COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

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PRE-STUDY CONSENT FORM

Study Title: *A Phase II Study with Orteronel as Monotherapy in Patients with Metastatic Breast Cancer (MBC) that Expresses the Androgen Receptor (AR)*

Principal Investigator: *Gina Chung, MD*
Principal Investigator's Phone Number: *203-785-6197*
24-Hour Phone Number: *203-785-4191*
Principal Investigator's Mailing Address: *333 Cedar Street, New Haven, CT 06520*
Funding Source: *SCRI Development Innovations, LLC*

Invitation to Participate and Description of Project

You are invited to take part in a research study. The research study is called "*A Phase II Study with Orteronel as Monotherapy in Patients with Metastatic Breast Cancer (MBC) that Expresses the Androgen Receptor (AR)"*. The research study is designed to look at anti-androgen drugs and their effect on breast cancer. You have been invited to take part because you have estrogen-receptor (ER) or progesterone receptor (PR)-positive breast cancer or "triple negative" breast cancer (negative for ER, PR, and HER2.

You are being asked to agree to provide a sample of your tumor tissue from a primary biopsy or from tissue where the cancer has spread (metastases). This will be used to see if you are eligible to take part in the main part of this clinical study. The study will assess how well a new cancer treatment (orteronel) works against breast cancer.

A condition of entry into the main study is that each subject's tumor tissue must have a certain concentration of androgen receptors on their cell membranes (≥10%). Because of this, before you can have tests to enter into the main study, you must agree to give a previous tissue sample to test for the presence of androgen receptors in your cancer. The presence of androgen receptors is thought to be necessary for the orteronel to work.

If your androgen receptors level is found to be suitable, you may decide to continue into the main study. If you do, the main study will also be discussed with you. A full informed consent form for the main study will be signed at that time. If your androgen receptors level is not suitable, your study doctor will discuss other treatment options with you.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: the purpose and nature of the research study, the procedures that will be performed, the risks of the procedures, possible benefits, possible alternatives, your rights as a participant and other information about the research study. You should take whatever time you need to discuss the research study with your physician and family. The decision to participate or not is yours. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign and date where indicated on this form.

If you choose to participate, you will be told of any significant new findings that develop during the course of your participation in this study that may affect your willingness to continue to participate.

The research study is being sponsored by SCRI Development Innovations, LLC (SCRI). SCRI Innovations is called the Sponsor and Yale University is being paid by SCRI Innovations to conduct this research study. Dr. Gina Chung is the principal investigator of this study at Yale Cancer Center.

Purpose

The purpose of this study is to test a new anti-androgen drug, Orteronel, as treatment for subjects with metastatic breast cancer. Subjects will be eligible only if androgen receptors are present on their tumor cells (tumor specimens from previous biopsies will be tested).

The study drug that will be used in this research study, Orteronel, is investigational drug. This means it has not been approved for use by the United States Food and Drug Administration (FDA) in any type of cancer. Orteronel has already been tested, however, in at least 1000 healthy volunteers and cancer patients. It is expected to suppress androgen levels in both the circulation and in relevant hormone-dependent cancers. Approximately 50% of breast cancers require the presence of estrogen (the major female hormone) to grow, and the anti-estrogen drugs block access of estrogen to the cancer cells. Breast cancers likely to respond to anti-estrogen therapy have estrogen “receptors” on the surface of the cancer cells – measurement of the estrogen receptors predicts whether anti-estrogen drugs should be used.

Some breast cancers also have androgen (male hormone) "receptors" on the cancer cell surface. Although the level of androgens in females is very low, there is evidence that even very low levels can stimulate cancer growth when androgen receptors are present. Recently, potent anti-androgen drugs have proven effective and well tolerated in the treatment of prostate cancer (another cancer that depends on the presence of hormones to grow), and some of these new anti-androgens are being tested in patients with breast cancer.

It is expected that approximately 86 men and women with advanced breast cancer will participate in this study (6 in the lead-in phase and 80 in the study treatment phase) at 15 sites around the United States. At Yale Cancer Center, it is expected that approximately 36 subjects will be tested for the presence of androgen receptors in their tumor and approximately 30 subjects will be enrolled.

Study Procedures

If you choose to take part in this study, your study doctor will ask for some basic details about you. These include things such as date of birth and race. You must be aged 18 years and older. He or she will also ask about previous treatments that you have had for your cancer. If you decide to take part, you will sign this form, and we will collect tumor tissue from a previous primary biopsy or from tissue where the cancer has spread to test your androgen receptor level.

Your tissue samples will be tested to determine your androgen receptor level. This testing will be performed by a laboratory chosen by SCRI Innovations. If your tissue has the required level of androgen receptors you will have tests to see if you can enroll in the main study. For those that do enter the main study, some of the tissue donated for this pre-study testing will be set aside for future exploratory testing that may help your doctors understand the nature of your disease.

Potential Risks, Side Effects, Discomforts and Inconveniences

You will be donating tissue samples that have already been taken. There are no side effects, risks, or discomforts associated with this pre-study testing.

For more information about risks and side effects, ask the researcher or contact their office at 203-785-6197.

Benefits

There is no direct benefit to you in taking part in this testing. However, following this initial testing, you may be able to take part in the main study.

If your androgen receptor level is found to be 10% or greater, you will be invited to take part in the main study. The possible benefits to you of taking part in the study are that orteronel may be an effective treatment for your cancer. However, this cannot be guaranteed. You may not experience any direct health benefits during or following completion of the study. However, your participation will provide information about the study drug and your type of cancer that may benefit others. The information we get from this study may help us to treat future subjects with breast cancer that has spread.

Economic Considerations

You will not be paid for taking part in this study. The collection of your tissue is being done as part of participation in the research. There will be no charge to you or your insurance provider.

You or your insurance provider will be charged for continuing medical care and/or hospitalization that are not a part of the research study.

Treatment Alternatives

You do not have to participate in this study. Other investigational treatments, standard anti-cancer therapies, or anti-cancer drugs may be available for you. You may choose not to have any anti-cancer therapy. Talk to your doctor about your choices before you decide if you will take part in this study.

Confidentiality and Authorization to collect, use and disclose Protected Health Information

For purposes of this study, Yale University, Yale-New Haven Hospital, and Dr. Gina Chung will use medical information collected or created as part of the study, such as medical records and test results, which identifies you by name or in another way. Your consent to participate in the study means you agree that Yale University, Yale-New Haven Hospital, and Dr. Gina Chung may obtain your medical information that they request for study purposes from your physicians and your other health care providers from the past or during your participation in the study.

The protected health information that will be collected in this study includes demographics, medical history, physical examinations, routine lab tests, review of adverse events and medications you take (past and present), vital signs, diagnostic tests such as MRI scans, response assessments

such as CT scans, ECHOs or MUGAs, pregnancy tests, blood samples for research purposes only, survival follow-up information and records about any study drug(s) that you received.

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases such as HIV or hepatitis. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the study staff will get information that identifies you and your protected health information. This may include information that might directly identify you, such as your name, date of birth, and medical record number**.** This information will be de-identified prior to providing it to the sponsor, meaning we will replace your identifying information with a code that does not directly identify you. The study doctor will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the Principal Investigator or selected members of the study team. Any information that can identify you will remain confidential.

The records for this trial will be stored in locked cabinets and/or offices and password protected computers. The study team will only give this coded information to others to carry out this research study or to sponsor representatives to comply with federal laws and regulations. It is anticipated that records containing the information that links you to your coded information will be maintained indefinitely, as there are no plans at this time to destroy these records at the end of the study.

Information about your study participation will be entered into your Electronic Medical Record (EMR). Once placed in your EMR, these results are accessible to all of your providers who participate in the EMR system. Information within your EMR may also be shared with others who are appropriate to have access to your EMR (e.g., health insurance company, disability provider.)

Information about you and your health which might identify you may be used by or given to:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University and the Human Investigation Committee (the committee or Institutional Review Board that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.

- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments

Those providers who are participants in the Electronic Medical Record (EMR) system

- The study doctor, Dr. Gina Chung, and the Yale study team
- The U.S. Food and Drug Administration (FDA). This is done so that the FDA can review information about the new drug product involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor, SCRI Innovations, the manufacturer of study drug, Millennium Pharmaceuticals Inc., and/ or their representatives
- Drug regulatory agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes. If you do not authorize the use of your medical record information, you will not be allowed to participate in this research study. If you cancel your authorization during the study, you will be removed from the study. Your authorization for use and disclosure of your medical record information will continue indefinitely.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at Yale School of Medicine and Yale-New Haven Hospital is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Authorized representatives of the Food and Drug Administration (FDA**)** and the manufacturer of the study drug being tested, Millennium Pharmaceuticals, Inc., may need to review records

of individual subjects. As a result, they may see your name, but they are bound by rules of confidentiality not to reveal your identity to others.

The sponsor will see the research information we collect about you when they come to Yale to monitor the conduct of this research study. The "Sponsor" includes any persons that work for or are hired by the sponsor to conduct research activities related to this study. For this study the sponsor is SCRI Innovations. Yale researchers will also send the sponsor your health information during the study or at the end of the study. When Yale researchers send information about you to the sponsor, they will not send information that directly identifies you such as your name.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. However, you will not be allowed to look at or copy your study related information until after the research is completed.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

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.

Voluntary Participation and Withdrawal

Participation in this study is voluntary. You are free to choose not to take part in this research study. Refusing to take part in this research study will not lead to penalty or loss of benefits to which you are otherwise entitled. Your health care outside the study and the payment for your health care will not be affected if you do not agree to participate. However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study. You do not give up any of your legal rights by signing this consent form.

Withdrawing From the Study:
If you decide to participate in this research study, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. They will make sure that proper procedures are followed and a final visit is made for your safety. This will cancel any future research study appointments.

The researchers may withdraw you from participating in the research if necessary. This may be done if it is in your best interest, you do not later consent to any future changes that may be made in the study plan, or for any other reason.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital.

If you fail to give your consent by not signing this document, or if you cancel your consent later, then you will not be eligible to participate in this study and will not receive any treatment provided as part of the study. Unless and until you do cancel the consent, it will remain valid and effective.

Withdrawing Your Authorization to Use and Disclose Your Health Information:
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by telling the study staff or by sending written notice to the study doctor, Dr. Gina Chung at the address listed on page one of this form. If you withdraw your permission, you will not be able to stay in this study.

Any medical record information already recorded as a result of your participation in this research study may continue to be used and disclosed by the study doctor for the purposes outlined above. If an unwanted effect of the study drug (adverse event) occurs, your entire medical record may need to be reviewed. Any data already collected for this research study and any new data about the adverse event will be sent to the study sponsor.

When you withdraw your permission, 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 until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project as described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use and give out information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to participate in this research.

Study Participant (print name)	Signature	Date
Person obtaining consent (print name)	Signature	Date
Person obtaining consent (print name) – only if applicable, otherwise blank	Signature	Date
Interpreter/ Witness (print name) – only if applicable, otherwise blank	Signature	Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at (203) 432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator, Dr. Gina Chung at 203-785-6197. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.