INFORMED CONSENT FORM AND AUTHORIZATION TO DISCLOSE PROTECTED HEALTH INFORMATION FOR A RESEARCH STUDY

TITLE:	Standard Chemotherapy versus Chemotherapy Chosen by Cancer Stem Cell Chemosensitivity Testing in the Management of Patients with Recurrent Glioblastoma Multiforme (GBM).
PROTOCOL NO.:	CG01-GBM WIRB® Protocol #20172720
SPONSOR:	ChemoID
INVESTIGATOR:	Tulika Ranjan, MD Allegheny Cancer Center 5th Floor Allegheny General Hospital 320 E. North Avenue Pittsburgh, PA 15212 United States
STUDY-RELATED PHONE NUMBER(S):	Tulika Ranjan, MD 412-770-3039 (24 Hours)

1 - ***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. There may be risks associated with being part of research studies. If there are any risks involved in this study then they will be described in this consent. Your participation is voluntary. Please take your time to make your decision, and ask your research doctor or research staff to explain any words or information that you do not understand.

2 - What you should know about a research study:

- Someone will explain this research study to you.
- You volunteer to be in a research study.
- Whether or not you take part is up to you.
- You can choose not to take part in the research study.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- Feel free to ask all the questions you want before you decide.

3 - Who can I talk to if I have questions?

If you have questions, concerns, or complaints, or think the research has hurt you, you should contact the principal investigator – Tulika Ranjan, MD, 412-770-3039, she can be reached 24 hours/day.

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research or for any of the reasons listed below:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research

You may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

If you have any questions regarding Allegheny Health Network Research, please contact 1-844-577-4621.

4 - Why is this study being done?

The investigational purpose of this study is to screen chemotherapy drugs currently used for the care of recurrent glioblastoma (a form of brain cancer) and to determine the most effective treatment based on results from a chemosensitivity assay.

Chemosensitivity drug assay refers to testing a patient's own cancer cells in the laboratory to drugs that are to be used to treat the patient's cancer.

Following surgery, you will be treated either as per chemotherapy agents chosen by the physician or with chemotherapies as suggested by the results of the chemosensitivity testing.

We would like to determine if patients treated with drugs predicted by the chemosensitivity test have better outcomes than patients treated with drugs chosen by the treating physician.

5 - How long will the research last?

We expect that you will be in this research study for 3 years. This study is designed to follow you for long-term survival as such – your doctor and his/her staff would like to follow your long-term health status for a period of not more than 36 months, by accessing your hospital records.

You can decide to 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 to discuss what follow up care and testing could be most helpful for you. The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped. If you decide to withdraw or if you are removed from the study, all data generated up to the date of withdrawal from the study will be collected.

6 - How many people will be studied?

About three hundred (300) people will take part in this study over a three year period. Allegheny Health Network is projected to enroll 60 participants per year in the trial; two additional sites are projected to enroll 40 participants per year.

7 - What happens if I say yes, I want to be in this research?

This study uses sample specimens obtained by the same surgical procedures that patients have to routinely undergo for the treatment of recurrent brain cancer.

Surgical resections are part of the established standard-of-care procedures to treat recurrent brain cancer. You will be asked to sign a separate consent form for this procedure as per standard of care.

As per standard-of-care, tumor biopsies from the surgical resections will be sent to the pathology laboratory for pathological confirmation of recurrent GBM and for MGMT methylation status assessment.

Biopsies will be also sent to the ChemoID laboratory for drug response assay assessment, which is a laboratory-developed test (LDT).

Participants will be randomized to receive either ChemoID guided chemotherapy with standard-of-care drugs, or standard-of-care drugs chosen by the Physician.

A computer will choose the treatment-group that you are assigned. Neither you nor the study doctor will choose what treatment-group you will be assigned. You will have one in two chance of being assigned to each treatment-group. You will not be told in which treatment-group you are, however your study doctor will know.

All diagnostic procedures (except for ChemoID test), therapeutic management and follow-up procedures will be conducted under standard-of-care for the disease.

- Administration of chemotherapy drugs will be under standard-of-care management of the disease.
- Follow-up visits will consist of a clinical evaluation with particular attention to neurological function, seizures and corticosteroid use, as per standard-of-care management of the disease.
- Indicated laboratory tests of blood counts, glucose level, and blood count, liver function tests, and the administration of corticosteroids and anti-epileptic drugs will be as per standard-of-care management of the disease.
- Radiological imaging with CT and/or MRI preferentially with contrast will be performed every 2 months as per standard-of-care management and follow-up of the disease.

8 - What happens if I say no, I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.

9 - What happens if I say yes, but I change my mind later?

If you agree to take part in the research now and stop at any time it will not be held against you. You may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

10 - What are the risks of the study?

Being in this study involves some risk to you, which are the same as the risks listed on your surgical consent. You should discuss with the study staff the risks of being in this study, which are the same as the risks of being treated with standard-of-care chemotherapy and radiation.

You should talk to your study doctor about any side effects that you have while taking part in the study. You will be provided with a US Package insert listing the risks and side effects for each drug that you will receive. Again, feel free to discuss with the study doctor this information and ask any questions about anything you feel needs to be explained to you.

There may be side effects 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.

PREGNANCY
Pregnant women or nursing mothers cannot participate in the study. Women of childbearing age must have a negative pregnancy test within 72 hours prior to study entry. Women of childbearing potential must practice medically approved contraceptive precautions. The study doctor will explain the pregnancy risks and the length and precautions you will need to take (depending of the treatment drugs you will be assigned to) not to become pregnant.

11 - Will being in this study help me anyway?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include prolonged response to treatment. Also, we hope the information learned from this study will benefit other people in the future.

12 - What other choices are there?

You do not have to be in this study to receive treatment. You may still receive the same chemotherapy treatments without being in the study.

The study doctor will discuss your alternative treatments option with you including comfort care.

If you decide that you don't want any more active treatment, one of your options is called "comfort care." Comfort care includes pain medication and other support. It aims to maintain your comfort and dignity rather than cure disease. Usually this care can be provided at home.

If you think you might prefer comfort care, please discuss this with your family, friends and your doctor.

13 - Will my information be kept confidential?

Your identity and medical records and data related to this study will be kept confidential, except as required by law and except for inspections by the Department of Health and Human Services, the Food and Drug Administration the sponsor (ChemoID), Allegheny Health Network, the Allegheny Health Network Research Institute, the Institutional Review Board (the committee that reviews, approves and oversees research) and the AHN Compliance Office. By law, anyone who looks at your records must keep them completely confidential. This is done to make sure that we are doing the study in the right way. They also need to make sure that we are protecting your rights and your safety.

Results of the research may be published for scientific purposes or presented to scientific groups; however, your identity will not be revealed.

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.

Federal law provides additional protections of your personal health information. These are described below in the **HIPAA Authorization Section below.**

14 - Can I be removed from the research without my OK?

The investigator in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include failure to follow instructions of the research staff or if the investigator in charge decides that the research study is no longer in your best interest. The sponsor can also end the research study early.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

15 - Are there costs of taking part in this study?

There are no costs to you for taking part in this study. The chemosensitivity assay that is required for this study will be provided to you at no cost and will be paid for by the study sponsor, ChemoID.

Costs for your regular medical care, which is not related to this study, will be your own responsibility. This kind of research study is not expected to result in any additional costs to you or your insurance company. If you require medical care for your glioblastoma or other health problems, as part of your routine care (care you receive even if you do not participate in this research study), either you or your insurance carrier will be billed for these charges. The cost for the standard-of-care items will be billed to you or your insurance company as usual. If you require additional medical care for your glioblastoma or other health problems, as part of your standard medical care, either you or your insurance carrier will be billed for these additional charges. Please talk with the study doctor about any expected costs or health insurance problems.

16 - Will I be paid to participate in this study?

You will not be paid for your participation in this research study.

17 - What if I am injured while taking part in this study?

If you are injured or made sick while taking part in this research study, emergency medical treatment will be provided at the usual charge. No funds have been set aside by Allegheny Health Network or Allegheny Health Network Research Institute to pay you in case you are injured. You do not waive any of your legal rights to compensation, if any, by signing this form.

18 - 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.

19 - Authorization to Use and Disclose Individually Identifiable Health Information for a Research Study

Before you can take part in this research study, the Allegheny Health Network is required to obtain your authorization to use and/or disclose (release) your health information. This section describes to you how, and to whom, your health information will be used and/or disclosed (shared) while you are participating in this research study. It is important that you read this carefully. Allegheny Health Network and its' researchers are required by law to protect your health information.

The following is a list of health information that will be used and/or disclosed:

- Age
- Gender
- Weight
- Pathology report
- Record of steroid and other medication doses over the course of treatment
- ChemoID test results
- MGMT gene methylation status
- IDH-1 mutation status
- Chemotherapy regimens including doses
- Radiation therapy schedule and doses (if part of therapy regimen)
- All brain imaging including but not limited to DICOM images of MRI and or CT scans as well as reports
- Clinical assessment of disease at baseline and during the course of therapy from neuro-oncologic progress notes
- Health-Related Quality of Life (HRQOL) questionnaires addressing physical, psychological, emotional, and social issues.

The following is a list of entities that may use and/or disclose your health information as part of this study:

<u>Internal Oversight</u>
Those who oversee the study will have access to your health information, including the following:

- Allegheny Health Network (AHN)
- Allegheny Health Network Research Institute
- AHN Compliance Office
- Study Doctor and Study Staff

<u>Governmental Oversight</u>
Your health information may also be shared with government agencies that have oversight of the study or to whom access is required under the law:

- Department of Health and Human Services (DHHS)
- Food and Drug Administration (FDA)

Others Outside Allegheny Health Network

The following persons and/or organizations outside of Allegheny Health Network may also use, disclose and receive your health information in connection with this study:

- Sponsor (and companies owned/affiliated with sponsor): ChemoID may need to view your medical records to make sure the study is being completed correctly.
- Western Institutional Review Board® (WIRB®) is a group of people who review the ethics of human research.
- A Data Safety Monitoring Board (DSMB) will be responsible to monitor data quality management and ongoing assessment of safety.
- ChemoID laboratory at the Translational Genomics Research Institute (TGRI) in Cabell Huntington Hospital will test patient's own cancer cells to drugs that are to be used to treat the patient's cancer.

In order to participate in this study, you must agree to share your health information with the persons and organizations listed above. If these persons or organizations that you authorize to receive and/or use protected health information, are not health plans, covered health care providers or health care clearinghouses subject to federal health information privacy laws, they may further disclose the protected health information and it may no longer be protected by the federal health information privacy laws.

Expiration of Authorization

This authorization will not expire unless you revoke it in writing. You may revoke or end this authorization by writing to the Principal Investigator:

Tulika Ranjan, MD
Allegheny Health Network
320 East North Avenue
Pittsburgh, PA 15212

If you revoke your authorization, you will also be removed from the study. Revoking your authorization only affects the use and sharing of your health information after the written request is received. Any health information obtained prior to receiving the written request may be used to maintain the integrity of the study.

Authorization
By signing this document (authorization), you authorize that your health information can be used and/or disclosed as described.

Your access to your protected health information created or obtained by Allegheny Health Network in the course of the research (that includes treatment) may be temporarily suspended for as long as the research is in progress. By signing this document, you are agreeing to the denial of access to your protected health information, created for the research, while you are participating in this research study. Your access to your protected health information will be reinstated upon completion of the research.

If you choose to not sign this document, you will not be permitted to participate in this research study.

20 - Consent for Future Use of Specimens

We would like to keep your specimens that are left over from the study for future research. Reports about future research will not be given to you or your regular doctor. These reports will **not** be put in your health record.

The specimens will be coded in such a manner that it should not be possible for others to find out that they came from you.

Even if you decide now that your specimens can be used for future research, you can later request, for up to 2 years from the end of your participation in the study, that they not be used for this research. To make this request, contact the study site and let them know that you now do not want your specimens to be used for research. Please understand that if the code identifying your specimens has been removed, we will not be able to find out which specimens are yours. In this case, they may still be used for research. Results from research that was done using your specimens before you changed your mind can still be used by the researchers. There is no end date for how long your specimens will be kept.

You agree that your leftover specimens may be used for other research purposes.

Please Initial.

_____*Yes, You agree* _____*No, you do not agree*

21 - Consent

Your signature below indicates your permission to take part in this research and to the use and disclosure of your protected health information:

Signature of Subject	Date
	Time
Printed Name of Subject	
Investigator Signature	Date
	Time
Printed Name of Investigator	
Signature of Witness to Signature	Date
	Time
Printed Name of Person Witnessing Signature	

My signature indicates that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

☐ ***Check box ONLY if the witness is an "impartial" witness*** *- an individual (greater than 18 years of age) with no affiliations to the patient (e.g. not a relative) and/or to the research study (e.g. not a study coordinator). An "impartial" witness is only required when a "short form" consent form is used or the subject is unable to read the consent form and the written informed consent document is read and comprehended by the subject or the subject's legally authorized representative and oral consent is given by either the subject or the subject's legally authorized representative.*

Signature of Witness to Signature	Date
	Time
Printed Name of Witness to Signature	