Protocol Title: Study of Precursor Hematological Malignancies to Assess the Relationship between Molecular Events of Progression and Clinical Outcome

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Information Sheet

A. INTRODUCTION

You are being asked to participate in a research study to help doctors and scientists understand why cancer occurs and to develop ways to better treat and prevent it. You are being asked to participate because you are at risk of developing cancer, you have had cancer in the past or you have cancer now. This form explains why this research study is being done, what is involved in participating, the possible risks and benefits of the study, alternatives to participation, and your rights as a participant. The decision to participate is yours. We encourage you to ask questions about the study now or in the future.

The Leukemia & Lymphoma Society is supporting this research study by providing funding. The National Cancer Institute is supporting this research study by providing funding.

We encourage you to take some time to think about your possible participation in this study, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

Blood cancers occur when the molecules that control normal cell growth are damaged. Many of these changes can be detected by directly examining parts of the cancer or cells in blood. Several alterations that occur repeatedly in certain types of blood cancers have already been identified, and these discoveries have led to the development of new drugs that target those alterations. More remain to be discovered.
Some of these abnormalities include alterations in genes. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work,

and determine physical characteristics such as hair and eye color. Genes are composed of DNA letters that spell out these instructions. Studies of the DNA molecules that make up the genes are called “molecular” analyses. Molecular analyses are ways of reading the DNA letters to identify errors in genes that may contribute to an increased risk of cancer or to the behavior of the cancer cells. Some changes in genes occur only in cancer cells. Others occur in the genes that are passed from parent to child. This research study will examine both kinds of genes. The best way to find these genes is to study large numbers of people. We expect that as many 1000 individuals will enroll in this study.

The purpose of this research study is to perform these molecular analyses on your tissues (obtained from biopsies), blood, or other body fluids such as saliva. Importantly, this study will use tissue specimens that have already been collected as part of your clinical care. Your tissue sample may be used to create a living tissue sample (called a “cell line”) that can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you. In this study, analyses will be performed on material only after all necessary clinical tests have been performed. In general, no additional procedures will be required. However, we are asking your permission to obtain additional samples of blood (2-4 tablespoons), bone marrow (up to 1.5 tablespoons), urine, and a gentle swab from the inside of your mouth or a mouthwash to obtain some cells. These are sources of normal, non-cancer cells which are needed for some types of analyses.

To fully understand the effects that molecular alterations have on blood cancers, they must be analyzed in the context of clinical behavior. Therefore, this study also asks your permission to link the molecular alterations in your precursor condition with clinical information that has been generated during the course of your clinical care. No additional clinical tests will be required. We will ask to see you for follow up at regular interval to follow your risk of progression.

Some of your specimens as well as some of the material generated during the analysis of your tissues or blood may be useful for future study. We are asking your permission to store these specimens and materials in a secure storage facility for possible later use.

Finally, rapid progress in understanding and treating cancer will occur when some of the molecular information derived from your tissues and blood can be shared with other researchers. In particular, the National Institutes of Health (NIH) and other organizations have developed special data (information) repositories that analyze data and collect the results of certain types of genetic studies. These central banks will store your genetic information and samples and give them to other researchers to do more studies. Therefore, we are also asking your permission to share your results with these special banks. Your information

will be sent with only a code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information and samples while they are stored in repositories and used for research. We do not think that there will be further risks to your privacy and confidentiality by sharing this information with these banks. However, we cannot predict how genetic information will be used in the future.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you may continue to obtain your clinical care without participating in the study. Your decision not to participate will not affect your clinical care in any way.

D. WHAT IS INVOLVED IN THE RESEARCH STUDY?

As a part of standard clinical care, your physician may collect samples of your blood, bone marrow, biopsy of your lymph nodes or other tissue in order to evaluate your disease. If you agree, an additional sample of each will be obtained at that time for the purposes of this study. The number of samples collected will be primarily determined by the frequency of clinic visits and blood and/or marrow samples needed for your clinical (non-research) management. Additionally, you will be asked to provide a one-time saliva sample or buccal swab (a gentle swab of the inside of your cheek) at any visit with your doctor.

In order to learn about you and your family's medical history, you will also be asked to complete a survey. Study personnel may contact you via postal mail, phone, or through secure electronic transmission to request you confirm your contact method to forward you study surveys and additional study communications.

In some cases, a research doctor may contact you to find out if you would be interested in participating in a different research study based on information that may have been found in your tissues or samples. Again, this would only happen if you have given your permission to be contacted. We will also ask you to provide the name and contact information for a relative who would know your whereabouts or could decide about using your information for research if you are not available to give permission yourself.

As a part of standard clinical care, you will be asked to follow up with your doctor at specific intervals (e.g., every 6 months or every year) to make sure that you are followed for the potential of clinical progression of your precursor condition. We ask to see you at these regular intervals (e.g., every 6 months or every year) or if you cannot come to our Institute, then we ask you to follow up with your local

oncologist at the same intervals to assess your clinical course. We ask your permission to contact your doctor to obtain information about your clinical course and whether there is progression of your disease.

E. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study until progression to active symptomatic disease that requires therapy. After progression, you will be followed for survival and disease status. You may inform your doctor that you no longer wish to participate at any time and your decision will not affect the care you receive.

F. WHAT KIND OF INFORMATION COULD BE FOUND IN THIS STUDY AND WILL I BE ABLE TO SEE IT?

These studies are being done to add to our knowledge of how genes and other factors affect cancer. We are gathering this knowledge by studying groups of people, and the study is not meant to test your personal medical status. For that reason, we will not give you the results of our research on your samples.

The tests being performed on your tissues or fluids are designed to look for changes that might be associated with cancer.

G. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

The major risk of participating in this study is that the analyses, including the identification of genetic abnormalities in you or your precursor condition, could be seen by unauthorized individuals. We have tried to minimize this risk by imposing rigorous controls on access to the computers that would house your information.

There is a small risk related to the breach of confidentiality and the loss of privacy of your identifying information. We have set strict controls to minimize this risk that involve a verification process in addition to the stringent controls already established for access to your information by authorized study personnel.

There are small risks associated with obtaining the 2-4 tablespoons of blood and/or up to 1.5 tablespoons of bone marrow. For the former, you may experience slight pain and swelling at the site of the blood draw. For the latter, you may experience pain and swelling along with some minor bleeding at the site of the marrow draw within a few days. There are no known risks and side effects related to saliva collection.

There is a small but real risk that if your samples are used for this research study, they might not be available for clinical care in the future. However, we have attempted to minimize this risk in three ways.

First, the pathologists in the department of pathology where your specimens are kept will not release your specimen unless they believe that the material remaining after the research test is performed is sufficient for any future clinical needs.

Second, many of the research tests (including tests from this trial) can only be performed if your physician orders the test. That way, your physician can decide whether your specimen contains enough material for both the research test and future clinical needs.

Finally, if your specimen is stored in a tissue bank or biorepository, then a designated group of clinicians and scientists who oversee the bank will release your specimen only if they think that the research being performed justifies the use of your material. This step is designed to help ensure that your specimens are being used for the best possible scientific purposes and to help minimize the possibility that your material will be used up.

H. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

It is important to understand that this is not a clinical study being done to benefit you directly. Therefore, taking part in this research study may not directly benefit you. However, the information gained from your participation is likely to generate important information which will help future patients with blood cancer and individuals at high risk of developing those diseases.

I. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign the consent associated with this study. If you decide not to sign, you cannot participate in this research study.

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Any samples of yours that were anonymized (identifying information removed) will not be discarded. Leaving the research study will not affect your medical care outside of the research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

Another reason to tell your research doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

J. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

We may use your samples and information to develop a new product or medical test to be sold. The sponsor and hospital may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

K. WHAT ARE THE COSTS?

There will be no additional costs to you for participating in this study.

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

L. WHAT HAPPENS IF I AM INJURED OR SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this information sheet.

There are no plans for Dana-Farber Cancer Institute Brigham & Women's Hospital to pay you or give you other compensation for the injury. You do not give up your legal rights by signing the consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

M. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database.

The results of this research study may be published. You will not be identified in publications without your permission.

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.

N. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Dana-Farber Cancer Institute
- Irene Ghobrial, MD: (617) 632-4198

Dana-Farber Cancer Institute at Milford Regional Cancer Center
- Michael Constantine, MD: (508) 488-3700

South Shore Hospital
- Meredith Faggen, MD: (781) 624-4800

Broad Institute
- Irene Ghobrial, MD: (617) 632-4198

Lowell General Hospital
- Blair Ardman, MD: (978) 937-6258

Faulkner Hospital
- Aric Parnes, MD: (617) 732-5190

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at DFCI (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

O. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health

information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

- For Studies Involving Tumor Samples: Rapid progress in understanding and treating cancer will occur when some of the genetic information derived from your tissues and blood can be shared with other researchers. In particular, the National Institutes of Health (NIH) and other organizations have developed special data (information) repositories that analyze data and collect the results of certain types of genetic studies. These central banks will store your genetic information and samples, and provide them to qualified researchers to do more research. Therefore, we are asking your permission to share your results with these public

databases. Some of this information may be made available over the internet and will be freely available to anyone who is interested (an open access database). Other, more detailed information may only be accessed by scientists at other research centers who have received special permission to review your de-identified data (a controlled access database).

Your information or samples will be sent only with a code number attached. Your name or other directly identifiable information will not be shared with these repositories or with other investigators. There are many safeguards in place to protect your information and samples while they are stored in these repositories and used for research. There is a slight risk of loss of privacy when sharing this information with these banks but we have established procedures to encode your samples and information and to protect your data. The repositories also have robust procedures in place to protect the confidentiality of the stored data. We will do everything we can to protect your data but we cannot absolutely guarantee its privacy or predict how genetic information will be used in the future.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health, and may prevent discrimination by health insurers and employers based on genetic information. GINA is intended to ease concerns about discrimination that might keep some people from getting genetic tests that could benefit their health, and enable people to take part in research studies such as this without fear that their DNA information might be used against them by health insurers or their workplace. This protection does not extend to disability or life insurance. Additional information can be found at http://www.genome.gov/10002328.

- For studies Involving Germline Research: Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all the safety measures that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters and other relatives. Consequently, it may be possible that researchers looking at your genetic information could guess your identity based on other genetic information that they might know about your relatives. Similarly, it may be possible that genetic information from you could be used to help identify your relatives.

In order to allow the greatest amount of research to be performed on the tissue that you donate, researchers for this study may share results of sequencing your genes (which shows how your DNA is organized) with other scientists. In particular, the National Institutes of Health (NIH) and other organizations have developed special data (information) repositories that analyze data and collect the results of certain types of genetic studies. These central banks will store your genetic information and samples, and provide them to qualified researchers to do more research. Some of this information may be made available over the internet and will be freely available to anyone who is interested (an open access database). Other, more detailed information may only be accessed by scientists at other research centers who have received special permission to review your de-identified data (a controlled access database). Neither type of database will contain information that is traditionally used to identify you, such as your name, address, medical record number, telephone number or social security number. However, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a relative) in another database and be able to identify you (or a relative). Because the DNA sequence of each individual is unique (with the exception of identical twins), there is a very remote possibility that if a complete sequence determination of your DNA were publicly disclosed, it could be used by a researcher to determine your identity. It is also possible that there could be violations to the security of the computer systems used to share the codes linking your genetic and medical information to you. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her relatives.

There may be other privacy risks that we have not foreseen. While we believe the risks to you and your family are very low, we are unable to tell you exactly what all the risks are.

The Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health, and may prevent discrimination by health insurers and employers based on genetic information. GINA is intended to ease concerns about discrimination that might keep some people from getting genetic tests that could benefit their health, and enable people to take part in research studies such as this without fear that their DNA information might be used against them by health insurers or their workplace. This protection does not extend to disability or life insurance. Additional information can be found at http://www.genome.gov/10002328.

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”

- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: “Whom do I contact if I have questions about the research study?”