Recurrent Glioblastoma Clinical Trial

Patient Study Guide

ReSPECT™ CLINICAL TRIALS

PLUS™ THERAPEUTICS

National Trial Reference Number: **NCT01906385**

ReSPECT™
CLINICAL TRIALS

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Introduction

What is the ReSPECT Recurrent Glioblastoma (ReSPECT-GBM) Clinical Trial?

Plus Therapeutics is developing a new targeted radiation therapy, **Rhenium (^{186}Re) Obisbemeda**, for central nervous system cancers such as Recurrent Glioblastoma. This clinical trial is for cancer patients with a glioma (type of brain tumor) that has come back after standard treatment options like surgery, radiation, or chemotherapy.

This FDA-approved **Phase 2** clinical trial can enroll up to 30-40 patients and is a prospective, multicenter, and open-label trial.

In this trial, the study doctor will give Recurrent Glioblastoma patients a single dose of Rhenium (^{186}Re) Obisbemeda, a specially designed radioactive drug.

The ReSPECT-GBM clinical trial is funded, in part, by the National Institutes of Health (NIH).

Clinical Study Plan

- This clinical research study is currently enrolling Phase 2 patients to evaluate the effectiveness of the investigationa treatment of Rhenium (^{186}Re) Obisbemeda.
- Rhenium (^{186}Re) Obisbemeda is given to the patient through tiny tubes placed into the skull by a skilled neurosurgeon.

  This tube is called a CED, or Convection-Enhanced Delivery, catheter and allows the therapeutic radiation to be delivered directly to the spot of the tumor with minimal or no harmful radiation exposure to healthy brain tissue (unlike traditional external beam radiation therapy).

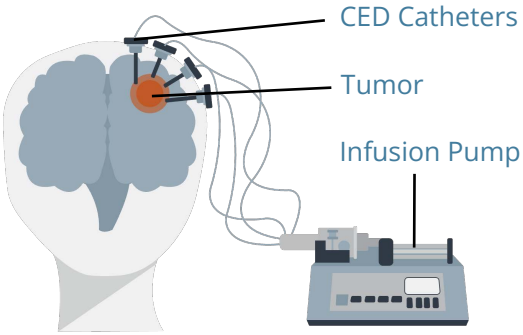
- This study consists of at least 9 visits with the researchers or study staff & the total length of the active part of the study fo each participant will be a minimum of 31 weeks.

Introduction (cont.)

What is the Rhenium (^{186}Re) Obisbemeda Treatment?

This study involves using an investigational treatment called **Rhenium (^{186}Re) Obisbemeda.** Rhenium-186 is a radioactive isotope of the element Rhenium which is intended to kill cancer cells.

The Rhenium is placed inside a "nano-liposome" carrier, which is a thin, bubble-like membrane that is like the material which makes up the membranes in your cells. Nanoliposomes increase the time that radiation is emitted to the tumor and have been **used in cancer treatment for over 25 years.**



About Targeted Radiotherapeutics

Receiving Rhenium (^{186}Re) Obisbemeda involves radiation, like x-rays. However, unlike x-rays, which require the use of a machine, multiple visits, and only administer a small dose of radiation due to potential toxicity to healthy cells, this targeted radiotherapeutic delivers a higher, single dose of "liquid radiation" directly to the tumor using a microcatheter. The radiation is concentrated on your tumor site via local, direct delivery, hence why this is known as a "Targeted Radiotherapeutic."

Please consult your physician for any questions or concerns regarding this radiation type.

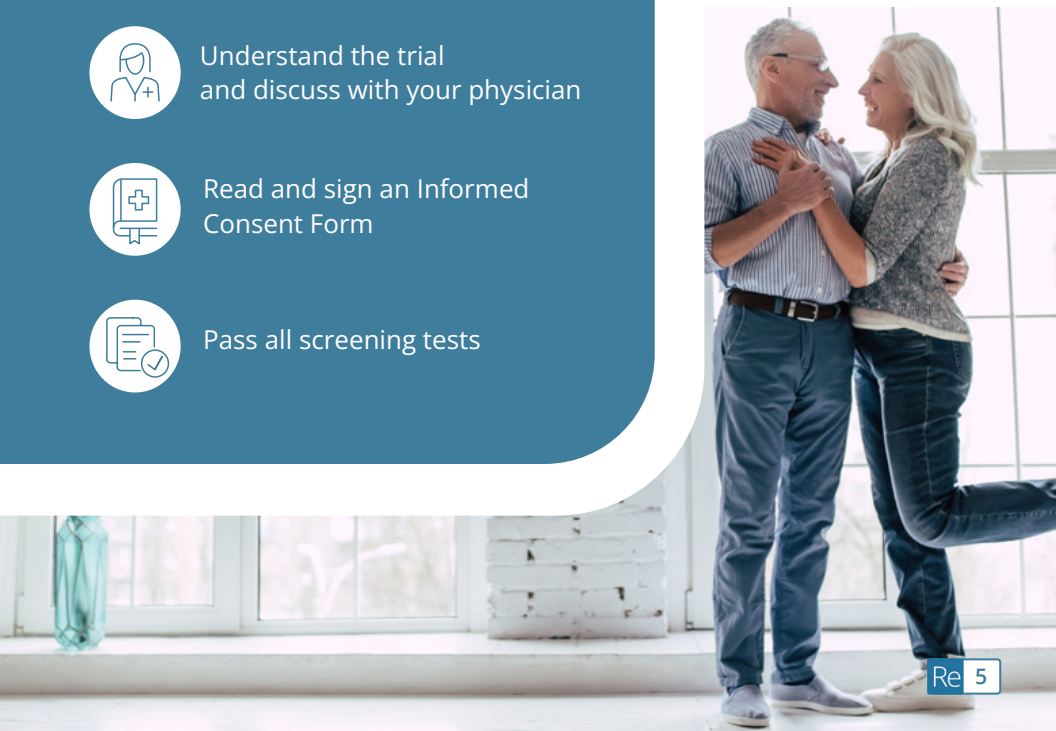
Study Inclusion Criteria

You may qualify if you meet the following criteria:

- 18 years old or older, any gender
- Able to undergo an MRI scan
- Able to walk about, capable of self-care (Karnofsky Performance Status ≥ 60)
- Have a life expectancy of at least 2 months.
- Diagnosed with recurrent Glioma of Grade III/IV *(confirmed by histology)* and within the treatment field volume *(< 20 cm^3)*
- Have acceptable kidney, liver, and hematological (blood) function

If you meet the criteria above you will need to:

- Understand the trial and discuss with your physician
- Read and sign an Informed Consent Form
- Pass all screening tests



Study Exclusion Criteria

You will be disqualified from this clinical trial if any of these apply:

- Acute internal bleeding in the brain or around the tumor
- Serious concurrent illness which would compromise your safety of the safety of the study
- Cancer progression in multiple areas *(multifocal)*
- Non-standard radiation therapy at the tumor target site
- Radiation therapy within 12 weeks of screening
- Prior Bevacizumab (Avastin) use at any point in time

Your physician will be able to **discuss the full list** of study qualifications and disqualifie

Summary Of Visits

A summary of visits for each subject is divided as follows:

- Screening period (up to 5 weeks)
- Up to 6 weeks for surgery, dosing, and recovery
- 4-week evaluation periods for toxicity and disease assessment

What are the Medical Screening Tests?

Within 35 days before Day 1 (Treatment Day)

The following screening tests will help us decide if you are eligible:

Your medical, surgical, medication and cancer history

A physical examination and measurement of your vital signs (e.g., blood pressure, pulse, respirations, temperature)

A blood (about 2 teaspoons) draw for routine clinical laboratory tests (including a pregnancy test)

Urine collection

An Electrocardiogram (ECG) to check your heart function

A neurological exam to check your mental status, reflexes, and gait

An MRI

MRI (Magnetic Resonance Imaging): a study performed to look at your brain and keep track of the brain tumor

This visit will take approximately 3-4 hours and will be completed by your referring physician at most 35 days before your treatment (Day 1).

Pre-Study Visit

May be repeated within 7 days before study treatment if initial screen visit was more than 21 days from Cathetr Placement Surgery Day.

- Physical examination
- Review of your medications
- MRI
- Blood draw (about 2 teaspoons)

Catheter Placement/Surgery Visit

One Day Before Drug Infusion (Treatment Day)

- Before the surgery begins, you will undergo:
  - Physical examination
  - Review of your medications, vital signs, and cognitive function

Intraoperative Placement of Catheters

- The study doctors will place catheters directly into your tumor. If you had a standard-of-care tumor biopsy, the catheters will be placed into your tumor after the biopsy is complete.
  - These catheters have been specifically designed to inject drugs into the brain
  - The number of catheters and location of the catheters will depend on the individual patient to provide the best possible coverage of their tumor
  - You may have a post-operative CT scan done to confirm the placement of the catheters
- Once the biopsy is complete (if done) and the catheters placed, you will then be sent to recover from the anesthesia
- After the catheter placement, the study care team will ask you if you are having any side effects

What to Expect on Treatment Day

Treatment Day: Day 1

- Physical examination
- Review of your medications, vital signs, and cognitive function
- Urine collection
- You will be given potassium iodide in a glass of water or juice at least **one hour** before your administration
  Potassium iodide is used to protect the thyroid gland from radiation.

You will receive the administration of radioactive study drug Rhenium (^{186}Re) Obisbemeda via the catheters placed during the surgery day.

- The drug infusion can take approximately 2-5 hrs, depending on which Phase of the study you are in, how many catheters were placed, and the rate of infusion (how fast the drug is pumped).
- You will undergo imaging (SPECT/CT / Whole Body Planar) at various time points
  - Imaging is performed using a dual SPECT/CT camera, which is a large circular device containing a camera that detects the radioactive tracer your body absorbs during infusion. During your scan, you lie on a table while the SPECT machine rotates around you; this is much more open than undergoing an MRI.

After Administration:

- Blood (about 2 teaspoons) will be collected for radioactivity testing at 0.5, 1, 2, 4, and 8 hours after you receive Rhenium (^{186}Re) Obisbemeda.

  Radioactivity testing measures the amount of study drug in the body at different time points.
- When drug administration is complete, you will go to a special hospital room for patients who have received radiation and will be watched for 48 to 72 hours before being discharged from the hospital.

Post-Treatment Day Events

Days 2 and 3:

- Physical examination
- Imaging will be done **24-hrs and 48-hrs** after your treatment.
- Blood (about 2 teaspoons) will be **collected for radioactivity testing** at 24-hr and 48-hr after your treatment.
- All your urine will be collected for the **first two days** to measure the amount of study drug excreted by your kidneys.
- **On Day 3**, you will have a physical examination and review any side effects

You may be discharged on **Day 2 or Day 3** at the study physician's discretion.

Day 4, 5, and 6 Visits

Day 4 Visit

- Imaging similar to **Day 2** and **Day 3**
- Review of any side effect
- Blood draw (about 2 teaspoons)

Day 5 Visit

- Review any side effects and medication

Day 6 Visit

- Imaging similar to **Day 2** and **Day 3**
- Review of any side effect
- Blood draw (about 2 teaspoons)

Day 7, 9, and 14 Visits

Day 7 Visit

- Physical and neurological exams including medical history, vital signs, and cognitive function
- Review of any side effect
- Blood draw (about 2 teaspoons)

Day 9 Visit

- Imaging similar to **Day 2** and **Day 3**
- Review any side effects and medication

Day 14 Visit

- Physical and neurological exams including medical history, vital signs, and cognitive function
- Review of any side effect
- Blood draw (about 2 teaspoons)

Day 28 Visit

and Every 28 Days Thereafter

- Review any side effects and medication
- Physical and neurological exams
- Blood draw (about 2 teaspoons)
- MRI of the head to check the status of the disease

Day 56 Visit

and Every 56 Days Thereafter

- Review any side effects and medication
- MRI of the head to check the status of the disease

End-of-Study Visit

- Review any side effects and medication
- Physical and neurological exams
- A MRI to check the status of the disease (if you have not had one within the past 4 weeks)

Study Follow-Up

Long Term Follow-Up Visits (every 3 months)

You may be seen in a clinic visit or contacted by phone every 3 months and review the following:

- Any side effects and medication
- Any treatments you have received along with the dates

Duration of Participation

You will remain in the study until one of the following occurs:

1. Your disease worsens (recurs)
2. You are withdrawn from the study related to noncompliance, serious or intolerable adverse events, physician's discretion, or need for other anti-tumor therapy
3. You voluntarily withdraw from the study
4. The Sponsor or Investigator terminates the study

Risks & Benefits

The main goal of a research study is to learn things to help patients in the future. While on this study, you are at risk for side effects. You should discuss these with the study doctor.

Side effects will vary from person to person, and some may occur after you have stopped receiving treatment. **Tell the study staff about any side effects you may have**, even if you do not think they are related to the study drugs/procedures.

Common side effects may include:

- Scalp redness or soreness
- Hair loss
- Dry mouth or altered taste
- Fatigue (tiredness)
- Sleepiness
- Temporary muffled heari

Depending on the individual, this study may result in symptomatic relief and/or improved survival. You will be given a gift card with a total of $599 for your time and travel for participating in this study after Day 56.

Resources

Visit ReSPECT-Trials.com to Learn More.

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To learn more about Recurrent Glioblastoma, check out our patient guide of the cancer at

ReSPECT-Trials.com/Patient-Guide-GBM

Notes