why is this study being done?

This study will look at the effects, good and/or bad, of the drug rosuvastatin (also called Crestor®). Rosuvastatin is a type of drug called a statin. The U.S. Food and Drug Administration (FDA) and Health Canada have approved rosuvastatin for use in lowering cholesterol. Reports of people who take statins to lower cholesterol suggest that statins may also lower the risk of certain cancers developing, including cancers of the colon or rectum (also called colorectal cancer or CRC). Rosuvastatin is considered to be investigational, which means it is still being tested, for use by people who have colon cancer to prevent adenomatous polyps and new CRC. Adenomatous polyps are a type of polyp that is more likely to become a cancer. In this consent form, adenomatous polyps will be referred to simply as "polyps".

- The main purpose of this study is to find out whether or not rosuvastatin is able to prevent colon polyps and CRC from occurring in patients who have already had a colon cancer removed by surgery. People who have had colon cancer have a greater than average risk of developing polyps in the colon and rectum that may become CRC in the future. Prevention of polyps may reduce the risk of a new CRC.
- Another reason for doing this study is to learn about the side effects of rosuvastatin when given to prevent the development of polyps and new CRC.
- This study will also evaluate the benefits of rosuvastatin in certain groups of patients, for example, patients who take daily aspirin and patients with a family history of colon or rectal polyps or CRC.

- This study will help researchers learn about how the study treatment affects your quality of life. Quality of life is your physical and emotional well-being.
- To learn more about your type of cancer, we would like to keep tissue samples from the colon cancer surgery you recently had and from any abnormal polyps or new CRC that are removed while you are in the study. We also would like to collect a blood sample when you join the study. Sample submission will be done only if you agree to the blood and tissue sample collections described at the end of this consent form.

How many people will take part in the study?

About 1740 men and women from different cancer centers will take part in this study.

What will happen if I take part in this study?

Before you begin the study:

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

- Physical exam and medical history
- Family history of CRC
- Colonoscopy (an exam in which your doctor inspects the inside of your colon) if you have not had one within 6 months before joining the study

You will also need to have the following tests that are not part of regular cancer care and **are being done for the purpose of this study**. If you have had some of them recently, they may not have to be repeated.

- Blood tests to check how well your liver and kidneys are working
- Blood test to check lipid (fat) levels (total cholesterol, LDL, HDL, and triglycerides)
- Pregnancy test (if you are a woman of childbearing potential)

During the study:

If the tests and exams show that you can be in the study, and you choose to take part, you will be randomized into one of the two study groups described below. Randomization means that you are put into a group by chance. A computer program will place you into one of two study groups. Neither you nor your doctor can choose which group you will be in. You will have an equal chance of being placed in either group.

Study therapy:

If you are in Group 1: You will take a placebo tablet that looks like the rosuvastatin tablet but does not contain any active drug. You will take 1 tablet every day for 5 years.

If you are in Group 2: You will take 1 rosuvastatin tablet (10 mg) every day for 5 years.

Neither you nor your study doctor will know whether you are taking rosuvastatin or placebo. The use of a placebo is important to make sure we can determine the side effects and benefits of giving rosuvastatin.

For all patients: You can take the rosuvastatin/placebo tablets with or without food. Your study doctor will ask that you keep track of the number of rosuvastatin/placebo tablets that you take. This can be done by writing the number of rosuvastatin/placebo tablets that you take in a diary or on a calendar or other type of record. You will also be asked to return any rosuvastatin/placebo tablets you did not take. Your study doctor or nurse will discuss this with you.

Please tell your study doctor or the study staff if you are taking any drugs other than rosuvastatin/placebo especially any medicines that you are taking to lower your cholesterol or to thin your blood (for example Coumadin®) or for pain (for example Celebrex® or Indocin®). You may have to stop taking some types of medications while you are taking the study drug. Before you stop taking any medications, you should discuss this with the doctor who prescribed the medication for you.

If you take daily aspirin to prevent a heart attack or stroke, you will be able to continue taking the same dose of aspirin. Your study doctor will ask if you are willing to continue taking the same dose of aspirin you are taking now. If you are not taking daily aspirin, your study doctor will ask if you are in agreement with not taking daily aspirin while you are taking the rosuvastatin/placebo.

You should let your study doctor or study staff know if you are regularly taking any over the counter drugs for headache or pain (for example aspirin, ibuprofen [Advil®, Motrin®], or naproxen [Aleve®]), for heartburn (for example, antacids [Maalox® or Mylanta®]), or drugs to lower your cholesterol (for example, niacin). Your study doctor will need to make sure that taking these drugs with rosuvastatin/placebo will not cause problems. Some drugs cannot be used when you take rosuvastatin/placebo. You should also let your study doctor know how much alcohol, including beer, you usually drink.

You should tell anyone who gives you medical care that you are in this research study and that you may be taking rosuvastatin (Crestor®).

Tests and exams during study therapy:

During the 5 years you are taking your study therapy, you will need to have the following tests and exams. They are part of regular cancer care.

- Blood tests at 6 and 12 months and then every year until 5 years after you join the study to check how well your liver is working
- Blood tests every year until 5 years after you join the study to check how well your kidneys are working
- Physical exam every 6 months for 5 years
- Colonoscopy about 1, 3, and 5 years after you join the study. The purpose of the colonoscopy is to make sure cancer has not returned in the colon and to check for polyps in the colon and rectum. If polyps are found, they will be removed during the colonoscopy.

You will need to have a blood test at about 3 to 4 months after you start taking rosuvastatin/placebo to check how well your liver is working. This test is not part of regular cancer care and **is being done for the purpose of this study.**

Tests and exams after you complete your study therapy:

Your study doctor or study staff will contact you about 6 months, 1 year, and 2 years after you complete your study therapy to ask how you are doing.

Quality of life questionnaires:

You may be asked to complete a questionnaire about any symptoms you are having and about your quality of life (your physical and emotional well-being). We want to learn about your view of how your life is affected by the study treatment and its side effects. This quality of life study will collect information from you about how you are feeling physically and emotionally during your study therapy. We also want to learn how well you are able to carry out your day-to-day activities. The questionnaire will take about 15 to 20 minutes of your time to complete. You will be asked to complete this questionnaire before you join the study, at 6 months after you join the study, and at 1, 3, 5, and 7 years after you join the study. If any questions make you feel uncomfortable or you do not wish to answer them, you may skip those questions and not give an answer.

How long will I be in the study?

You will be in the study for 7 years. During that time, you will take the rosuvastatin/placebo for 5 years. After you stop taking the rosuvastatin/placebo, the study doctor or study staff will contact you to ask how you are doing every 12 months through 7 years from the time you joined the study.

Can I stop being in the study?

Yes. You can decide to stop at any time. 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 related to the therapy can be evaluated by your doctor. Another reason to tell your study doctor is to discuss what follow-up care and testing would be most helpful for you.

You can choose to stop in one of two ways:

- You can stop taking rosuvastatin/placebo but still allow the study doctor to report your health status to the NSABP.
- You can stop taking rosuvastatin/placebo and request that no new information about you be reported to the NSABP.

Also, your study doctor may stop you from taking part in this study if he or she believes it is in the best interest of your health, if you do not follow the study rules, or if the study is stopped by the NSABP.

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

You may have side effects while on the study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person. Everyone taking part in the study will be watched carefully for any side effects. You should talk to your study doctor about any side effects that you have while taking part in the study.

Side effects may be mild or very serious. Your health care team may give you medicines to help lessen the side effects. Many side effects go away soon after you stop taking the study therapy. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

Possible

These side effects occur in **about 1% to 5%** of patients taking rosuvastatin (10 mg):

- headache
- muscle pain
- weakness
- nausea
- constipation

Rare but serious

These side effects occur in **less than 1%** of patients taking rosuvastatin (10 mg):

- allergic reaction including rash, itching, and swelling
- blood tests that show changes in liver function. There were no reported cases of severe or permanent liver damage.
- blood tests that show damage to muscles. Rare cases of muscle damage have been reported in patients receiving rosuvastatin. *Myopathy* is a muscle disease in which the muscle fibers do not function, causing muscle weakness, cramping, and/or spasms. *Rhabdomyolysis* is a condition caused by the rapid breakdown of muscle cells. When rhabdomyolysis occurs, the byproducts of the breakdown of muscle cells are released into the bloodstream and may cause damage to the kidneys. This risk can occur at any dose, but is more common at higher doses than those used in this study. Most of the patients who were found to have myopathy and/or rhabdomyolysis had known medical problems that increased their risk, and/or were receiving lipid lowering medicines that were known to cause muscle problems in addition to rosuvastatin. Be sure to let your study doctor know if you are having any unexplained muscle pain, tenderness, or weakness, especially if you do not feel well or have a fever.

Risks related to fertility and pregnancy: You should not become pregnant or father a baby while on this study because rosuvastatin can affect an unborn baby. Men and women must use an effective method of birth control during therapy and for at least 3 months after their last dose of rosuvastatin/placebo. Both male and female patients should ask about counseling and more information about preventing pregnancy. Female patients who feel they might be pregnant, even though they practiced birth control, must notify their study doctor immediately. The study doctor will talk about the appropriate action to be taken. A pregnancy test may be performed. If you are pregnant, you will have to stop taking the rosuvastatin/placebo. Women should not

breastfeed a baby while taking rosuvastatin/placebo and for at least 3 months after their last dose of rosuvastatin/placebo.

What are my responsibilities?

- Keep your study appointments. If you cannot keep an appointment, contact your study doctor or study staff to reschedule as soon as you know that you will miss the appointment.
- Tell your study doctor or study staff about any medications you are taking.
- Take the rosuvastatin/placebo as directed by your study doctor and study staff.
- Do not share the rosuvastatin/placebo with anyone else. Keep the rosuvastatin/placebo out of the reach of children and persons of limited capacity to read or understand.
- The study doctor or study staff will talk to you about any food or medicines that you should not take while on the study.
- Accurately fill out your study diary or calendar.
- Return unused rosuvastatin/placebo as directed by the study doctor or study staff.
- Tell your study doctor or study staff about any side effects, doctor visits, or hospitalization that you may have whether or not you think they are related to the study therapy.
- Tell your study doctor if you have been in a research study in the last 30 days or are in another research study now. While participating in this research study, you should not take part in any other research project without approval from your study doctor. This is to protect you from possible injury arising from such things as extra drawing of blood samples, possible reaction between research drugs, or other hazards.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that rosuvastatin will be useful in cancer prevention, there is no proof of this yet. A possible benefit may be the prevention of colon or rectal polyps that could lead to cancer. We hope the information learned from this study will help patients in the future who are at increased risk for developing polyps of the colon and rectum.

What other treatment options are there?

Your other choices may include:

- Taking part in another study
- Receiving treatment for polyps or colon cancer without being in a study
- Taking over the counter products such as aspirin or calcium, or adding fiber to your diet
- No additional 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.

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

- the NSABP;
- AstraZeneca Pharmaceuticals, (the company that makes the rosuvastatin and placebo);
- your local Institutional Review Board (IRB), a group of people who review the research study to protect your rights; and
- government agencies, including the NCI or its authorized representatives, the FDA, the Office for Human Research Protections (OHRP), and Health Canada. These agencies review the research to see that it is being done safely and correctly.

What are the costs?

Taking part in this study may lead to added costs for you or for your insurance company. 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.

The extra costs are:

Tests that are not part of regular cancer care and are being done for the purpose of this study. These tests (blood tests and a pregnancy test for women of childbearing potential) are described in earlier sections of this consent form.

There is no charge in this study for the following:

- Rosuvastatin and placebo will be provided for this study at no cost to you by AstraZeneca Pharmaceuticals through the National Cancer Institute.
- There will be no cost to you for the collection, shipment, testing, and storage of your blood and tissue samples for research purposes.

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://www.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.

Institutional Funding:

Funds are provided from the study sponsor to Marquette General Hospital on a per patient basis to help with the institution's costs of participating in this study.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, _____ if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him/her at _____.

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 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.

To ensure the safety of those who take part in this study, an independent group of experts called the Data Monitoring Committee (DMC) will be reviewing the data from this research throughout the study. 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. You may be asked to sign another consent form in response to new information.

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.

WHOM DO I CALL IF I HAVE PROBLEMS OR QUESTIONS?

In the event that physical injury occurs as a result of this research, facilities for treatment of injury will be available; however, you will not automatically be provided with reimbursement for medical care or other compensation. For more information concerning the research and research-related risks or injuries, you can notify Dr. _____, or his/her associates, who may be reached by phoning the office at (906) 225-3922. During the evenings, weekends, or holidays you may phone Marquette General Hospital at (906) 228-9440, and request to speak with the oncology physician on call. You can also call the Patient Advocate at Marquette General Hospital at (906) 228-9440, if you have any questions, comments, or concerns about the study or your rights as a research subject.

Tissue and blood sample collection for the NSABP P-5 Study

Optional collection of blood and tissue samples:

The NSABP would like to have samples of your blood collected at one time point. Collection of a blood sample is not required for participation in the P-5 study. If you agree, a blood sample will be collected before beginning rosuvastatin/placebo. The blood sample will be kept and may be used in future research to learn more about cancer and other diseases.

The NSABP would like to keep some of the tissue (tumor and normal colon tissue) that was removed during your colon cancer surgery. If you develop abnormal polyp(s) or a second cancer in the colon or rectum while you are in the study, the NSABP also would like to keep samples of these tissues. If you agree, the tissue samples will be kept and may be used in future research to learn more about cancer and other diseases.

Using the blood and tissue for research: The research that will be done with your blood and tissue samples is not designed to specifically help you. It might help people who have cancer in the future. Reports about research done with your samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your blood and tissue samples will not affect your care.

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

The NSABP will study the samples and may give them to other researchers approved by the NSABP. Any research using your samples must also be approved by an Institutional Review Board (IRB). An IRB is a group of people who review the research to determine if it is being done correctly and safely.

People who do research with your blood and tissue samples may need to know more about your health. While the NSABP may give them reports about your health, they will not give them your name, address, phone number, or any other information that will let the researchers know who you are. Your blood and tissue samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future, but you will not be paid.

If you change your mind after your blood or tissue samples are sent to the NSABP, just *contact your study doctor* and let him or her know that you no longer want the NSABP to use your blood and tissue samples, and they will no longer be used. Otherwise, your blood and tissue samples will be kept until used up or until the NSABP decides to destroy them.

Benefits and risks: The possible benefits of research using your blood and tissue samples include learning more about what causes cancer and how to treat it.

There is a risk of the release of information from your health records. The NSABP will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.

Costs of the sample collections: There will be no cost to you or your insurance company for the collection, shipping, testing, and storage of any of the tissue and blood samples in this study.

Making your choices

Please read each question below and think about your choice. After reading each question, circle “yes” or “no.” If you have questions, please talk to your study doctor or health care team member.

Participation in the optional tissue and blood collections: Remember, no matter what you decide about the ***optional*** collection and use of the tissue and blood samples in this research study, you may still take part in the P-5 study.

1. My blood and tissue samples may be kept by the NSABP for use in future research to learn about, prevent, detect, or treat cancer.

YES

NO

2. My blood and tissue samples may be used for research about other health problems (for example, causes of heart disease, osteoporosis, diabetes).

YES

NO

Contact in the future for other research: No matter what you decide, you may still take part in the P-5 study.

3. My study doctor (or someone he or she chooses) may contact me in the future to ask me to take part in more research.

YES

NO

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/>

You will receive 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 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 take part in this research study.

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