PRINCIPAL INVESTIGATOR: Eric Burton, M.D.

STUDY TITLE: Phase II Trial of LB100, a Protein Phosphatase 2A Inhibitor, in Recurrent Gliomas

STUDY SITE: NIH Clinical Center

Cohort: Affected Study Patient

Consent Version: 06/02/2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator: Eric Burton, MD
240-760-6030
eric.burton@nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research interventions in which they would want to participate. Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This study will test an investigational drug called LB100. The safety profile of LB100 is uncertain since only 29 people have been treated and most of those were not treated at the dose used in this study. An "investigational drug" is a drug that is being tested and is not approved for sale in the United States by the Food and Drug Administration (FDA). The purpose of this research study is to find out if LB100 can pass into your brain. Your brain is separated from the rest of your blood stream by a membrane called the "blood- brain barrier." This is like a filter that protects your brain but is also a challenge when medications need to get into your brain. You have a brain tumor that

requires surgery. We want to give you a dose of LB100 before your surgery and then take samples of your blood during and after surgery; and the tumor tissue that is being removed during surgery. We will then measure how much LB100 is in your blood and how much gets into your brain. This may help us use LB100 to treat brain tumors in the future.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

We are asking you to be in this study because you have a brain tumor that has recurred after your standard treatment and requires surgery.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 25 participants will take part in this study.

DESCRIPTION OF RESEARCH STUDY

What will happen if you take part in this research study?

If you agree to be in this study, we will ask you to do the following things:

Before you begin the study

Before you can start this protocol, we will do an evaluation to see if you are eligible to participate in this study. This will include a physical examination and blood laboratory studies. We may also need to collect all the urine you produce over 24 hours. You will need to see a neurosurgeon to be evaluated for surgery. You will also need to have an MRI of the brain if you have not had one in 28 days. If you are unable to have an MRI, you may have a CT Scan instead of an MRI. Your healthcare provider will tell you which one you will have. An EKG will be done. We must also be certain we have complete information about your history any past treatments, including surgeries. If available, we will request surgical tissue samples from prior surgeries. Women who are capable of having children will have a pregnancy test. You cannot take part in this study if you are pregnant. Also, you must not be taking certain medications or eating foods that strongly alter liver function.

These include cimetidine, ketoconazole, fluconazole, erythromycin, ciprofloxacin, omeprazole, phenytoin, phenobarbital, carbamazepine, or drinking a large volume of alcohol or any grapefruit juice. If you are unsure about the other medications that you are taking, please discuss them with the study team.

Any concerns you or your clinician may have can be further explored, and you may be referred to a specialist for further evaluation or treatment if necessary.

During the study

If you are found to be eligible to take part in this study, you will be scheduled for removal of your brain tumor in the operating room. You will be admitted to the Clinical Center for your surgery.

You will receive LB100 at a dose of 2.33 mg/m2 though a temporary plastic tube which is placed into a vein (IV) over 2 hours 2-4 hours prior to surgery.

Blood samples will be collected at the following time points: 1) Before LB100 infusion; 2) At the completion of LB100 infusion); 3) 30 minutes after LB100 infusion; 4) 1 hour after LB100

infusion; 5) 2 hours after LB100 infusion; 6) 4 hours after LB100 infusion; and 7) 8 hours after LB100 infusion.

Glioma tissue sampling to measure LB100 will be performed in the operating room during your surgery. The number of tumor samples taken will depend on the length of your surgery.

You will receive an EKG at the end of the infusion. An electrocardiogram (EKG) is a test that gives us a measure of the heart's electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.

Study visits

During the first week after infusion with LB100, you will have routine blood tests to check your kidney and liver function.

Two to three weeks after you are discharged from the hospital after your surgery, you will come into the clinic or see your physician to have an exam and some routine blood tests performed.

About a month after the surgery, you will be contacted either in person or by phone to discuss any problems or concerns you may have. After that contact, if you are doing fine, you will no longer be a participant of the study. A member of the study team will not contact you again unless you are experiencing problems when we talk to you.

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment and for 30 days after the last dose of study medication. If you think that you or your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- intrauterine device (IUD)
- hormonal [birth control pills, injections, or implants]
- tubal ligation
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

While on the study, you are at risk for these side effects. You should discuss these with your doctor. There also may be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and uncomfortable.

LB100 risks

COMMON, SOME MAY BE SERIOUS

The following possibly related risks were reported for ≥ 25% of people receiving LB100:

- Fatigue.

OCCASIONAL, SOME MAY BE SERIOUS

The following possible related risks were reported for ≥ 10% but ≤ 25% of people receiving LB100

- Temporary elevation of blood measures of kidney function.
- Temporary elevation of blood measures of liver function.
- Headache
- Increase blood concentration of sodium.
- Decrease in a blood measure of liver function.
- Nausea.
- Fever.
- Abdominal discomfort.
- Abdominal distension.
- Anemia.
- Joint pain.
- Yeast infections.
- Chest pain.
- Chills.
- Constipation.
- Decreased appetite.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think they are related to the study drug.

You should inform the study doctor before you start any new medications, including prescription, over-the-counter, or herbal products. If you are having stomach upset, consult with your physician for recommended medications.

Other Risks

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

EKGs may cause some redness or itching where the pads are placed. Other than the minor skin irritation from the electrodes there are no expected risks related to the EKG.

LB100 may involve unpredictable risks to the study participants.

Risks for MRI

MRI scans cannot be done on people who have a cardiac pacemaker, neural pacemaker, surgical metal clips in the brain or on blood vessels, cochlear implants, or foreign metal objects within the eye. At the time of your MRI, you will be asked about these things. When you are in the scanning machine, a feeling of claustrophobia may come over you, and there will be a repetitive thumping noise. Cool air will surround you, and the room is lit so you will not feel like you are in a cave or underground. It is important to remain still during the MRI scan. If you are very claustrophobic in MRI scanners, you may ask your physician for a mild sedative for the procedure. If you do this, you must not drive a vehicle after the MRI. You can notify the MRI technologist of any discomfort you feel. The medicine that is used for the injection may rarely (1:2000) cause an allergic reaction such as hives, shortness of breath, or low blood pressure. The medical personnel in the MRI room are prepared to treat you for this kind of reaction. The MRI study will be stopped.

Risks for gadolinium enhanced MRI scans:

Procedure

During part of the MRI you will receive gadolinium, a contrast agent, through an intravenous (iv) catheter. It will be done for research and medical purposes.

It is not known if MRI with contrast is completely safe for a developing fetus. Therefore, all women of childbearing potential will have a pregnancy test performed no more than 24 hours before each MRI scan with contrast. The scan will not be done if the pregnancy test is positive.

Risks

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given. People with kidney disease are at risk for a serious reaction to gadolinium contrast called “nephrogenic systemic fibrosis (NSF)”. This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive

gadolinium for a research MRI scan if your kidney function is below the safe level. Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The effects of the retained gadolinium are not clear. At this time, retained gadolinium has not been linked to health risks in people whose kidneys work well. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body, whenever possible. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

CT Scans

In addition to the radiation risks from the scans, you may experience an allergic reaction to the dye we inject into your veins to help us view the scan better. You might experience hives, itching, headache. More serious reactions that would include difficulty breathing, increased heartrate and swelling of your throat or other body parts.

What are the risks of radiation from being in the study?

During your participation in this research study, you will be exposed to radiation from a CT Scan. This is considered a low exposure. The risk of this exposure is too low to be reliably measured. Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation". No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The radiation you will get by participating in this study is less than the average yearly background radiation in the United States.

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The aim of this study is to determine if LB100 can cross the blood- brain barrier. We do not yet know whether LB100 can help treat brain tumors, or even whether it can cross the blood-brain barrier. Because there is not much information about the drug's effect on your cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

What other choices do I have if I do not take part in this study?

Instead of being in this study, you have these options:

- Instead of being in this study, you have could have a different treatment including surgery without LB100 for your relapsed brain tumor. You do not have to join this study.

- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if during the time of surgery, it is confirmed that you do not have tumor tissue in your brain that can be sampled, you will not have the blood samples performed

In this case, you will be informed of the reason therapy is being stopped. Your participation in this study will end approximately one month after your surgery.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Lixte Biotechnology Holdings, Inc. or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study have developed a drug being used in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of LB100.

The National Institutes of Health and the research team for this study are using LB100 developed by Lixte Biotechnology through a joint study with your researchers and the company. The company also provides financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used.

Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.

Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The Study Sponsor, Center for Cancer Research, NCI or their agent(s)
- Qualified representatives from Lixte Biotechnology Holdings, Inc., the pharmaceutical company who produces LB100

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for

research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Eric Burton, M.D., Bldg. 82, Room 243, Telephone: 240-760-6030. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.