MC1572 / 16-002965

Phase II Study of Pembrolizumab (MK-3475) in Combination With Standard Therapy for Newly Diagnosed Glioblastoma

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MAYO CLINIC

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: MC1572, Phase II Study of pembrolizumab (MK-3475) in combination with standard therapy for newly diagnosed glioblastoma

IRB#: 16-002965

Principal Investigator: Dr. Ian Parney and Colleagues

Please read this information carefully. It tells you important things about this research study. A member of our research team will talk to you about taking part in this research study. If you have questions at any time, please ask us.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- You are free to change your mind at any time if you choose to participate.
- Your decision won't cause any penalties or loss of benefits to which you're otherwise entitled.
- Your decision won't change the access to medical care you get at Mayo Clinic now or in the future if you choose not to participate or discontinue your participation.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you a copy of this form to keep. A copy of this form will be put in your medical record.

CONTACT INFORMATION

You can contact …	At …	If you have questions about …
Principal Investigator: Ian F. Parney, M.D., Ph.D. (Minnesota) Alyx B. Porter, M.D. (Arizona)	**Phone:** Minnesota: (507) 284-2511 Arizona: (480) 301-8000 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905 Mayo Clinic Hospital 5777 E. Mayo Boulevard Phoenix, AZ 85054	▪ Study tests and procedures ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints ▪ Withdrawing from the research study ▪ Materials you receive ▪ Research-related appointments
Mayo Clinic Institutional Review Board (IRB)	**Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681	▪ Rights of a research participant
Research Participant Advocate (The RPA is independent of the Study Team)	**Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu	▪ Rights of a research participant ▪ Any research-related concerns or complaints ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study
Patient Account Services	**Toll-Free:** (844) 217-9591	▪ Billing or insurance related to this research study

Other Information:
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.

1. Why are you being asked to take part in this research study?

You are being asked to participate in this study because you have been diagnosed with a brain tumor called glioblastoma.

The plan is to have about 52 people take part in this study at Mayo Clinic.

2. Why is this research study being done?

In this study, we want to find out more about how effectively a new drug for cancer called pembrolizumab fights against your tumor, when combined with standard chemotherapy and radiation. We also want to find out how safe and tolerable this combination is since there are limited clinical data to support the safety of combining pembrolizumab with radiation therapy (RT) or temozolomide (TMZ), the standard treatment for glioblastoma. Everyone in this study will receive pembrolizumab, which is experimental in the treatment of this cancer. This drug is approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with melanoma, lung cancer, kidney cancer, colorectal cancer, and several other types of cancer. It is not approved by the FDA for brain cancers. However, the FDA has allowed the use of this drug in this research study.

3. Information you should know

Who is Funding the Study?
Merck & Co. and Mayo Clinic are funding the study. Merck will pay Mayo Clinic to cover costs related to running the study.

4. How long will you be in this research study?

This study will last approximately three years. You will be in the study for as long as your cancer is responding to the treatment and you are not having side effects that cannot be managed.

5. What will happen to you while you are in this research study?

Before starting this study

Before starting this study, you will participate in a screening period. The screening period will help the study doctor find out if you are eligible to enter the study. You will need to have the following exams, tests or procedures as part of your standard clinical care to find out if you can be in the study:

- Physical exam including complete medical history, height, weight and vital signs
- ECOG performance status (assessment of your ability to carry out daily activities)
- Routine blood and urine tests
- Pregnancy test if you are a woman who is able to become pregnant
- Consultation with a radiation oncologist
- Consultation with a neurosurgeon
- Consultation with a medical oncologist
- MRI scan of your brain
- Stereotactic biopsy of your tumor, if not done previously

These exams, tests or procedures are part of regular clinical care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This decision will be up to the Principal Investigator.

You will also have the following required tests which are part of the research study:

- Research blood tests (32 ml or about 2.5 tablespoons)
- Research tissue samples (taken during the biopsy or from your previous surgery)

While you are on this study

Treatment on this study will be divided into two groups:
Group 1 for neoadjuvant patients who will have surgical resection of their cancer at Mayo Clinic and
Group 2 for adjuvant patients who have already had a surgical resection of their cancer.

Pembrolizumab is given through a needle in a vein in your arm. You have to come to the clinic for these infusions.

Temozolomide is pills or tablets that you take once a day at home. Temozolomide is part of regular cancer care for glioblastoma. The study staff will tell you when and how to take your temozolomide. You may be given other medicines to take with the temozolomide to help with nausea or other side effects.

For Group 1:
The treatment portion will be divided into four stages:

1) Neoadjuvant treatment with pembrolizumab (Cycle 1)
2) Surgery to remove your tumor and a rest period prior to starting radiation therapy (RT) (Cycle 2)
3) Concurrent treatment with temozolomide and radiation therapy and pembrolizumab (Cycle 3)
4) Adjuvant treatment with temozolomide and pembrolizumab (Cycles 4-8)

Cycle 1 (Neoadjuvant): Prior to surgery-one dose of pembrolizumab will be given with an IV infusion.

Cycle 2 (Surgery): You will have surgery to remove your tumor about four days after you receive pembrolizumab.

Cycle 3 (Concurrent): Starting 3-4 weeks after your surgery and along with standard radiation therapy (RT) and daily temozolomide (beginning on Day 8 after RT starts), pembrolizumab will be given Day 1, Day 22 and Day 43 of a 53 day cycle.

Cycles 4-8 (Adjuvant): Starting 4-5 weeks after completing radiation, pembrolizumab be given Days 1, 22 and 43 (in 63 day cycles for up to 5 cycles) combined with standard therapy using temozolomide chemotherapy.

As part of your regular cancer care, you will take temozolomide (TMZ) every day for five days in a row every four weeks. If the temozolomide causes any side effects, your physician may decrease the dose, delay treatment, or eliminate any remaining doses of temozolomide per standard treatment. We will give you diaries to help you track your temozolomide doses. Please remember to bring your diaries and your pill bottles with you to every appointment.

For Group 2:

The treatment portion will be divided into two stages:

1) Concurrent treatment with temozolomide and radiation therapy and pembrolizumab (Cycle 1)
2) Adjuvant treatment with temozolomide and pembrolizumab (Cycles 2-6)

Cycle 1 (Concurrent): Starting 3-4 weeks after your surgery and along with standard radiation therapy (RT) and daily temozolomide (beginning on Day 8 after RT starts), pembrolizumab will be given Day 1, Day 22 and Day 43 of a 53 day cycle.

Cycles 2-6 (Adjuvant): Starting 4-5 weeks after completing radiation, pembrolizumab be given Days 1, 22 and 43 (in 63 day cycles for up to 5 cycles) combined with standard therapy using temozolomide chemotherapy.

As part of your regular cancer care, you will take temozolomide (TMZ) every day for five days in a row every four weeks. If the temozolomide causes any side effects, your physician may decrease the dose, delay treatment, or eliminate any remaining doses of temozolomide per standard treatment. We will give you diaries to help you track your temozolomide doses. Please remember to bring your diaries and your pill bottles with you to every appointment.

Table for Group 1 (Neoadjuvant Patients)

Timing	What will happen
Pre-Study	- Complete medical history and physical exam including vital signs (height, weight, blood pressure, temperature, etc.) - Routine blood and urine tests - Routine pregnancy test for women of childbearing potential - Routine brain MRI - Research blood collection (~3.5 tablespoons) - Stereotactic biopsy and research tissue sample collection
Cycle 1 Neoadjuvant (25 days)	- Pregnancy test (women of childbearing potential) only if more than 7 days since previous test - Treatment with pembrolizumab one time prior to surgery
Cycle 2 Surgery and rest period prior to RT	- Surgery to remove your cancer - Research blood collection (~3.5 tablespoons) ≤7 days prior to RT
Cycle 3 Concurrent treatment with temozolomide, radiation therapy, and pembrolizumab (up to 54 days)	- Routine tests and exams Day 1 prior to treatment with pembrolizumab - Treatment with pembrolizumab Days 1, 22 and 43 - Temozolomide starting Day 8 and continuing daily until end of RT - Radiation therapy (RT) every weekday (Monday through Friday) beginning Day 8

Timing	What will happen
Cycles 4-8 Adjuvant therapy (Each cycle is 63 days)	- Prior to treatment on Cycle 4, Day 1: Research blood and samples - Prior to treatment on Day 1 of each cycle: o Routine blood and urine tests o Routine physical exams and MRI scan - Treatment with pembrolizumab Days 1, 22, 43 of each cycle - Treatment with temozolomide 5 days every 28 days
End of treatment for any reason	- Routine blood and urine tests and exams
Observation (30 days after last dose of pembrolizumab)	- Routine tests and exams - Research blood samples

Table for Group 2:

Timing	What will happen
Pre-Study	- Complete medical history and physical exam including vital signs (height, weight, blood pressure, temperature, etc.) - Routine blood and urine tests - Routine pregnancy test for women of childbearing potential - Routine brain MRI - Research blood collection (~3.5 tablespoons) - Stereotactic biopsy and research tissue sample collection
Cycle 1 Concurrent treatment with temozolomide, radiation therapy, and pembrolizumab (up to 54 days)	- Routine tests and exams Day 1 prior to treatment with pembrolizumab - Treatment with pembrolizumab Days 1, 22 and 43 - Temozolomide starting Day 8 and continuing daily until end of RT - Radiation therapy (RT) every weekday (Monday through Friday) beginning Day 8
Cycles 2-6 Adjuvant therapy (Each cycle is 63 days)	- Prior to treatment on Cycle 4, Day 1: Research blood and samples - Prior to treatment on Day 1 of each cycle: o Routine blood and urine tests o Routine physical exams and MRI scan - Treatment with pembrolizumab Days 1, 22, 43 of each cycle - Treatment with temozolomide 5 days every 28 days
End of treatment for any reason	- Routine blood and urine tests and exams
Observation (30 days after last dose of pembrolizumab)	- Routine tests and exams - Research blood samples

Both Groups 1 and 2:
If your tumor comes back, we would like to obtain additional research blood samples. If you have another biopsy at this time, we would like to obtain additional research tissue samples.

6. What are the possible risks or discomforts from being in this research study?

Risks and side effects of pembrolizumab (MK-3475)
Pembrolizumab works by helping your immune system to fight your cancer. However, pembrolizumab can also cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e., causing hospitalization or be life-threatening), may result in death, and/or may occur after you stop taking pembrolizumab. These side effects can affect more than one of your normal organs and tissues at the same time.

Very common side effects (>10%) seen in people taking pembrolizumab include the following:

- Itching of the skin
- Frequent or excessive bowel movements or diarrhea
- Cough

Common side effects (5-20%) seen in people taking pembrolizumab include the following:

- Pain in joints (arthralgia)
- Rash
- Fever
- Back pain
- Pain or uncomfortable feeling in the belly
- Loss of skin color (vitiligo)
- Low levels of salt in the blood (hyponatremia) that may cause you to feel confused, have a headache, have pain or cramping in a muscle or group of muscles, or make you feel sick to your stomach
- Decreased release of thyroid hormone that may appear as feeling tired, weight gain, feeling cold easily, or bowel movements occurring less often than usual

Uncommon (less than 5%) side effects seen in people taking pembrolizumab include the following

- Inflammation of the lungs (pneumonitis) – you may feel short of breath and cough
- Increased release of thyroid hormone which may cause anxiety, irritability, or trouble sleeping, weakness, trembling, sweating, feeling uncomfortable in warm weather, fast or uneven heartbeats, feeling tired, weight loss, and frequent or excessive bowel movements.
- Severe infusion reaction, which may be life-threatening - you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e., peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection (Severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis syndrome (TENS))

Rare (*No event occurred in >1% of everyone treated with pembrolizumab*)

- Inflammation of the pancreas - symptoms may include: abdominal pain that radiates to the back, swollen or tender abdomen, fever, nausea and vomiting (pancreatitis)
- Inflammation of the muscles that may result in weakness or pain in the muscles (myositis)
- Inflmmation of the eye - you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters, or have headaches (uveitis)
- Inflammation of the kidneys causing them not to work as well, you may pass less urine, cloudy or bloody urine, have swelling and low back pain (nephritis)
- Inflammation of the pituitary gland, which may cause headache, nausea, vomiting, a sensation of the room spinning around you (dizziness), changes in behavior, double vision, few to no menstrual cycles, or weakness (hypophysitis)
- Inflammation of the liver which may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, a mild pain in the right side of your belly, cause yellowing of the skin or eyes and dark urine (hepatitis)

- Adrenal glands (glands on top of the kidneys) may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, having joint, muscle, and bellyaches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type 1 diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination, and weight loss – you may need to take insulin
- Inflammation of the heart muscle (middle layer of your heart), usually caused by infection which may be serious and require hospitalization. may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath, and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (immune-mediated myorcarditis)
- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- Lambert-Eaton Myasthenic Syndrome, myasthenia gravis, or worsening of existing myasthenia gravis (nerve damage that causes muscle weakness and muscle fatigue) may make you feel weak and tired and may cause drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- Guillain-Barre Syndrome - Inflammation of the nerves that may cause pain, weakness, or tingling in your hands and feet, and may spread to your legs, arms, and upper body, leading to severe muscle weakness and possible temporary paralysis
- Formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoidosis)
- Vasculitis – inflammation of the blood vessels – symptoms will depend on the blood vessels involved - for example, if it is your skin you may have a rash. If your nerves are not getting enough blood, you could have numbness or weakness, and may cause fever, weight loss, and fatigue
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord (with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, or constipation (myelitis))
- Low levels of parathyroid hormone (a hormone made by 4 tiny glands in your neck) which may result in low blood calcium and cause muscle cramps or spasms; fatigue or weakness; numbness, tingling, or burning in your fingertips, toes or lips (hypoparathyroidism)

- Inflammation of the stomach (gastritis). You may have pain in your belly, feel full, or sick to your stomach. You may also experience nausea, vomiting or loss of appetite.
- Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, or have a fast heartbeat. You may also have difficulty with physical exercise, pale or yellow skin, dark urine, or fever.
- Not enough pancreatic enzymes (proteins that break down food) that leads to poor digestion of food (exocrine pancreatic insufficiency). You may have bloating, gas, discomfort in your belly, diarrhea, abnormal stool that is oily, or weight loss.

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of this side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This reaction may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis (HLH))
- Vogt-Koyanagi-Harada (VKH) Syndrome – an immune response of skin cells (melanocytes) which affects eyes, ears, nervous system and skin; damage from VKH may be permanent
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver) - which can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis)
- Optic neuritis – may have pain when moving your eyes, sudden temporary loss of vision, loss of color vision, and/or loss of peripheral vision in one or both eyes

We do not know all the side effects that may occur with pembrolizumab. The side effects of pembrolizumab may cause delays to your treatment with radiation and/or chemotherapy with temozolomide and may also delay your surgery.

Patients with brain tumors and patients who have had prior brain radiation therapy may be at increased risk for neurotoxicities (nervous system side effects) that can also be associated with pembrolizumab including cerebral edema. There is a risk you may not be able to receive all the

radiation therapy and/or temozolomide doses, which have been shown to prolong survival for patients with newly diagnosed glioblastoma.

Other less common side effects have been reported. The study doctor or staff can discuss these with you.

It has been reported that immune-related side effects from pembrolizumab including some that could be life-threatening can occur even after patients are no longer taking the drug.

There may be other side effects or risks that are not known at this time.

Standard of Care Risks
Your doctor will discuss the risks of these tests and procedures, which are part of regular care for your cancer:

- MRI or CT scans
- Biopsy and/or surgery to remove the cancer
- Chemotherapy with temozolomide, such as decreased white blood cell count (which may make you more likely to get an infection)
- Radiation therapy

Other Risks

Blood draws
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Pregnancy and Birth Control:
It is not known if the study drugs may affect an unborn or nursing baby or if the study drugs have an effect on sperm. Chemotherapy can cause harm to an unborn child. If you are pregnant, trying to become pregnant or breast-feeding, you may not be in the study. The study doctor will perform a blood or urine pregnancy test before the start of and during the study, if you are able to have a baby.

For Persons Able to Become Pregnant
If you are sexually active and able to become pregnant, you must agree to use **one** of the birth control methods listed below:

- Intrauterine device (IUD)
- Vasectomy of a female subject's male partner
- Contraceptive rod implanted into the skin

OR

You must agree to use **two** of the methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, or vaginal ring
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- For persons able to become pregnant who have never given birth to a child the following options are also allowed in combination with another method:
    - Cervical cap with spermicide
    - Contraceptive sponge

You must use birth control for the entire study and for at least 120 days after your last dose of pembrolizumab.

If you miss a period, or think you might be pregnant during the study, you must tell the Principal Investigator immediately. The Principal Investigator may ask for your permission to collect information about the outcome of your pregnancy and your newborn.

For Persons Able to Father a Child

If you are sexually active, and able to father a child, you must agree to use **one** of the birth control methods listed below:

- Vasectomy
- Intrauterine device (IUD) used by female partner
- Contraceptive rod implanted into the skin of female partner

OR

You must agree to use **two** of the methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, or vaginal ring used by female partner
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)

You must use birth control for the entire study and for at least 120 days after your last dose of pembrolizumab.

If your partner thinks she might have become pregnant while you are in the study or for 30 days after your last dose of pembrolizumab, you must tell the Principal Investigator immediately.

The Principal Investigator may ask for your partner's permission to collect information about the outcome of her pregnancy and her newborn. You won't have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Risk Summary
Many side effects go away shortly after the pembrolizumab is stopped, but in some cases side effects can be serious, long lasting, or may never go away There may be a risk of death. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

7. Are there reasons you might leave this research study early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- if the study is stopped.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

8. What if you are injured from your participation in this research study?

Where to get help:

If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

9. What are the possible benefits from being in this research study?

This study may not make your health better. However, it may help other cancer patients in the future.

10. What alternative do you have if you choose not to participate in this research study?

You don't have to be in this study to receive treatment for your condition. Your other choices may include:

- Treatment for your cancer without being on a study
- Treatment on a different research study
- No treatment

Talk to the Principal Investigator or your doctor if you have any questions about any of these choices.

11. What tests or procedures will you need to pay for if you take part in this research study?

You will not need to pay for tests and procedures which are done just for this research study.

These tests and procedures are:
- Study drug pembrolizumab
- Research testing on your blood and tumor tissue

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular medical care. These tests and procedures include:
- Biospy of your cancer, if needed for your care
- Craniotomy and tumor resection, if not done previously
- Clinical blood tests
- Exams and consults
- Pregnancy tests (if applicable)
- Brain MRIs or CTs
- Administration of study drug (pembrolizumab)

Before you take part in this study, you should call your insurer to find out if the cost of these tests and/or procedures will be covered. Some insurers will not pay for these costs. You will have to pay for any costs not covered by your insurance, Including copayments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

12. Will you be paid for taking part in this research study?

You will not be paid for taking part in this study.

13. What will happen to your samples?

Submission of blood and tissue samples is required to take part in this study. These samples will be collected prior to starting the study, at the time of surgery to remove the cancer, and at the end of your treatment on this study. We would also like to get a blood sample if your cancer comes back.

In addition, we would like to keep your sample for future research. You can still take part in this current study even if you don't want your sample used for future research. If you agree to give your sample, it will be the property of Mayo Clinic.

Other researchers at Mayo Clinic who aren't involved with this study may ask to use your sample for future research. Researchers at other institutions may also ask for a part of your sample for future studies. Your sample will be sent to researchers in a coded format, which protects your identity.

Some future studies may examine your DNA, which is the genetic information you inherited from your parents (genetic testing). The Principal Investigator may contact you if there are findings which may be useful for your health care. You would be given general information on the potential risks, benefits, and costs of choosing to learn about the findings.

Please read the following statements and mark your choices:

1. I permit my sample to be stored and used in future research of brain cancer at Mayo Clinic:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo Clinic to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

3. I permit Mayo Clinic to give my sample to researchers at other institutions:

☐ Yes ☐ No Please initial here: _____Date: _____

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you won't be offered a share in any profits.

You may request to have your sample destroyed by writing to the Principal Investigator. The address is found in the "Contact Information" section of this consent form.

Because we cannot predict how your sample will be used in the future, we cannot promise that samples can be retrieved and destroyed.

14. How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

Various methods are used to safeguard confidentiality. Some or all of the following may be used in this study: assigning a specific code or registration number to each participant's data and samples, research materials stored in locked areas, password protected data stored on a computer. If the results of the research are made public, information that identifies you will not be used.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so.

Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission.

Health information may be collected about you from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Why will this information be used and/or given to others?

- To do the research.
- To report the results.
- To see if the research was done correctly.

If the results of this study are made public, information that identifies you will not be used.

Who may use or share your health information?

- Mayo Clinic research staff involved in this study.

With whom may your health information be shared?

- The Mayo Clinic Institutional Review Board that oversees the research.
- Other Mayo Clinic physicians involved in your clinical care.
- Researchers involved in this study at other institutions.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other US or government agencies in other countries) that oversee or review research.
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- A group that oversees the data (study information) and safety of this research.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy, however once your information is shared outside Mayo Clinic we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Privacy Rights

You do not have to sign this form, but if you do not, you cannot take part in this research study. If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your own doctors or with Mayo Clinic.

You can cancel your permission to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number, and /or study name, and
- Your contact information.

Your permission lasts forever, unless you cancel it.

ENROLLMENT AND PERMISSION SIGNATURES:

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature