Trial Using Pembrolizumab and a Vaccine to Determine if Survival Improves

A Study for Newly Diagnosed Glioblastoma Patients

What is a glioblastoma?

Glioblastomas are highly malignant (cancerous) tumors that arise from astrocytes (supportive cells) in the central nervous system (brain and spine).

What is standard treatment for glioblastoma?

The standard treatment for glioblastoma is to have surgery to remove as much of the tumor as possible, followed by radiation therapy and chemotherapy (a drug called Temozolomide). This treatment course is outlined on the standard treatment timeline chart on the right.

What is the purpose of this study?

The purpose of this study is to find out if adding immunotherapy (Pembrolizumab) with or without a vaccine (HSPPC-96) to standard treatment for glioblastoma improves survival.

- **Vaccines:** Vaccines are substances that stimulate the body's immune system and when injected into a patient, it may cause their body's immune system to attack cancer cells.
- **Pembrolizumab:** Pembrolizumab is an antibody drug that has been approved for use in other cancers, but has not yet been approved to treat glioblastoma. This antibody drug may help the cells that are already in your body to fight the cancer cells.

How will they create the vaccine?

You will first have a surgery to remove the tumor. Once you undergo surgery, the tissue removed during surgery will first be used to confirm the glioblastoma diagnosis. The remaining tissue will be sent to Agenus, the manufacturer that will create a vaccine that is prepared specifically from your tumor.

If the surgeons are unable to obtain enough tumor to make the vaccine, you will be assigned to group 1. If enough vaccine was created, you will be assigned to group 2 or 3 (more details shown on the next page). If your tumor does not meet certain criteria, you will be removed from the study and not receive any additional treatment on this study.

Standard Treatment Timeline

Surgery

Radiation Therapy + Chemotherapy
(given daily over 6 weeks)

Chemotherapy
(given daily for 5 consecutive days every 28 days for 6 months to one year)

What will happen during the study?

Your study doctor will not know if you are eligible to take part in the study until tissue tests are completed. This process may take several weeks after your surgery and your doctor will let you know if you are eligible before radiation begins.

Group 1: If your tumor does not provide adequate vaccine, then you will be assigned to group 1.

Group 2 and 3: If you are eligible and once your radiation is almost complete, you will be randomly assigned to group 2 or 3. Randomly means by chance. You will have a 50-50 chance of being in group 2 or 3. If you are randomly assigned to group 2, you will be receiving the active vaccine treatment. If you are randomly assigned to group 3, you will not be receiving the active vaccine treatment. **You and your doctor will not know if you have been assigned to group 2 or group 3.**

A = Active
P = Placebo

A placebo is a pill that looks like the study drug but is not.

A OR P

You will be assigned to one of these groups:

Group 1:

Radiation + Chemotherapy + Pembrolizumab

Group 2:

Radiation + Chemotherapy + Pembrolizumab + HSPPC-96 Vaccine

A

Group 3:

Radiation + Chemotherapy + Pembrolizumab + Placebo Vaccine

P

What are the possible risks?

Some possible risks include side effects from the study drugs, surgery, or radiation therapy, which are found in the consent document. Possible risks will be discussed with you in detail by the NIH health care team.

What are the possible benefits?

Because there is not much information about the drug or vaccine's effect on glioblastoma, we do not know if you will benefit from taking part in this study.

You may benefit from this study in the following ways:

- your tumor may shrink
- your symptoms, such as pain, that are caused by the cancer may lessen
- you may help others in the future who have cancer

How long will I take part in the study?

We expect that you will be participating in this study for up to 2 years. For 1 year, you will receive study treatment, plus an additional year if your doctor feels that you are benefiting from Pembrolizumab.

What happens if I decide to quit the study?

You may decide to stop taking part in the study at any time and withdraw your consent for any reason. Taking part in a NIH study is entirely voluntary. However, to receive care at the NIH, you must be taking part in a research study or be under evaluation for study participation.

What is the treatment for this study?

If you decide to participate in this study, you will receive standard treatment (outlined on the first page) and additional study treatment.

Step 1: You will sign a consent form, then have screening tests to determine that you can have surgery and that you are healthy except for your tumor. These tests are part of regular surgical care. Within 14 days approximately from signing your consent, you will have surgery.

Step 2: After surgery, you will have some time to recover. During this time (3-6 weeks approximately), the tissue removed during your surgery will be tested to confirm your diagnosis and determine if you are eligible to continue with the study. If eligible, you will then receive standard treatment (radiation and chemotherapy) and Pembrolizumab (3 separate infusions during radiation over 6 weeks).

Step 3: After 6 weeks of standard treatment and Pembrolizumab, Agenus will inform the study team if there was enough tumor to make the vaccine. You will be assigned to a group (see previous page). If you are in group 1: you will have a break; group 2: you will receive the HSPPC-96 vaccine; group 3: you will receive the Placebo vaccine. The HSPPC-96 vaccine or Placebo vaccine is given weekly for 4 weeks. You will then begin standard therapy (chemotherapy) and Pembrolizumab (infusion given once every 3 weeks) with or without vaccine for 54 weeks (or 6 cycles, each cycle is 9 weeks). If you are in group 1: no vaccine; group 2: you will receive the HSPPC-96 vaccine; group 3: you will receive the Placebo vaccine. The HSPPC-96 vaccine or Placebo vaccine is given by injection twice per cycle.

This additional study treatment course is outlined on the timeline chart on the right.

What are the costs of taking part in this study?

If you take part in this study at the NIH, you will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the NIH.

Can I take part in this study?

People who are recently diagnosed with (or have a suspected) glioblastoma and are eligible for surgery.

All research studies have specific guidelines on who can or cannot take part. Before you can take part, your doctor will review the study requirements and details with you. If you meet the requirements and decide to participate, we will ask you to sign a consent form and you may have screening tests.

Whom can I contact for more information?

National Institutes of Health
Brain Tumor Trials Collaborative Research Nurse: 240-760-6060

Your Care Team *(insert your care team's contact information below)*

Radiation Oncologist _____

Neurosurgeon _____

Neuro-Oncologist _____

Other Care Team _____

Other Care Team _____

Trial Timeline

STEP 1

Consent > Screening > Surgery
(14 days)

STEP 2

Surgery Recovery >
Diagnosis/Eligibility
Confirmation
(3-6 weeks)

Standard Treatment
+ Pembrolizumab
(6 weeks)

STEP 3

Vaccine Production
Success/Failure >
Break or
HSPPC-96 or Placebo Vaccine*
(4 weeks)

Standard Treatment
+ Pembrolizumab
+ HSPPC-96 or Placebo Vaccine*
(54 weeks)

**Given if assigned to group 2 or 3*

Learn more about this trial by visiting: **clinicaltrials.gov** ID: NCT03018288.