COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL/SMILOW CANCER HOSPITAL CARE CENTERS/SAINT FRANCIS HOSPITAL

***BRCA* mutation testing for patients with unknown *BRCA* mutation status for participation in a study testing the drug olaparib with placebo in early breast cancer**

Study Title: A Randomised, Double-Blind, Parallel Group, Placebo-Controlled Multi-Centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients with Germline BRCA1/2 Mutations and High Risk HER2 Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy

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What is the usual approach to my breast cancer?

You have been diagnosed with a type of breast cancer that is HER2-negative and is not sensitive to hormone treatment **or** breast cancer that is HER2-negative and is sensitive to hormone treatment, and your doctor thinks that you should have genetic testing for a *BRCA* mutation. People who are not in a study have genetic testing if their doctor thinks it should be done; others do not have genetic testing.

What are my other choices if I do not have the *BRCA* testing?

If you decide not to have the *BRCA* testing, you have another choice:

- you may choose to take part in a different study, if one is available

Why is this *BRCA* testing being done?

BRCA1/2 testing is being done to see if you have a mutation in your DNA. A mutation is a change in your DNA. If you have this mutation, you may be eligible to participate in a clinical trial that looks at how people with this mutation respond to a study drug after the usual treatment for breast cancer.

We do not know how many people will agree to take part in this *BRCA* testing. About 1500 people worldwide will take part in the B-55/6-13 treatment study.

What will happen if I have *BRCA* testing done?

You will only have this blood test done if your doctor thinks that you should have genetic testing. Your doctor will explain the local procedures before having a genetic test which should include genetic counseling where available, to help you understand what this result could mean for you or your blood relatives, such as your siblings and children. You should discuss with your doctor how hereditary cancer risk is inherited. Siblings and children of an

individual with a *BRCA* mutation are at 50% risk of also having the mutation. Individuals who have inherited the mutation are at an increased lifetime risk of developing breast and ovarian cancer. Individuals who have not inherited the mutation have the same risk of developing breast and ovarian cancer as the general population. The *BRCA* test looks only at the *BRCA1* and *BRCA2* genes. There are other genes, known and unknown, associated with hereditary breast and ovarian cancer for which the *BRCA* test does not test. By signing this consent form, you are agreeing to have two blood samples (about 4 teaspoons) collected. One sample will be sent to Myriad, a company that does *BRCA* testing. At Myriad, one sample of your blood will be tested to find out if you have a *BRCA* mutation. Every person who is considering joining the B-55/6-13 study will have a blood sample tested at Myriad. Testing all of the samples at Myriad will also make sure that the *BRCA* testing was done in the same way for everyone. Blood remaining after the *BRCA* testing will be stored at Myriad and used by Myriad (and any other companies with whom Myriad decides to work) for future research purposes of the B-55/6-13 study including exploratory testing and to help develop tests, which may be used in the future to assess the *BRCA* status of other patients. The second sample will also be used by AstraZeneca (and any other companies with whom AstraZeneca decides to work), for the future research purposes of the B-55/6-13 study as well as to also to help develop tests, which may be used in the future to assess the *BRCA* status of other patients and to assess the status of other genes known or predicted to have a role in breast cancer. Even if your test result shows that you do not have a specific type of mutation and that you cannot take part in the treatment study, your second sample will still be used for the future research purposes of the B-55/6-13 study.

Your study doctor may be asked to provide additional information such as your age, gender, race, ethnicity, and previous treatment for your breast cancer.

Your doctor will be given the results of your *BRCA* testing within about 2 weeks after Myriad receives your blood sample. If the test shows that you have a *BRCA* mutation, and you meet all other study requirements, you can join the B-55/6-13 study. You will need to sign another consent form that explains the B-55/6-13 treatment study. If the test shows that you do not have a *BRCA* mutation, you will not be able to take part in the B-55/6-13 study.

CAUTION – Please be aware that the test that will be used in this study, to determine if you have a mutation in *BRCA1* or *BRCA2*, is an experimental test (Investigational Device) and is limited by Federal (or United States) law to experimental (investigational) use. Experimental means that the test is not approved by the U.S. Food and Drug Administration (FDA) and is still being tested in research studies. If the result confirms that your *BRCA1* or *BRCA2* gene is mutated, you may be provided with some additional cancer risk information (this information has not been reviewed or approved by the Food and Drug Administration [FDA] and does not form part of the research study).

How long will I be in this study?

Your samples will be kept by AstraZeneca and their partners and Myriad and until they are used up or this study is over and the samples are destroyed.

What possible risks can I expect from allowing *BRCA* testing?

If you choose to have the *BRCA* testing:

- There is a risk someone could get access to the personal information in your medical records or other information researchers have kept about you.
- There is a risk that someone could trace the information in a central database back to you. Even without your name and 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. In some cases, this information could be used to make it harder for you to get or keep a job. There are laws against misuse of genetic information, but they may not give full protection. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.
- There can also be a risk in finding out new genetic information about you. New health information about inherited traits that might affect you or your blood relatives could be found during a study.
- The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
- There may also be risks we do not know at this time.

There are three major risks associated with the experimental *BRCA* test

- Risk of a false-positive test result

  A false positive result is when the results of the test show that you have a *BRCA* mutation when in fact a mutation is not there. Measures have been put in place to make sure that test results are of high quality and are accurate. Patients included on the study based on an incorrect test result would be given study treatment but are less likely to respond to this treatment.

- Risk of a false-negative test result

  A false negative result is when the results of the test show that you do not have a *BRCA* mutation when in fact a mutation is there. Measures have been put in place to make sure that test results are of high quality and are accurate. Patients with a false negative result would not be included on the study and would not receive study treatment. Your family doctor or the study doctor can explain the other treatment options that may be available.

- Risk of a delayed test result

  If test results are delayed for any reason, it is possible that a patient may choose not to wait for results and may decide not to take part in the study but choose to be treated with another available treatment. If this is the case, the patient may be denied access to study treatment. Measures have been put in place to make sure that the risk of a delay to test results is low.

What possible benefits can I expect from taking part in this study?

There is no direct benefit to you in taking part in this screening process other than finding out if you have a *BRCA* mutation. However, depending on the test result, you may be eligible to participate in the B-55/6-13 study.

Can I stop *BRCA* testing on my blood sample?

Yes. You can withdraw permission for testing on your blood sample. Tell the study doctor immediately if you are thinking about withdrawing permission for *BRCA* testing. If you withdraw your permission for *BRCA* testing, you will not be able to join the B-55/6-13 treatment study. Depending on when you withdraw permission, testing may have already been done on your blood sample, and it is possible that there may be no remaining blood to destroy. If you are thinking about withdrawing permission for the use of your sample to develop tests which may be used in the future to assess the *BRCA* status of patients and for the use of your samples to assess the status of other genes known or predicted to have a role in breast cancer, tell the study doctor. Any remaining blood sample will be destroyed. If you withdraw permission for developing tests, you may still take part in the B-55/6-13 study.

Even if the *BRCA* testing has been done, and the test showed you have a *BRCA* mutation, you can choose not to take part in the B-55/6-13 treatment study.

What are the costs of *BRCA* testing?

There will be no charge to you or your insurance company for the collection, shipping, *BRCA* testing, and storage of your blood sample at Myriad to determine if you have a *BRCA* mutation or the storage of your blood sample at AstraZeneca and their partners. The cost of the genetic counseling will be covered by the study.

If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

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

What are my rights if I allow the *BRCA* testing?

To have the *BRCA* testing done to determine if you may be eligible for the B-55/6-13 treatment study is your choice. ***If you decide to have the testing done and you have a BRCA mutation, you do not have to join the B-55/6-13 treatment study.*** No matter what decision you make, and even if your decision changes, there will be no penalty to you. Not having the *BRCA* testing done will not affect your medical care. You will not lose medical care or any legal rights.

For questions about your rights, call the Yale University Institutional Review Board at (203) 785-4688.

Confidentiality

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.)

Who will see my medical information?

Your privacy is very important to us, and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

The protected health information that will be collected in this study includes demographics, medical and surgical history, family history of cancer, physical examinations, routine lab tests, review of adverse events and medications you take (past and present), vital signs, MRI scans, CT scans, pregnancy tests, blood samples for research purposes, tumour samples for research purposes, and information recorded in study questionnaires.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The study sponsor, NRG Oncology (The NSABP has joined with two other clinical trials groups to form NRG Oncology as required by the National Cancer Institute.)
- Alliance for Clinical Trials in Oncology
- ECOG-ACRIN Cancer Research Group
- SWOG
- AstraZeneca, the drug company supporting this study
- Breast International Group
- Frontier Science
- Myriad, the company testing blood samples for *BRCA* mutations
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to promote greater access to clinical trials.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.
- 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
- Your providers who are participants in the Electronic Medical Record (EMR) system

- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The study doctor, Dr. Erin Hofstatter, and the Yale study team
- 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.

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 the Yale School of Medicine and Yale-New Haven Hospital are 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.

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

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 sample is sent to Myriad, your date of birth will be included but no other information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) When your sample(s) is sent to other researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
3) The list that links the unique code to your name will be kept separate from your sample and health information. Any NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.

4) Researchers to whom NRG Oncology sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
5) Information that identified you will not be given to anyone, unless required by law.
6) If research results are published, your name and other personal information will not be used.

Neither you nor your doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples. Your doctor will only be given the results of your *BRCA* testing.

Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

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 may withdraw your permission by telling the study staff or by writing to Dr. Erin Hofstatter at the Yale University, 300 George Street, Suite 120, New Haven, CT 06511.

If you withdraw your permission, you will not be able to stay in this study.

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.

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 the *BRCA* testing?

You can talk to the study doctor about any questions or concerns you have about this testing. Contact the study doctor, Dr. Erin Hofstatter, at (203) 785-2876.

My Signature Agreeing to *BRCA* testing

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 have my blood collected and sent to Myriad for *BRCA* testing. I also agree to have my blood sent to Myriad to help develop tests to be used in the future to assess the *BRCA* status of patients and for future research purposes of the B-55/6-13 study. I also agree to have my blood sent to AstraZeneca to help develop tests to be used in the future to assess the *BRCA* status of patients and to assess the status of other genes known or predicted to have a role in breast cancer.

Print patient's name_____

Patient's signature_____

Date of signature_____

Print name of person(s) conducting the informed consent discussion_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

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. Erin Hofstatter, at (203) 785-5876. 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.