PRINCIPAL INVESTIGATOR: Christine Alewine, M.D., Ph.D.

STUDY TITLE: A Phase I Study of Mesothelin-Targeted Immunotoxin LMB-100 in Combination with tofacitinib in Persons with Previously Treated Pancreatic Adenocarcinoma, Cholangiocarcinoma and other Mesothelin Expressing Solid Tumors

STUDY SITE: NIH Clinical Center

Cohort:	*Standard*
Consent Version:	*8/10/20*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

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.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you to in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

You are being asked to take part in this study because you have pancreatic cancer, bile-duct cancer, or solid tumor that has a protein called mesothelin on the surface. Your disease has either gotten worse after previous treatment or you are unable to receive standard treatment.

The purpose of this study is to find a better way to treat your cancer. LMB-100 is an investigational drug, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat your cancer. LMB-100 has been given in other clinical trials, but its effect has not lasted for as long as we hoped.

The purpose of this study is to test LMB-100 in combination with another drug, tofacitinib, to find out if the effects of the combination last longer than the effects of LMB-100 alone. We would also like to find a safe dose for the combination by testing different doses of LMB-100. Tofacitinib is a drug used for rheumatoid arthritis. It is not used in cancer and has never been tried in combination with LMB-100. However, the FDA has given us permission to use tofacitinib in combination with LMB-100 in this study.

LMB-100 targets cancer cells that make a protein called mesothelin. Most (>85%) pancreatic adenocarcinomas, extrahepatic cholangiocarcinomas and epithelioid-subtype mesotheliomas

make mesothelin, but some do not. Testing to see if your tumor makes mesothelin is not required before you start study treatment if you have one of these tumor types.

There are other drugs that can be used to treat your disease, and these can be prescribed/given by your regular cancer doctor, even if you are not in this study. For example: If you have pancreatic cancer, you could receive further chemotherapy with gemcitabine alone or with nab-paclitaxel, nanoliposomal irinotecan, fluorouracil or other standard chemotherapeutic drugs that you have not received before. If you have extrahepatic cholangiocarcinoma, you could receive fluorouracil alone or with oxaliplatin, or gemcitabine with or without cisplatin if you have not received these drugs before. The delivery of drugs in this study happens much the same way that the delivery of chemotherapy does. Some side effects from treatment are expected to be the same but others are different. Our current ways to treat pancreatic and bile-duct cancers have not been very effective at preventing it from getting worse in other patients so we are studying this new treatment combination. Giving the drugs together as part of this study, we can learn more about how the treatment affects your cancer by also collecting and studying research blood and tissue samples. If you would prefer other treatments over what you would receive in this study, you should consider not joining this trial.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- We will first do some basic tests to make sure you qualify for the trial. We will confirm your cancer diagnosis. Also, you must have a cancer that has started growing again after previous treatment.
- You will take tofacitinib by mouth for 10 days in a row every 3 weeks, and LMB-100 that you will receive as an injection in your blood 3 times every 3 weeks. The dose of LMB-100 that you receive may be different (higher or lower) from what others will receive in the study depending on when you enroll.
- You may have side effects from taking part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include: nausea, swelling, tiredness, fever, infections, etc. Other side effects are described further on in this consent form. It is important that you read these.
- Your involvement is expected to last for at least three months. You will be seen regularly during the study. You will have clinical, laboratory, and imaging tests to see how you are doing and to assess your disease. We will also collect required samples from you (such as blood and tissue biopsy) for both clinical and research purposes.
- After the study treatment has ended we will contact you or your physician by telephone to ask about any other cancer therapies you may have started and about your survival status.

Just as we cannot predict what side effects you personally will have, we cannot know if you will benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

If you are a sexually active person with a partner capable of becoming pregnant, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use

birth control during the study and for three months after treatment if you want to take part in this study. If you think your partner has become pregnant during your participation in this study, please contact a research team member identified at the top of this document as soon as possible. If you and your partner plan for your partner to become pregnant after your participation in this study, please discuss this with the study team.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure you are not having side effects from the treatment that you already received.

The remaining document will now describe more about the research study. 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 treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

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 is a research study. The purpose of this research study is to find a safe dose of LMB-100 plus tofacitinib in patients with pancreatic, bile-duct and other solid tumors that make a protein called mesothelin. Mesothelin is found on many different tumors, including pancreatic and some bile-duct tumors, but on very few non-cancer cells.

We are asking you to join this research study because you have pancreatic cancer, bile-duct cancer, or any other solid tumor with mesothelin. You have either received, refused, or are unable to receive standard therapy. If you have received standard therapy, your disease has gotten worse after that treatment.

If you decide to enroll to this study and have not received standard therapy, then you are refusing or ineligible to receive cancer therapy with proven clinical benefit.

LMB-100 is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat cancers that make mesothelin, including pancreatic

and bile-duct cancers. Tofacitinib is an FDA approved drug but it has never been used to treat these cancers. It has only been used to treat specific kinds of arthritis and bowel inflammation.

LMB-100 is a manufactured protein that contains two parts. The first part of LMB-100 is similar to a toxin that some bacteria make. The toxin can only kill if it gets inside a cell but cannot enter cells by itself. The second part of LMB-100 directs the toxin to get into cancer cells. This is similar to germ-fighting proteins made by your immune system and can make LMB-100 stick to cells that have the mesothelin protein on their surface. LMB-100 is attracted to the mesothelin protein. After LMB-100 binds to the mesothelin on tumor cells, the cancer cells can bring LMB-100 inside where the toxin can attack and kill the cancer cell.

Another reason for this study is to find out if using tofacitinib along with LMB-100 will allow for longer and more effective LMB-100 treatment. Sometimes after patients receive several doses of LMB-100 the patient's body creates substances (called antidrug antibodies – ADAs) that will attack LMB-100 and limit how well it can work. We believe that tofacitinib could be effective at stopping this, and that giving it with LMB-100 could potentially make LMB-100 more effective at killing tumor cells.

WHAT WILL HAPPEN DURING THE STUDY?

Before you begin the study

Before beginning the study, you will need to have tests and/or procedures to help your doctor verify whether you can participate. This is called screening. The exams, tests, and procedures you will have are part of the usual approach for your cancer. Most must be performed within 28 days before enrollment. Briefly, these tests, which may be performed under a separate protocol or a separate consent for, include:

- Confirmation of diagnosis (You must provide a sample tumor tissue for formal evaluation by the NCI Laboratory of Pathology. The tissue may be from a previous surgery or biopsy. If none is available, we will ask you to have a biopsy to provide a fresh sample).
- Medical history and physical examination including weight and height
- Test to measure blood oxygen levels
- Lab blood and urine tests
- Pregnancy test in women who can have children. Pregnant women will not be allowed on study.
- CT Scans and/or MRI and/or PET scan
- Electrocardiogram (ECG)
- Echocardiogram
- Tests for certain infections

During the study

Once it is determined that you are eligible, and you have signed the consent for the study, you will take tofacitinib by mouth, twice a day, on days 1-10 of each cycle. Each cycle is 21 days long. You also will keep a pill diary. This helps you keep track of when you take your tofacitinib pills.

The study doctor will show you how to use this diary. Each time you visit the clinic, you must bring the pill diary, any remaining pills, and the pill bottle. Since pancreatic cancer or other solid tumors can cause blood clots, you will need to take blood thinner medications every day while you are taking tofacitinib and until two weeks after study treatment is finished. These medications are taken by mouth or by injection under the skin.

You will also receive LMB-100 on day 4, 6, and 8 of each cycle through a mediport or central line (a secure IV line located in your arm). This will last for about 30 minutes, though it may take longer if you have side effects. You will be monitored for side effects during all infusions. Your blood pressure, pulse rate, oxygen levels and temperature will be monitored before the infusions start, and periodically until the infusions are completed. You will be given standard pre-medications that include an antihistamine, such as diphenhydramine (Benadryl), and also acetaminophen (Tylenol) and ranitidine (Zantac). If ranitidine is not available, it can be substituted with famotidine (Pepcid). If you develop infusion related side effects, you will also receive Dexamethasone.

You will receive LMB-100 in combination with tofacitinib for three cycles unless your disease worsens or you have intolerable side effects.

If you show benefits from the treatment, the study doctor may give you the option to continue to receive treatment beyond cycle 3 until you stop benefiting from the treatment or you show intolerable side effects. If you choose to continue the treatment, you may initiate it immediately after the end of cycle 3 or start it at a later time during which you would be allowed to take other anti-cancer drugs. If you choose to defer the treatment beyond 6 weeks or to have a different intervening therapy, you may be required to repeat some screening safety evaluations.

We will continue to follow you after you have finished taking the study drug to keep track of your disease status (progression), your survival status or whether you have taken any additional cancer therapy. The specific procedures you will have are described below.

Study Procedures

While you are taking study medication, we will perform some tests and examinations for safety and to test the effect of the study therapy.

During the course of the treatment, we will ask you questions to monitor your symptoms and perform physical exams including vital signs. You will have routine blood and urine tests and a weight check. You will have a pregnancy test once per cycle if you are a woman who can have children. You will have scans done about every 9 weeks until your tumor starts to grow, and ECGs will be done twice during the first cycle that you receive LMB-100. Before starting each cycle, a chest x-ray will be done for patients who already have a mediport. If you don't have a mediport, chest x-ray will be performed each cycle that requires new placement of a central line.

Additional research testing

In addition to the tests that we will do to check whether you are having side effects or if you are responding to the study therapy, we will also collect samples from you for purposes of research only. The samples are being collected to find out how your body handles the drugs, how your

body, including your immune system, reacts to the drug and how certain side effects of the LMB-100 might be caused.

The samples included for these studies include:

- Blood
- Tumor tissue

An optional biopsy may be collected at cycle 1 day 1 and on day 3 of cycle 2. The biopsies to be performed are only for research purposes and will not benefit you. What we learn from those biopsy samples might help other people in the future. You will be given the opportunity to decide whether you want to have these samples collected at the time of each biopsy. Please see Tumor Biopsies and Tumor Effusions below for the risks of a biopsy.

When you are finished taking the drugs

- *Safety Visit*

If you need to stop participating in the study treatment for any reason (including that your disease has started to grow while you are receiving the treatment), then you will be asked to return to the NIH approximately 3 – 6 weeks after you have had last dose of study drug for a safety visit.

The visit will include the following clinical tests:

- Medical history and physical exam including weight
- Routine blood and urine tests
- Pregnancy test if you are a woman who can have children
- ECG
- CT Scans and/or MRI
- Blood for tumor markers

The visit will include the following research tests

- Research blood sample

- *Long term follow up*

This will be encouraged. Only patients who are removed from study therapy for reasons other than disease progression will be asked to return to the NIH (about every 6 weeks) for the required scans and labs until disease progression.

About once a year, regardless of whether your disease has gotten worse, we will contact you or your physician by telephone to ask about any other cancer therapies you may have started and about your survival status.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for at least three months.

You will be seen several times during treatment. The outpatient visits during and after treatment usually take about 3 hours but should not take longer than 8 hours. During long term follow-up after the treatment, we will contact you by phone to ask about your health conditions.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 45 people participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

Because LMB-100 is still being tested for safety, we do not know all the possible side effects. However, below is a list of the most common and most serious side effects occurring on earlier and ongoing studies. Some of these side effects occurred at higher doses of LMB-100 than will be used in this study.

1 *The most common side effects (some were serious) were:*

- Low levels of the blood protein albumin which may lead to swelling, muscle weakness or loss of appetite
- Tiredness
- Swelling of the arms and legs
- Nausea
- Fever
- Decreased appetite
- Shortness of breath
- Pain in muscles
- Increased protein in the urine
- Reactions during or following the infusion of the drug which may cause fever, chills, rash or low blood pressure

2 *Less common, but serious side effects included:*

- Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles. This can include swelling of the heart muscle which has led to temporary lowering of heart function and decreased blood pressure.
- Abnormal heartbeat
- Pain in joints
- Kidney damage which may cause swelling, or could require dialysis
- Heart inflammation which may cause chest pain, swelling and shortness of breath

3 *Other possible side effects*

Other possible side effects discussed below are based on side effects that occurred when testing a similar agent, SS1P and, also in animal studies of LMB-100. It is possible that there may be other unexpected side-effects that occur in addition to those listed below.

LMB-100 may cause inflammation to membranes causing chest pain, shortness of breath, low blood pressure, and heart failure. In animals, some mild kidney damage was seen, that is, increased enzymes and protein in the urine. We will check for this with regular blood and urine tests.

As with other drugs like LMB-100, there is a chance that the drug could cause the body to produce an unwanted response called 'Anti-drug antibodies' (ADAs). These might not cause problems however there is a chance they could lead to a severe anti-drug response in the body.

There may also be pain and swelling at the infusion site.

It is important that you contact your doctor as soon as you experience any side effects whether you think the treatment has caused them or not. You must also tell your doctor if you have started any new medication or had a change to your existing medication. This includes medications available without a prescription (over the counter) and alternative medicines. If you have any questions or concerns about any of the information provided above, about the possible side effects of treatment, or the possible consequences of treatment for those side effects, please ask the principal investigator or the research staff for more information.

The most important symptoms you need to report to your doctor <u>immediately</u> are:

- possible infusion or allergic reactions (symptoms that start during or within a few hours of the infusion, e.g. wheezing, tightness in the throat or chest, rash, and facial swelling)
- chest pain
- shortness of breath
- palpitations (fast heart beat)
- bleeding and high fever
- impaired brain function (e.g., dizziness, blurred vision, confusion)

If you experience any severe or dangerous side effect, you should:

1. Seek professional medical help immediately.
2. Call your study doctor.
3. If necessary, go to the nearest emergency room.

Risks and Possible Side Effects of tofacitinib.

Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, lymphoma and other malignancies,

gastrointestinal perforations, low lymphocyte and neutrophil count, low hemoglobin levels, and elevation of liver enzymes and cholesterol have occurred in patients receiving tofacitinib. Tofacitinib treatment can increase the risk of getting blood clots in the lungs or deep veins of the legs.

Risks from pre-medications and medications to prevent blood clots

Acetaminophen (Tylenol)

Acetaminophen is considered to be safe and effective in the recommended doses. However, when taken incorrectly acetaminophen can cause liver damage. Your risk of liver damage may be increased if you drink more than three alcoholic drinks every day, take more than the recommended dose (overdose), or if you take any additional drugs that also contain acetaminophen at the same time.

Diphenhydramine (Benadryl)

Drowsiness, dizziness, constipation, stomach upset, blurred vision, or dry mouth/nose/throat may occur when taking diphenhydramine.

Ranitidine (Zantac)

Constipation, diarrhea, headache, nausea or upset stomach may occur when taking ranitidine. Rare serious side effects include severe allergic reaction with rash, hives, itching, difficulty breathing; confusion, dark urine, depression, fast or slow heartbeat, unusual bruising or bleeding, yellowing of the eyes or skin (indicating liver damage).

Dexamethasone:

Stomach upset, headache, dizziness, changes in your period, trouble sleeping, increased appetite, or weight gain may occur. Rarely patients using dexamethasone have experienced increased infection, bone/joint pain, thirst, increased urination, irregular heartbeat, eye pain, vision problems, black stools, vomit that looks like coffee grounds, puffy face, swelling of the feet and ankles, pain/redness/swelling of the arms or legs, tiredness, mood changes, unusual hair/skin growth, muscle cramps, weakness, easy bruising/bleeding, slow wound healing, thinning skin and seizures.

Enoxaparin (Lovenox), Rivaroxaban (Xarelto) and Apixaban (Eliquis)

These medications that cause thinning of the blood can increase the risk of bleeding which can be serious or fatal. Allergic reactions are also possible with all three drugs. Allergic reaction to enoxaparin (called HIT for heparin-induced thrombocytopenia) can cause increased risk of blood clotting and decreases in platelets, the cells that clot blood.

Risks from Study Research Procedures

The following study procedures and treatments may have risks and cause discomfort while you participate on this study:

Blood draws

There is the risk of slight pain, bruising or infection when your blood is drawn. Drawing blood may cause some people to faint.

Electrocardiogram (ECGs)

The glue used to keep the electrodes in place during the ECG may irritate your skin and cause redness.

Central Line Insertion

- Contamination of the catheter which would result in a serious blood stream infection, requiring admission to the hospital and giving you antibiotics through the vein.
- Collapsed lung particularly if the central line is placed in the vein under your collarbone. Collapsed lung is treated with a chest tube when necessary.
- During the insertion of some types of central lines, the heart may be irritated by the process while the line travels through the blood vessels near the heart, causing an alteration in the heart's rhythm. This typically gets better once the line is in place but may require medication for some rare individuals.
- Air embolism, a condition where air enters the blood stream and begins to travel through the body. This condition, which is very serious, is also very rare and largely preventable.

Tumor Biopsies and Tumor Effusions

Tumor biopsies and tumor effusions: local anesthesia of the skin will be given prior to any tumor biopsy or effusion collection to prevent painful sensations. However, you may still experience pain or discomfort at the biopsy site. Irritation, redness, swelling and/or bleeding may also occur. There is a risk of abnormal healing, fever, infection or of an allergic reaction to the anesthetic agent used to anesthetize the skin at the biopsy site. Once the sample has been obtained, a stitch may be used to close the wound and assist in healing.

Risks for MRI

Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of the body. We will obtain pictures of your abdomen for this study. The MRI scanner is a metal cylinder surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the cylinder. It is very important for the experiment that you do not move your head or body inside the scanner. We will place soft padding or a coil around your abdomen to help keep it in place. You will be in the scanner about 45-60 minutes. You may be asked to lie still for up to 10-15 minutes at a time. While in the scanner you will hear loud knocking noises, and you will be fitted with earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff at all times during your scan, and you may ask to be moved out of the machine at anytime.

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for

these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks from Gadolinium

Gadolinium is an FDA-approved medication used to improve MRI images. About 98% of patients receiving gadolinium have no symptoms related to the injection of this medication. Mild symptoms that may occur include: coldness in the arm at injection, a metallic taste, headache, and nausea. In an extremely small number of patients, more severe symptoms have been reported including: shortness of breath, wheezing, and lowering of blood pressure.

MRI contrast agents containing gadolinium can cause a rare disease known as Nephrogenic Systemic Fibrosis (NSF) mostly in patients with severe kidney disease. NSF has been nearly eliminated by screening kidney function prior to MRI. To try and avoid NSF, we do not give gadolinium to patients with severe kidney disease in this research study. NSF can cause tight rigid skin, trouble bending joints, pain, weakness, and can scar body organs. NSF is debilitating and may cause death.

Recent reports indicate that some gadolinium may be retained in the brain, bone, and skin. In May 2018, the FDA stated that no harmful effects have been identified related to gadolinium in the brain, but it is continuing to study the issue. You will receive additional information called a "medication guide" about the contrast medication you will receive.

Gadolinium will be administered as clinically indicated. We will check your kidney function before giving you any gadolinium contrast.

What are the risks related to pregnancy?

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 3 months after you finish study treatment (the restricted period). If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails during the restricted period. If you think or know you have become pregnant during the restricted period, please contact the study team as soon as possible.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during the restricted period. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during the restricted period, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after the restricted period, please discuss this with the study team.

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 CT scans, CT-guided biopsies, and chest X-rays. The amount of radiation exposure you will receive from these procedures is equal to approximately 7.28 rem. A rem is a unit of absorbed radiation.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The CT scans, PET scans, CT-guided biopsies, and chest X-rays that you get in this study will expose you to the roughly the same amount of radiation as 23.8 years' worth of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is 0.7 out of 100 (0.7%) and of getting a fatal cancer is 0.4 out of 100 (0.4%).

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. .

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be shrinking of your tumor or lessening of your symptoms, such as pain, that are caused by the cancer. Because there is not much information about the drugs' effect on your cancer, we do not know if you will benefit from taking part in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because of the knowledge gained from this therapeutic intervention.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could:

- get treatment or care for your cancer without being in a study, including standard options
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to receive comfort care, also called palliative care, to relieve symptoms. 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.

You should discuss with your doctor your other choices and their risks and benefits.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

The results from all standard clinical test results will be reported to you. However, we will not return to you results from research studies conducted with your samples.

EARLY WITHDRAWAL FROM THE STUDY

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

- if he/she believes that it is in your best interest
- if your disease worsens or comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if LMB-100 may become unavailable
- if new information shows that another treatment would be better for you
- if you do not follow the study rules
- if the study is stopped for any reason

In this case, you will be informed of the reason therapy is being stopped.

After therapy is stopped we would like to see you for a safety visit 3-6 weeks after your last dose.

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 collaborators or designated representatives.

WILL YOUR SPECIMENS OR DATA BE SAVED FOR USE IN OTHER RESEARCH STUDIES?

As part of this study, we are obtaining specimens and data from you. We plan to use these specimens and data for studies going on right now, as well as studies in the future. These studies may provide additional information that will be helpful in understanding pancreatic cancer, bile-duct cancer, or other mesothelin-expressing solid tumors, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you. By agreeing to let us use your specimens and data, you give the NIH any rights you may have in the samples and data.

We may share your specimens and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or industry sponsors of research.

In addition to the use and sharing of your specimens and data described above, we might remove any information from your samples and data that can identify you such as name, address, or medical record number, and then use the samples and data for additional research studies at the NIH or other places. If we do this, we might not contact you to ask your permission or otherwise inform you.

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your samples. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw the specimens and data.

Please place your initials in the blank next to Yes or No for each of the questions below:

My specimens and data may be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

My specimens and data may be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

How Long Will Your Specimens and Data be Stored by the NIH?

Your samples and data may be stored by the NIH indefinitely.

Risks of Storage and Sharing of Specimens and Data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

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.

The NCI generally does not cover expenses during screening. If you are scheduled for and begin treatment, 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. Someone will work with you to provide 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.

- If some tests and procedures are performed outside the NIH Clinical Center, 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

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

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. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of LMB-100.

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

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

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

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the

insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens and data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

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 information that 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 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, Christine Alewine, Christine.alewine@nih.gov, 240-760-6146. 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

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

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: _____.