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Department/Section of *Hematology & Oncology*

PRECISION MEDICINE FOR PATIENTS WITH IDENTIFIED ACTIONABLE MUTATIONS AT WAKE FOREST BAPTIST COMPREHENSIVE CANCER CENTER (WFBCCC): A PRAGMATIC TRIAL

Informed consent to participate in research
WFBCCC # 04519
Stefan C. Grant, MD, JD, MBA, Principal Investigator (PI)

SUMMARY

You are invited to participate in a research study. The purpose of this research study is to determine how feasible it is to use Next Generation Tumor analysis to direct your cancer care. You are invited to be in this study because your body has not responded to at least two previous cancer therapies and you have had a test performed on a tumor sample of your cancer. The test on your tumor sample was to identify any changes in the tumor that are different from your normal genetic material. These changes are called mutations. Your physician has received a report about changes that were identified and some drug recommendations based on these changes. Sometimes the recommended drugs may not be approved by the FDA for your particular cancer, but there may be scientific evidence that suggests that the drug could be helpful. The length of participation in this study will vary for each person and will be determined by the number of treatment cycles you receive.

Participation in this study will involve allowing the Investigator to make recommendations for your cancer care using information learned from the reports about the genetics of your cancer. All research studies involve some risks. A risk to this study that you should be aware of is that the treatment chosen from your tumor mutation report using methods developed in this study may cause your cancer to worsen or may change nothing about your current cancer status. Additionally, there may be side effects due to the different types of drugs used to treat the cancer. However, there is a possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include receiving the same drugs without participating in a study, participating in a different research study, or receiving comfort care for your cancer. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study **is Dr. Stefan Grant**. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted]2 or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have cancer that has not responded to previous treatment or has recurred after a previous treatment and you have had molecular genetic testing performed on a piece of your cancer tissue. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to test the effect of using drugs targeted at genetic mutations as well as the method of choosing the best treatment option for you based on a genetics report.

As part of your routine cancer care, you recently have had or will have a tumor (or bone marrow) biopsy performed. Samples from this biopsy are sent to a company (either Foundation One, Caris, or Guardant360) and DNA testing is done on them. The results of this testing are sent back to your cancer physician in a report with a list of genetic mutations in your tumor that might respond better to specific (targeted) chemotherapies. If you would like a copy of this genetics report, your physician can provide one for you. This can be done whether or not you participate in this study. You are eligible for this study if: a) you have a mutation listed on the genetics report that does not have an FDA-approved treatment regimen, b) you have already completed a non-FDA-approved treatment regimen and your cancer did not respond to it, or c) you are medically unable to receive an FDA-approved treatment for your condition.

Genetic testing of cancer tumors is a relatively new process. Although a lot of information is learned from this testing, doctors do not always know what the best approach for treatment of

cancer is. This is because tumors can have many different kinds of genetic mutations and there is not always a known treatment for these mutations.

For this study, the treating physician will select a medication for your treatment based on the report's genetic information about your cancer and a new method that the investigators have developed for interpreting the report's results. Ultimately, your physician will choose the best drug(s) possible for your overall medical situation and health care coverage. The investigators will also collect information about your health and any side effects that occur on any of the medication(s) prescribed.

Drugs used in this study have been approved by the US Food and Drug Administration (FDA), but may not have been approved for use in your particular cancer.

How Many People Will Take Part in the Study?

337 people at this research site will take part in this study.

What Is Involved in the Study?

After your study doctor has answered all your questions about this study and you have given written consent by signing this form, several tests will be done to be sure you are able to enter this study. Many of the tests are the same as those you have had in the past to diagnose and treat your disease. Some of these same tests will also be done during the study to follow your progress.

Pre-Study Tests

The following tests may be completed over a four-week period before receiving medication:

- If your doctor has been monitoring your cancer with CT scans, you will undergo an imaging scan known as a CT scan. A CT scan uses computers and x-rays to take detailed pictures of areas inside your body.
- If you have a hematologic malignancy such as leukemia or myeloma and your doctor has been following your disease with bone marrow biopsies, you will undergo a bone marrow biopsy.
- The study doctor or study staff will ask you about your medical history, and obtain a list of all medications that you are currently taking.
- The study doctor or study staff will examine you and determine your performance status.
- A physical examination with your vital signs (heart rate, blood pressure, breathing rate, and body temperature), will be recorded.
- You will be asked about any problems you are having with your medication.

- You will be asked to complete some surveys that ask questions about your medical care, your day to day activities, and your emotional health. These surveys usually take about 30 minutes to complete.

The following test must be completed within one week before receiving medication:

- Pregnancy test for women who can become pregnant. This must be done within one week of starting treatment.

If the results of these tests show that you are eligible to enroll in this study, your participation on the study can begin.

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will be randomized based on the number of genetic mutations present on your tumor report. This is because researchers do not know which mutation is more important to treat. The drug chosen for your treatment will also be from your tumor report. It will be chosen randomly. For example, if the report lists 4 different drugs that have shown effectiveness in fighting a certain type of mutation, you will be randomly assigned to receive one of these 4 drugs.

Study Treatment and Procedures
This clinical research study consists of multiple (three, four or six-week) cycles of treatment with a medication selected by one of the doctors participating in this study. Cycle length will be determined by prescribing information for the specific medication that you will receive.

Study Visits
You will have a Pre-Study visit before you start the study. Your next visit will be in four to six weeks. At this visit, you will receive the following:

- If applicable, you will undergo an imaging scan known as a CT scan. A CT scan uses computers and x-rays to take detailed pictures of areas inside your body.
- The study doctor or study staff will ask you about your medical history, and obtain a list of all medications that you are currently taking.
- The study doctor or study staff will examine you and determine your performance status.
- A physical examination with your vital signs (heart rate, blood pressure, breathing rate, and body temperature), will be recorded.
- You will be asked about any problems you are having with your medication.
- You will be asked to complete some surveys that ask questions about your medical care, your day to day activities, and your emotional health. These surveys usually take about 30 minutes to complete.

Your remaining visits will be scheduled every 6-12 weeks for as long as you are receiving benefit from the medication. At these visits, the following will occur:

- If applicable, you will undergo an imaging scan known as a CT scan. A CT scan uses computers and x-rays to take detailed pictures of areas inside your body.
- The study doctor or study staff will ask you about your medical history, and obtain a list of all medications that you are currently taking.
- The study doctor or study staff will examine you and determine your performance status.
- A physical examination with your vital signs (heart rate, blood pressure, breathing rate, and body temperature), will be recorded.
- You will be asked about any problems you are having with your medication.

Schedule of events

	Pre-Study [a]	Cycle 2, Day 1	Day 1 of every even cycle (after cycle 2)	End of Treatment ±7 days	Follow Up Visit [c]	Bimonthly after End of Treatment
Informed Consent	X					
Medical History	X					
Physical Exam	X	X	X	X	X	
Vital Signs	X	X	X	X	X	
Imaging[b]	X	X	X	X		
Bone Marrow Biopsy[b]	X	X	X	X		
Lab work	X	X	X		X	
Pregnancy Test for women who can become pregnant	X					
Adverse Event Evaluation		X	X	X	X	
Surveys	X	X		X		
Telephone Follow Up						X

[a] Pre-study requirements listed in table must be completed **within** 30 days prior to registration.
[b] If clinically indicated as part of your Standard Care
c Follow up visit will happen at least 30 days after your end of treatment visit *only* if you were experiencing side effects at your end of treatment visit

End of Treatment Visit
When you decide to leave the study or when your cancer stops responding to the medication, you will be asked to return for a final study visit. At this visit, you will be asked to complete surveys about your health. You will also receive a physical exam at this time.

Telephone Follow up
After you complete treatment, the study team would like to follow up with you every 2 months. Every 2 months, someone from the study team will call to check in with you.

How Long Will I Be in the Study?

The length of participation in this study will vary for each person and will be determined by the number of treatment cycles you receive. All participants will be in the study until it is determined that your cancer is no longer responding to treatment.

For example, if the PET/CT scan that is performed at the end of cycle two shows that your cancer has responded to treatment, you will receive two more cycles of treatment. If the scan shows that your cancer has stopped responding, you will not receive any further treatment.

Once you have finished treatment as part of this study, you will receive a phone call from the research staff once every two months to check and see how you are doing if you do not return to the clinic for follow-up. These phone calls will continue long term as long as you give permission.

If your initial medication does not show any effect on your cancer, it is possible for you to try a different medication based on your cancer genetics.

In addition, you can stop participating at any time. It is important to tell the study doctor if you are thinking about stopping so that any risks from your medication can be evaluated by your study doctor. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What Are the Risks of the Study?

Being in this study involves some risk to you. There is a risk that your cancer will not respond to treatment long-term, at all, or it may get worse. Receiving targeted chemotherapy based on genetic mutations in your cancer is not a guarantee that the treatment will work. It is possible that only some of your tumor's cells will have the mutation being targeted, there may be no evidence that the drug(s) chosen for you will work on your specific type of cancer, or that your tumor cells will/could continue to change and become unresponsive to the drug(s) chosen for you. There may also be side effects associated with your chosen medication(s). You should discuss the risk of being in this study with the study staff and your physician. Specific risks and side effects related to your condition and specific medication(s) will be provided to you before you begin treatment and you will be able to discuss these with the prescribing physician.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other risks that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any

medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, OrthoEvra patch, NuvaRing, intrauterine devices (IUD), Nexplanon implant, DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a diaphragm with spermicide with Plan B used for any noticed condom or diaphragm failures. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because NO method of birth control is 100% reliable, a pregnancy test is required within 10 days of the pre-study visit.

Contraceptive Measures for Males

Your participation in this research study may damage your sperm, which could cause harm to a child that you may father while on this study. Such harm may be currently unforeseeable. If you are sexually active, you must agree to use a medically acceptable form of birth control in order to be in this study and for (at least 6 months afterwards. Medically acceptable contraceptives include: (1) surgical sterilization (such as a vasectomy), or (2) a condom used with a spermicide. Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. You should inform your partner of the potential for harm to an unborn child. She should know that if pregnancy occurs, you will need to report it to the study doctor, and she should also promptly notify her doctor.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: a delay in the return of your cancer.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:
You could receive treatment outside of the study based on your physician's discretion. You may participate in another research study or you may choose to receive comfort care for your cancer.

WHAT ARE THE COSTS?

You or your insurance company will be responsible for all of the medical care you receive. The study doctors will seek out every chance to get your insurance to cover the costs for your chosen treatment or to get you financial assistance through one of our patient assistance programs.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Cancer Institute which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL YOU BE PAID FOR PARTICIPATING?

You will not be paid for participating in this study. Parking validation will be provided for all study-related visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest Baptist Comprehensive Cancer Center. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. However, the researchers do not hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted]

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call *Dr. Stefan Grant* at [redacted] or After Hours at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** information about your medical visits, information from your imaging scans, and information regarding your cancer and treatment of your cancer.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations. We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a

password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Grant that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Stefan C. Grant, MD, JD, MBA
[redacted]

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Laboratory test results and other clinically relevant medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because such as, it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you

may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, *Dr. Stefan Grant* at [redacted] or after-hours at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm