

Northwest Community Clinical Oncology Program (NWCCOP)
MultiCare Health Research Institute
315 Martin Luther King Jr. Way
Tacoma, WA 98405
Phone: (253) 403-1461 Fax: (253) 403-1615
Sponsored and Funded by the National Cancer Institute

CONSENT FORM

CIRB S0500: A Randomized Phase III Trial to Test the Strategy of Changing Therapy Versus Maintaining Therapy for Metastatic Breast Cancer Patients Who Have Elevated Circulating Tumor Cell Levels at First Follow-up Assessment.

INVESTIGATORS:

Lauren K. Colman, MD; Chris Chen, MD; Xinda Wang, MD; Daniel Moore, MD;
Troy Wadsworth, MD; Katharine Barford, MD; Umesh Chitale, MD; Yoshio Inoue, MD;
315 MLK Jr. Way, 4th Floor, Tacoma, WA 98405 (253) 403-1677.

Robert McCroskey, MD; Sibel Blau, MD; Andrea Rose, MD; Ronald Goldberg, MD;
400-15th Avenue SE, Puyallup, WA 98372 (253) 841-4296.

Frank Senecal, MD; Thomas Baker, MD; Lorrin Yee, MD; Moacyr Oliveira, MD;
1624 South I Street, Tacoma, WA 98405 (253) 383-3366.

Paul Robertson, MD; Steven Gorton, MD; James Lechner, MD; Harry Griffith, MD;
Xingwei Sui, MD; Hui Wang, MD; Michael Harris, MD; Maury Blitman, MD;
4525 Third Ave. SE, Suite 200, Lacey, WA 98503 (360) 754-3934.

Dustan Osborn, MD; Robert Witham, MD; Nicole Grous, MD; Min Kang, MD; 3920 Capital
Mall Drive SW, Suite 100, Olympia, WA 98502 360-753-4700 and 121 North Division Street,
Suite 100, Auburn, WA 98002 (253) 887-9333.

John Rieke, MD; Suraj Singh, MD; Carolyn Rutter, MD; Rizwan Nurani, MD;
315 Martin Luther King Jr. Way, 1st Floor, Tacoma, WA 98405 (253) 403-4994.

Michael Liao, MD, 400 -15th Ave SE, Puyallup, WA 98372 (253) 697-4829

Oliver Batson, MD; James Congdon, DO; Mark Coughenour, MD; Peter Y.Z. Jiang, MD;
Elie Saikaly, MD; Luke Walker, MD; Xiaowen Wang, MD; Steve Adam, MD;
B. Sharon Cole, MD; Darren Little, MD; William Wisbeck, MD; Thomas Smith, MD;
1717 13th Street, Third Floor, Research, Everett, WA 98201 (425) 297-5532

James Pelton, MD; William Reece, MD; Tanya Wahl, MD; Kathryn Crossland, MD;
11135 116th Avenue NE #230, 3rd Floor, Bellevue, WA 98201 (425) 454-2148

Sushma Pant, MD; Thomas Drake, MD; Katrina Popham, MD; Gerardo Midence, MD;
Binay Shah, MD; 1250 Idaho Street, Lewiston, Idaho 83501 (208) 743-7427

CIRB S0500: A Randomized Phase III Trial to Test the Strategy of Changing Therapy Versus Maintaining Therapy for Metastatic Breast Cancer Patients Who Have Elevated Circulating Tumor Cell Levels at First Follow-up Assessment.

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 study because you are a woman with breast cancer that has spread to other parts of your body.

Why is this study being done?

The purpose of this experimental study is to find out if the CellSearch® blood test, which identifies tumor cells in the blood, can predict survival outcome in patients with metastatic breast cancer. These tumor cells are called circulating tumor cells (CTCs). The CellSearch® blood test may allow doctors to tell if your current chemotherapy is not working before you show signs that your cancer is getting worse. This is based upon a prior study that showed that most women with high numbers of CTCs had worsening of their breast cancer within 1-3 months. In this prior study, increase in the size of a tumor or spread of cancer in the body was determined by standard clinical tests such as physical examinations, x-rays and scans, and not by the CellSearch® blood test. This study will test whether switching to another form of treatment based upon the results of the CellSearch® blood test helps people live longer. In addition, this study will be used to further confirm results of the prior study, which showed that patients with < 5 CTCs before they begin treatment are more likely to live longer than those with ≥ 5 CTCs.

How many people will take part in the study?

About 500 women will take part in this study.

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

Before you begin the study ...

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
- Weight and Performance Status
- Disease Assessment including CT scans, MRI scans, bone scan, PET scans and/or x-rays. Routine laboratory blood tests (to measure your kidney and liver function)
- Pregnancy test (if determined to be appropriate by your treating physician)

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. They are part of regular cancer care.

- Medical history and physical exam
- Weight and performance status
- Disease assessment including CT scans, MRI scans, bone scans, PET scans and/or x-rays.
- Routine laboratory blood tests (to measure your kidney and liver function).

The timing of the exams and tests above will be determined by the treatment that is given to you by your study doctor. The dates of these clinical visits will be discussed with you by your study doctor.

You will need these tests and procedures that are either being tested in this study or being done to see how the study is affecting your body.

- Measurement of circulating tumor cells (CTCs) in the blood (**all patients**): about 2-3 teaspoons of blood will be collected for this test. Blood will be collected before treatment begins. All patients will be told the results of this first CTC test.

Patients with < 5 CTCs will continue to receive their regular treatment without change, and no further blood draws will be performed. These patients will be followed to find out how long they respond to treatment and how long they live. This group of women with < 5 CTC is called **Arm A**.

- Repeat measurements of circulating tumor cells (CTCs) in the blood (**only for patients with $CTC \geq 5$ at the time of initial screening**): about 2-3 teaspoons of blood will be collected for these tests. Blood will be collected at Day 22, Day 50 or 57, Day 85, Day 169, Day 253, and at the time your cancer becomes worse or when the doctor decides to discontinue this protocol strategy.

Except for the initial blood test, neither the patient nor the doctor will be given the results of any of the CTC blood tests.

- The CTC blood drawing procedure requires that a separate tube of blood be drawn first to prevent contamination with skin cells. This separate tube of blood (about 10 mL or 2 - 3 teaspoons) will be submitted to a special laboratory and used to measure the breast cancer tumor markers CA 15-3 and CEA. The results of these tests will be compared to the results of the CTC testing. In addition, we will ask your permission to save any leftover serum from this blood sample for future research. This will be discussed in more detail below.

Your study doctor will choose a treatment program that is believed to be best for you. For women with ≥ 5 CTCs at baseline the CellSearch® test will be performed 3 weeks after your first dose of chemotherapy and will be used to determine if you are at higher risk of having your cancer worsen on this current therapy. You and your study doctor will not be told the results of the CellSearch® blood test.

- **Approximately half of the women on this study will have low numbers of CTCs (< 5 CTCs) after completing one cycle of chemotherapy.** These women are not believed to be at higher risk. These women will continue on the same chemotherapy. They will continue to be followed on study until the doctor finds evidence that the breast cancer has become worse. These women are in the "maintain current therapy" group or Arm B.
- **Approximately half of the women on this study will have elevated numbers of CTCs (≥ 5 CTCs) after completing one cycle of chemotherapy. These women will be randomized to either maintain current therapy or switch therapy.** Randomization means that you are put into a group by chance. 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 an equal chance of being placed in any group.

Women randomized to the "maintain current therapy" group or Arm C1 will remain on the same therapy. The doctor will monitor the cancer using standard methods including physical exam, CT scans, bone scans, and x-rays. These patients will continue to be followed on the study until the doctor finds evidence that the breast cancer has become worse.

Women randomized to the "switch therapy" group or Arm C2 will change chemotherapy to a different drug or combination of drugs. The selection of the new chemotherapy will be made by the patients own doctor based upon what they believe is best. The study does not specify what therapy the doctor should choose. The doctor will monitor the cancer using standard methods including physical exam, CT scans, bone scans, and x-rays. These patients will continue to be followed on the study until the doctor finds evidence that the breast cancer has become worse.

If your doctor is told that you are to "maintain current therapy", neither you nor your doctor will know whether you are in the Arm B group or in the Arm C1 group.

Only chemotherapy will be changed based on the CTC results. If your study doctor is also prescribing a hormonal therapy or a biological therapy at the same time as chemotherapy, then these hormonal or biological therapies will continue at the discretion of you and your doctor regardless of the CTC level.

How long will I be in the study?

You will be followed with collection of blood specimens and information about your treatment and progress until your doctor finds evidence your cancer has worsened. This will be different for each patient and may vary from weeks to months to years. After your cancer worsens we will no longer collect the blood specimens. Further follow-up and treatment decisions will be made between you and your doctor. We would like to keep track of your medical condition for a minimum of 5 years after you start the study. Every 6 months your doctor will send us an update on your condition.

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. 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 that you can discuss what follow-up 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 study?

It is possible that you will not have any benefit in the control of your cancer from participation in this trial. This study is being performed to determine whether changing therapy based on CTC levels improves outcome.

There is also a chance that participation in this trial will be detrimental to the treatment of your cancer. Not all patients with elevated CTCs after one cycle of chemotherapy have rapid worsening of their cancer. As a result some of the women who are randomized to switch to alternative therapy (about 15-20% of the women randomized to switch therapy) will be switched off chemotherapy that was working.

After you complete this study, your doctor will have the option of using the original chemotherapy drug(s) again.

The chemotherapy you receive will be determined by your doctor, not by the study. To find out more about the risks of your own chemotherapy ask your doctor.

One risk is the release of information from your health records. The Southwest Oncology Group will protect your records so that your name, address, and telephone number will be kept private. The chance that this information will be given to someone else is very small. This is discussed in greater detail below in the section called "Will my medical information be kept private?"

For more information about any other risks, ask your study doctor.

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 the CellSearch® blood test will improve the effectiveness of cancer treatment compared to the usual methods of monitoring of breast cancer, there is no proof of this yet. We do know that the information from this study will help doctors learn more about the CellSearch® blood test in monitoring cancer. This information could help future cancer patients.

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

Your other choices may include:

- Getting treatment or care for your cancer 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.

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

- Local Institutional Review Board (IRB)
- The National Cancer Institute (NCI)
- The Food and Drug Administration (FDA), involved in reviewing and inspecting the data and results of this clinical study, and in keeping research safe for participants in this study.
- The Southwest Oncology Group
- The Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.
- Veridex, LLC: manufacturer of the CellSearch® blood test and sponsor of this investigation.
- Veridex Pharma Laboratory Services: The laboratory that will be performing CTC enumeration.
- Data Safety and Monitoring Board (DSMB), an independent group of experts will be reviewing the data from this research throughout the study.

What are the costs of taking part in this study?

The cost of the CellSearch® CTC, CA 15-3, and CEA blood tests will be paid for by the study. Neither you nor your insurance company will be billed for these blood tests.

The treatments received during this clinical trial are not experimental. They will be determined by your doctor and are considered standard of care. The costs of these treatments are not paid for by the study, and you and/or your health plan/ insurance company will need to pay for all of the costs of treating your cancer in this study. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

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 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 doctor in person or call him/her at the number on the cover page.

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.

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 study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor at the number on the cover page.

For questions about your rights while taking part in this study, call the MultiCare Health System Institutional Review Board (a group of people who review the research to protect your rights) at 253-403-3877.

***You may also call the Operations Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only).**

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.

Future Contact

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

Yes No

Additionally, we would also like to bank any leftover serum specimens for future, unspecified scientific testing. An additional consent form and information is attached for this purpose.

Consent Form for Use of Specimens for Research

About Using Specimens for Research

We would like to keep leftover serum specimens for future research. If you agree, these specimens will be kept and may be used in research to learn more about cancer and other diseases. Please read the information sheet called "How are Specimens Used for Research" to learn more about specimen research.

The research that may be done with your specimens are 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 specimens 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.

Your specimens will be kept at:

SWOG Solid Tumor Tissue Bank
University of Colorado HSC at Fitzsimons
Department of Pathology
RC-1 South, Room L18-5400A
12801 East 17th Avenue
Aurora, CO 80045
Phone: 303/724-3086

Things to Think About

The choice to let us keep specimens 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 specimens 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 specimens, then any specimens that remain will no longer be used for research.

In the future, people who do research may need to know more about your health. While the Southwest Oncology Group 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 specimens are used for genetic research (about diseases that are passed on in families). Even if your specimens are used for this kind of research, the results will not be put in your health records.

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

Benefits

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

Risks

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 253-403-3877.

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

- 1. My specimens may be kept for use in research to learn about, prevent, treat or cure cancer.**

Yes No

- 2. My specimens may be kept for use in research about other health problems (for example: diabetes, Alzheimer's disease, or heart disease).**

Yes No

3. Someone may contact me in the future to ask me to allow other uses of my specimens.

Yes No

If you decide to withdraw your specimens from a Southwest Oncology Group Specimen Repository in the future, a written withdrawal of consent should be submitted through your treating physician to the Southwest Oncology Group Operations Office. If you decide to withdraw your permission from the banking part of the study, then any remaining blood specimens will be destroyed.

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

Signature

I have been given a copy of all 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.

Patient's name (printed or typed)

Patient's Signature Date

Physician name (printed or typed)

Physician Signature Date

Signature of person conducting the
Informed consent discussion

Date

Authorization to Use or Disclose (Release) Identifiable Health Information For Research

1. What is the purpose of this form?

The **Southwest Oncology Group** is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your identifiable health information, you must sign and date this form to give them your permission.

2. What health information do the researchers want to use?

The researchers want to abstract and use the portions of your medical record that they will need for their research. If you enter a Southwest Oncology Group research study, information that will be used and/or released may include your complete medical record, and in particular, the following:

- the history and diagnosis of your disease
- specific information about treatments you received
- information about other medical conditions that may affect your treatment
- medical data, including laboratory test results, tumor measurements, CT scans, MRIs, X-rays, photographs of radiation therapy target areas, and pathology results
- information on side effects (adverse events) you may experience, and how these were treated
- long-term information about your general health status and the status of your disease
- tissue and/or blood samples, associated data related to the analysis of the samples

You may request a blank copy of the Southwest Oncology Group data forms from the Northwest Community Clinical Oncology Program (NWCCOP) to learn what information will be shared.

3. Why do the researchers want my health information?

The Northwest CCOP will collect your health information and share it with the Southwest Oncology Group if you enter a Cooperative Group research study, or to evaluate your eligibility for a study. The Southwest Oncology Group researchers will use your information for the following cancer research study.

S0500, "A Randomized Phase III Trial to Test the Strategy of Changing Therapy Versus Maintaining Therapy for Metastatic Breast Cancer Patients who Have Elevated Circulating Tumor Cell Levels at First Follow-Up Assessment"

The purpose of this experimental study is to find out if the CellSearch™ blood test, which identifies tumor cells in the blood, can predict survival outcome in patients with metastatic breast cancer. These tumor cells are called circulating tumor cells (CTCs). The CellSearch™ blood test may allow doctors to tell if your current chemotherapy is not working before you show signs

that your cancer is getting worse. This is based upon a prior study that showed that most women with high numbers of CTCs had their breast cancer getting worse within 1-3 months. In this prior study, increase in the size of a tumor or spread of cancer in the body was determined by standard clinical tests such as physical examinations, x-rays and scans, and not by the CellSearch™ blood test. This study will test whether switching to another form of treatment based upon the results of the CellSearch™ blood test helps people live longer. In addition, this study will be used to further confirm results of the prior study, which showed that patients with <5 CTCs live longer than those with ≥ 5 CTCs.

4. *Who will be able to use my health information?*

The Northwest CCOP will use your health information for research. As part of this research, they may give your information to the following Groups taking part in the research. The Northwest CCOP may also permit staff from these Groups to review your original records as required by law for audit purposes.

- the Southwest Oncology Group
- the Northwest CCOP
- the Cancer Trials Support Unit (CTSUS), a research group sponsored by the National Cancer Institute to provide greater access to cancer trials
- public health agencies and other government agencies (including non-U.S.) as authorized or required by law
- other people or organizations assisting with Southwest Oncology Group research efforts.
- central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed above.

5. *How will information about me be kept private?*

The Southwest Oncology Group will keep all identifiable health information confidential to the extent possible, even though they and other federal research groups are not subject to the same federal privacy laws governing clinical centers. The Southwest Oncology Group will not release identifiable health information about you to others except as authorized by this form, or required by law. If your identifiable health information must be shared with other organizations, the privacy laws that govern those organizations would apply.

6. *What happens if I do not sign this authorization form?*

If you do not sign this authorization form, you will not be able to take part in a research study for which you are being considered.

7. *If I sign this form, will I automatically be entered into the research study?*

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a separate research consent form.

8. What happens if I want to withdraw my authorization?

You can change your mind at any time and withdraw this authorization. This request for withdrawal must be made in writing. Beginning on the date you withdraw your authorization, no new identifiable health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your authorization, you will be removed from the research study at that time.

To withdraw your authorization, please contact the person below. She will make sure your written request to withdraw your authorization is processed correctly.

Karyn Hart, RHIT, CCRP
Program Coordinator
Northwest CCOP
315 Martin Luther King Jr., Way
Tacoma, WA 98405
(253) 403-1461

9. How long will this authorization last?

If you agree by signing this form that researchers can use your identifiable health information, this authorization has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding my identifiable health information?

You have the right to refuse to sign this authorization form. You have the right to review and/or copy records of your health information kept by the Northwest CCOP. You do not have the right to review and/or copy records kept by the Southwest Oncology Group or other researchers associated with the research study.

Signature

I agree that my personal health information may be used for the research purposes described in this form.

Signature of Patient
or Patient's Legal Representative: _____ Date: _____

Printed Name of Legal Representative (if any): _____

Representative's Authority to Act for Patient: _____

Signature of Person Obtaining Permission: _____ Date: _____

Printed Name of Person Obtaining Permission: _____