THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH

A Phase I Trial of Ipilimumab (Immunotherapy) and MGN1703 (TLR Agonist) in Patients with Advanced Solid Malignancies
2015-0135

Study Chair: David S. Hong

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

STUDY SUMMARY

The goal of this clinical research study is to find the highest tolerable dose of MGN1703 that can be given in combination with ipilimumab to patients with advanced tumors. The safety of this drug combination will also be studied.

This is an investigational study. MGN1703 is not FDA approved or commercially available. It is currently being used for research purposes only. Ipilimumab is FDA approved and commercially available for the treatment of unresectable (cannot be removed with surgery) or metastatic (has spread) melanoma.

The study drug may help to control the disease. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment/prolonged stay out of town.

You can read a list of potential side effects below in the Possible Risks section of this consent.

You may receive MGN1703 in combination with ipilimumab for up to 4 cycles. After that, you may continue taking MGN1703 alone for as long as the doctor thinks it is in

your best interest. You will no longer be able to take the study drug if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

You participation on this study will be over 90 days after your last dose of study drug.

MGN1703 will be provided at no cost to you while you are on study. You and/or your insurance provider will be responsible for the cost of ipilimumab.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive chemotherapy, radiation therapy, and/or surgery. If you have melanoma, you may choose to receive standard ipilimumab treatment without taking part in this study. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will have a physical exam.
- Blood (about 3 teaspoons) will be drawn for routine tests and for biomarker testing (including genetic biomarkers). Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug
- Urine will be collected for routine tests.
- You will have imaging scans (such as magnetic resonance imaging [MRI], bone scans, x-rays, and/or computed tomography [CT] scans) to check the status of the disease.
- You will have an electrocardiogram (EKG) to check your heart function.
- If you can become pregnant, blood (about 1 teaspoon) will be drawn for a pregnancy test. To take part in this study, you must not be pregnant.
- If you are in dose expansion and depending on when you join the study, you will have a core needle tumor biopsy for biomarker testing (including genetic biomarkers). If this applies to you, this will be discussed with you.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other options will be discussed with you.

Study Groups

If you are found to be eligible to take part in this study, you will be assigned to a dose level of MGN1703 based on when you joined this study. Up to 4 dose levels of MGN1703 will be tested. Up to 6 participants will be enrolled at each dose level. The first group of participants will receive the lowest dose level of MGN1703. Each new group will receive a higher dose of MGN1703 than the group before it, if no intolerable

side effects were seen. This will continue until the highest tolerable dose of MGN1703 is found. This is called dose escalation.

In another part of the study (called dose expansion) up to 3 groups of up to 12 additional participants will be enrolled. Two (2) groups will receive MGN1703 at the highest tolerable dose that was found in dose escalation. One (1) group will receive the first dose level of MGN1703 (if it is found to be tolerable). The study doctor will tell you which dose of MGN1703 you will receive.

All participants will receive the same dose level of ipilimumab. You will receive ipilimumab at standard doses.

Up to 60 participants will be enrolled in this study. All will take part at MD Anderson.

Study Drug Administration
Each study cycle is 21 days.

You will be given MGN1703 as an injection under the skin on Days 1, 8, and 15 of each cycle. Each administration will be between 1-4 injections in multiple parts of your body (such as your upper arms and thighs, your abdomen and thighs, or your abdomen and upper arms). The study doctor will tell you how many times you will be injected.

If you are in dose expansion, you may receive MGN1703 as an injection directly into the tumor. The study doctor will tell you if you will receive the study drug this way.

You will also receive ipililumab by vein over about 90 minutes on Day 8 of Cycles 1-4.

Study Visits
During **Week 1 of every cycle,** blood (about 1 teaspoon) will be drawn for routine tests.

During **Week 2 of Cycles 1-4**, you will have a physical exam.

During **Week 3 of Cycles 1 and 3,** blood (about 5 teaspoons) will be drawn for routine tests and biomarker testing.

During **Week 3 of Cycles 2 and 4:**

- Blood (about 5 teaspoons) will be drawn for routine tests and biomarker testing.
- Urine will be collected for routine tests.
- You will have an EKG.
- You will have imaging scans to check the status of the disease.
- If you can become pregnant, blood (about 1 teaspoon) will be drawn for a pregnancy test.

If you are in dose expansion and depending on when you join the study, on Day 1 of Cycle 3 you will have a biopsy for biomarker testing (including genetic biomarkers).

During **Cycle 4 and then every even-numbered cycle after that** (Cycles 6, 8, 10, and so on):

- You will have a physical exam.
- Blood (about 5 teaspoons) will be drawn for routine tests and biomarker testing.
- You will have imaging scans to check the status of the disease. After 1 year on study, you will have these scans every 4 cycles.

During **Cycle 4 and then every 4 cycles after that** (Cycles 8, 12, 16, and so on):

- Urine will be collected for routine tests.
- You will have an EKG.
- If you can become pregnant, blood (about 1 teaspoon) will be drawn for a pregnancy test.

Every **30 days for 90 days** after your last dose of study drug, you will be called by a member of the study staff and asked about any new anticancer drugs you may have started and how you are feeling. You may also be asked these questions during a routine clinic visit or this information may be collected from your medical record. If you are called, each call should last about 10-15 minutes.

Additional Information

- You should talk to your study doctor before taking any new drugs or supplements.
- You cannot receive any vaccinations within 1 month of each ipilimumab dose.
- You cannot receive other cancer treatments, experimental (research) treatments, drugs that affect the immune system, or long-term steroids while taking part in this trial. The study doctor will discuss this in more detail with you.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the study drug/procedures.

MGN1703 Side Effects

This is an early study of MGN1703, so the side effects are not well known. Based on early human and animal studies, MGN1703 may cause:

• fever • dizziness • chills • headache • fatigue/lack of energy	• increased sweating • itching • skin rash • loss of appetite • weight gain • nausea	• vomiting • increased risk of bleeding • pain (muscle/joint) • injection site swelling, pain, and/or heat

The drug may cause a low white blood cell count, which increases your risk of infection, such as pneumonia and/or severe blood infection. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

MGN1703 may also cause an abnormal sensation such as pins and needles. However, this side effect was seen in participants who were also receiving another anticancer drug called oxaliplatin and it is a well-known side effect of that drug. It is unclear if this side effect is a result of oxaliplatin or MGN1703.

Ipilimumab Side Effects

Common (occurring in more than 20% of patients)

• fatigue • headache • itching and/or skin rash • weight loss • nausea • diarrhea	• loss of appetite • vomiting • abnormal digestive blood test (possible inflammation of the pancreas)	• constipation • low red blood cell counts • abnormal liver tests (possible liver damage)

Ipilimumab may cause low red blood cell counts. A low red blood cell count (anemia) may cause difficulty breathing and/or fatigue. You may need a blood transfusion.

Occasional (occurring in 3-20% of patients)

• fever • difficulty sleeping • death of skin tissue and skin sores • very severe blistering skin disease (with loss of large portion of skin) • very severe blistering skin disease (with ulcers of the skin and digestive tract)	• skin rash with blisters or bleeding • pituitary gland failure (possible endocrine gland abnormality) • abdominal pain • inflammation of the intestines • abnormal blood test (possible pancreas	• abnormal liver tests (possible yellowing of the skin and/or eyes) • liver damage • abnormal kidney test (possible kidney damage) • cough • difficulty breathing

	damage)	

Rare but serious (occurring in fewer than 3% of patients)

• blood vessel disease • blood vessel inflammation (possible bleeding and/or bruising) • leakage of fluids from blood vessels into surrounding tissue (possible difficulty breathing) • heart inflammation • inflammation of the tissue around the heart (possible chest pain) • brain inflammation (possible paralysis and/or coma) • immune system damage to the nervous system (causing numbness and/or paralysis) • immune response (causing muscle weakness) • nerve damage (loss of motor or sensory function) • Cushing's syndrome (possible weakness, diabetes, and/or bone weakness) • red, dry, scaly patches of thickened skin (psoriasis)	• skin rash (possible fever/lymph node swelling/inflammation of internal organs/abnormal blood cell counts) • allergic skin reaction • inflammation of the thyroid gland (possible tenderness in the neck) • decreased production of adrenal hormones (possible weakness and/or low blood pressure) • overactive thyroid gland (possible weight loss, heart rate changes, and/or sweating) • underactive thyroid gland (possible weight gain, heart failure, and/or constipation) • hole in the intestines (possibly leaking contents into the abdomen) • inflammation of the pancreas (possible abdominal pain) • stomach and/or small intestine ulcer	• anemia due to destruction of red blood cells • bone marrow failure due to abnormal tissue growth • liver failure • liver damage due to inflammation • muscle inflammation and weakness • inflammation inside the eye (possible vision problems) • partial hearing loss • kidney failure • bronchiolitis obliterans (damage of the small airways with difficulty breathing) • lung inflammation (possible difficulty breathing) • multi-organ disease causing lesions, most often in the lungs • severe life-threatening infection (possible low blood pressure, kidney failure, and/or heart failure) • immune response • infection

Ipilimumab may cause dehydration that may be severe enough to require hospitalization.

Ipilimumab may cause an increased risk of infection, such as pneumonia. This infection may occur anywhere (such as the brain/spinal cord, lungs, and/or blood). It may become life-threatening. Symptoms of infection may include fever, pain, redness, and difficulty breathing.

Other Risks

Using the study drugs together may cause side effects that are not seen when each is given alone. The study drug combination may also increase the frequency and/or severity of the side effects, which may delay further standard treatment of your disease.

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.

The type of **genetic testing** being performed in this study will not provide you or your doctor information about diseases that are passed down in families. It will not tell the study researchers anything that will prevent you from getting health insurance, and it will not tell the study researchers anything about any diseases or conditions you may get in the future.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study and at least 2 months after your last dose of study drugs if you are sexually active.

Birth Control Specifications: Acceptable forms of birth control include:

- Intrauterine device (IUD) or birth control pills, implants, or injections (such as Norplant® or Depo-Provera® started at least 3 months before joining the study) plus a barrier method, such as a condom or diaphragm
- Double-barrier methods, such as a condom used in combination with a diaphragm

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or Mologen for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. David S. Hong, at 713-563-1930) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, Mologen, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: Mologen.

10. In a medical emergency, you may be cared for by someone who has a financial interest with the study sponsor(s)/supporter. If you have any questions about this, you may call the IRB at 713-792-6477.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and Mologen and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by Mologen may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing

is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:

- Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
- The IRB and officials of MD Anderson
- Mologen, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
- any future sponsors and/or licensees of the study technology and National Institute of Health (NIH)/Office of Biotechnological Activities (OBA)/Recombinant DNA Advisory Committee (RAC)
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol **2015-0135.**

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people

(Name of Language)

obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____

NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, PARENT/GUARDIAN, OR STUDY CHAIR) DATE