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Principal Investigator:	Joanna Kolodney, MD
Department:	Department of Medicine, Division of Oncology/Hematology
Protocol Number:	WVU020318 - WVU IRB Number: 1808261484
Study Title:	A Pilot Study: Effect of Carvedilol with Standard Treatment in Frontline Setting of Glioblastoma Multiforme and Response of Peripheral Glioma Circulating Tumor Cells
Co-Investigator(s):	Michael Kolodney, MD-PhD, Geraldine Jacobson, MD, Gary Marano, MD, Rashi Mehta, MD, Christopher Cifarelli, MD-PhD, Robert Marsh, MD, and Todd Tenenholz, MD-PhD
Sponsor:	Novocure

Contact Persons

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In the event you experience any side effects or injury related to this research, you should contact Dr. Kolodney at (304) 598-4500. (After hours, contact, contact the medical oncologist on call at (304) 598-4500). If you have any questions, concerns, or complaints about this research, you can contact Dr. Joanna Kolodney at (304) 598-4500.

For information regarding your rights as a research subject, to discuss problems, concerns, or suggestions related to the research, to obtain information or offer input about the research, contact the Office of Research Compliance at (304) 293-7073.

In addition, if you would like to discuss problems, concerns, have suggestions related to research, or would like to offer input about the research, contact the Office of Research Integrity and Compliance at 304-293-7073.

Introduction

You, _____, have been asked to participate in this research study, which has been explained to you by _____.
This study is being conducted by Dr. Joanna Kolodney in the Department of Department of Medicine/ Division of Oncology/Hematology at West Virginia University with funding provided

by West Virginia University with funding provided by the West Virginia University and Novocure.

Purpose(s) of the Study

It has been explained to you that you have a new diagnosis of glioblastoma multiforme and you have completed surgery. Your medical oncologist has recommended standard of care therapy with radiation therapy given in conjunction with oral chemotherapy followed by oral chemotherapy over a 6-month span. You have been invited to participate in this research study which involves the additional use of a generic blood pressure medication called carvedilol to be taken while receiving standard therapy. Carvedilol is a commonly used medication for high blood pressure, heart failure, and liver cirrhosis. This drug has been extensively studied in preclinical research (preliminary testing of an investigational drug in laboratory and animal studies) to have anti-cancer effects, especially in brain tumors. The purpose of this study is to evaluate the effects of the combination of a carvedilol with standard chemotherapy in the front line setting of glioblastoma. It is considered investigative because carvedilol is not approved for glioblastoma. In addition, we are evaluating a marker in the bloodstream that may be able to determine the extent of the cancer you have with a new developed assay, or procedure, in the lab. WVU will see how the response of cancer cells from the brain tumor corresponds to response to treatment and to the corresponding brain MRI that is used to measure response to treatment. WVU expects to enroll 30 subjects to participate in this study.

Description of Procedures

All patients who are enrolled in this study will receive the standard of care for their cancer. Standard front-line treatment is oral temozolomide with radiation therapy followed by 6 cycles of Temodar. All patients will receive standard of care and will be monitored with standard imaging which is usually a brain MRI. In addition to standard of care, all patients will also receive carvedilol, a known high blood pressure drug, and will be given a diary to record the date, number of pills, and time taken. Blood pressure and heart rate will be monitored closely on the medication. In addition, blood samples for evaluation of cancer cells will be obtained at the same time as routine blood samples are obtained. We will stop the blood pressure medication at the end of the 6th cycle of chemotherapy. Our last blood sample will be obtained after the 6th cycle of chemotherapy. The study will last for approximately 2 years with monitoring of response with standard brain imaging as routinely done. If the anti-hypertensive medication needs to be discontinued due to intolerance or progression of disease, then further treatment will be determined by your medical oncologist and you will come off of the study.

Prior to the first course of treatment at the routine follow-up appointment with your medical oncologist, you will be asked to provide a blood sample of approximately 2 teaspoons of blood (1 tube) to evaluate the quantity of cancer cells. You will be asked to do this before starting radiation treatment, after radiation treatment, at beginning of cycle 1 of chemotherapy and then after 3 months of chemotherapy and after 6 months of chemotherapy. This blood sample will mostly be drawn at the same time as other routine blood work is being performed per the orders of your treating medical oncologist. This blood sample will be sent to a lab off campus without any patient identification to evaluate the quantity of cancer cells in the blood and this data will

solely be used for the purpose of this study. You will also be monitored closely regarding generalized symptoms, blood pressure, and heart rate while on the blood pressure medication. If you are on another blood pressure medication, we will either add carvedilol or switch to carvedilol depending on your blood pressure and heart rate evaluation at the time of consent.

There are anticipated circumstances under which your participation may be terminated by the investigator without regard to your consent, particularly if your physician determines that continuing treatment is not in your best interest. You may also withdraw from the study at any time.

Discomforts

There are no known additional risks in terms of cancer management from participating in this study as you will be receiving the standard of care treatment. Additional risks that can occur from the blood pressure medication include the known side effects of a blood pressure medication. Carvedilol is used to control heart rate and high blood pressure. This medication can cause blood pressure to go low or a slower heart rate, and if this occurs at a significant level, then you may feel dizzy or light-headed. There are no known permanent adverse effects from this medication. Dose modification or termination of the drug will resolve any of the side effects of dizziness or light-headedness. Some patients also complain of a fatigue or malaise with some of the beta-blocker medications.

Alternatives

You do not have to participate in this study. You are free to withdraw your consent to participate in this study at any time. Refusal to participate or withdraw will involve no penalty to you and will not affect your future care.

In the event new information becomes available that may affect your willingness to participate in this study, this information will be given to you so you can make an informed decision about whether or not to continue your participation.

Alternatives that could be considered in your case include chemotherapy as offered by your treating oncologist or comfort care measures only.

Benefits

Possible benefits that may result from your participation in this study include improvement of your health, but since it is not known whether the addition of a beta-blocker to chemotherapy will be effective in your case, it is possible you may not receive any direct benefit from this study. The knowledge gained from this study may eventually benefit others.

Financial Considerations

You may wish to consult your insurance carrier prior to entering this study. With the exception of special correlative blood tests, which will be paid for by the study sponsor, all other treatments, tests, and procedures you will undergo as part of this study will be billed to your

insurance company (e.g. doctor visits, imaging tests, chemotherapy, and standard bloodwork). The portion of these costs that you will be responsible for personally will depend on your agreement with your insurance provider. No treatments will be undertaken by your physicians unless authorization is received by your insurance provider. There may be some additional expenses related to this study, such as transportation, parking, or meals. There are no special fees for participating in this study, and you will not be paid for participating in this study. If your insurance company will not cover carvedilol, then the study will reimburse you for this drug.

There is no money set aside to help treat you if you get hurt or sick in this study. The study doctor and WVUMedicine or its partners do not have special funds to pay for research study injuries if they occur.

Confidentiality

Any information about you that is obtained as a result of your participation in this research will be kept as confidential as legally possible. Your research records and test results, just like hospital records, may be subpoenaed by court order or may be inspected by the study sponsor or federal regulatory authorities without your additional consent.

In addition, there are certain instances where the researcher is legally required to give information to the appropriate authorities. These would include mandatory reporting of infectious diseases, mandatory reporting of information about behavior that is imminently dangerous to your child or to others, such as suicide, child abuse, etc

In any publications that result from this research, neither your name nor any information from which you might be identified will be published without your consent.

HIPAA

We know that information about you and your health is private. We are dedicated to protecting the privacy of that information. Because of this promise, we must get your written authorization (permission) before we may use or disclose your protected health information or share it with others for research purposes.

You can decide to sign or not to sign this authorization section. However, if you choose not to sign this authorization, you will not be able to take part in the research study. Whatever choice you make about this research study will not have an effect on your access to medical care.

Persons/Organizations Providing the Information

Patient/West Virginia University Hospitals/WVU Medicine/West Virginia United Health System (WVUHS)

Persons/Organizations Receiving the Information

- The research site(s) carrying out this study. This includes UHA or UHA Affiliated, WVU, WVU Medicine, WVU Hospitals, West Virginia United Health System

(WVUHS), or the covered entities under the purview of West Virginia University, collaborating institutions, affiliate institutions, and component institutions. It also includes each site's research staff and medical staff.
- Health care providers who provide services to you as part of this research study.
- Laboratories and other people and groups that look into your health information as part of this study in agreement with the study protocol.
- The United State Department of Health and Human Services (which includes the National Institutes of Health (NIH), Food and Drug Administration (FDA)) and other groups that have the right to use the information as required by law.
- Foreign Regulatory Agencies
- The members and staff of any Institutional Review Board (IRB) that oversees this research study.
- West Virginia University Office of Research Compliance and Office of Sponsored Programs.
- West Virginia University Clinical Research Unit.

The Following Information Will Be Used

Information from your existing medical records and new information about you that is created or collected during the study such as: history and physicals, clinic visit notes, nursing and staff notes, laboratory results, x-rays, EKG results, demographic data, pulmonary tests, imaging scans and study forms.

The Information is Being Disclosed for the Following Reasons

- Review of your data for quality assurance purposes
- Publication of study results (without identifying you)
- Other research purposes such as reviewing the safety or effectiveness of the study drug and other products or therapies; conducting performance reviews of the study drug; evaluating other products or therapies for patients; developing a better understanding of disease; improving the design of future clinical trials

You May Cancel this Authorization at Any Time by Writing to the Principal Investigator

Joanna Kolodney, MD
West Virginia University School of Medicine
Department of Medicine/ Division of Oncology/Hematology
1 Medical Center Drive
Morgantown, WV 26506

If you cancel this authorization, any information that was collected already for this study cannot be withdrawn. Once information is disclosed, according to this authorization, the recipient may re-disclose it and then the information may no longer be protected by federal regulations.

You have a right to see and make copies of your medical records. You will not be able to see or copy your records related to the study until the sponsor has completed all work related to the

study. At that time you may ask to see the study doctor's files related to your participation in the study and have the study doctor correct any information about you that is wrong.

This authorization will expire at the end of the study unless you cancel it before that time.

Voluntary Participation

Participation in this study is voluntary. You are free to withdraw your consent to participate in this study at any time.

Refusal to participate or withdrawal will not affect and will involve no penalty to you. Refusal to participate or withdrawal will not affect your future care, or your employee status at West Virginia University.

In the event new information becomes available that may affect your willingness to participate in this study, this information will be given to you so that you can make an informed decision about whether or not to continue your participation.

You have been given the opportunity to ask questions about the research, and you have received answers concerning areas you did not understand.

Upon signing this form, you will receive a copy.

I willingly consent to participate in this research.

Signatures

Signature of Subject Date Time

_____

Printed Name

_____

The participant has had the opportunity to have questions addressed. The participant willingly agrees to be in the study.

Signature of Investigator or Co-Investigator Date Time

_____

Printed Name

_____