Leptomeningeal Metastases Clinical Trial

Patient Study Guide

ReSPECT™ CLINICAL TRIALS

PLUS™ THERAPEUTICS

National Trial Reference Number: **NCT05034497**

ReSPECT™
CLINICAL TRIALS

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Introduction

What is the ReSPECT Leptomeningeal Metastases (ReSPECT-LM) Clinical Trial?

Plus Therapeutics is developing a new targeted radiation therapy, **Rhenium (^{186}Re) Obisbemeda**, for central nervous system cancers such as Leptomeningeal Metastases.

This FDA-approved **Phase 1** clinical trial will enroll approximately 27 patients and is a prospective, multi-center, and open-label trial.

In this trial, the study doctor will give Leptomeningeal Metastases from any primary cancer a single dose of Rhenium (^{186}Re) Obisbemeda through a small catheter placed under the patient's scalp.

The ReSPECT-LM clinical trial is funded, in part, by the Cancer Prevention & Research Institute of Texas, the second largest public funding source for cancer research in the world.

Clinical Study Plan

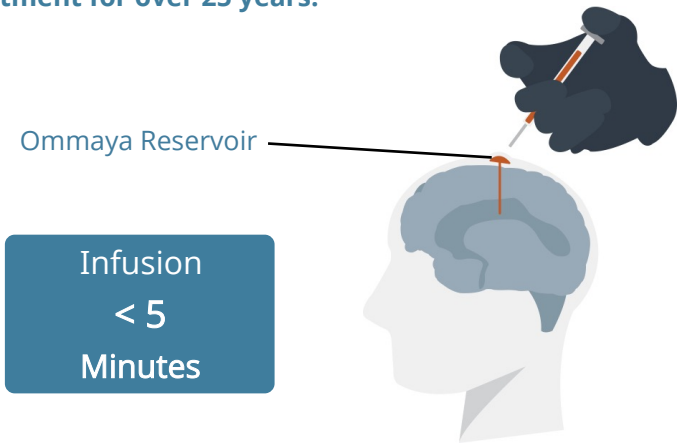
- This clinical research study aims to find the maximum tolerable dose of Rhenium (^{186}Re) Obisbemeda and evaluate the safety & effectiveness of the investigational treatment.
- This drug is administered in less than 5 minutes in a hospital setting, and the patient will go home the same day.
- This study consists of at least 13 visits with the researchers or study staff & the total length of the active part of the study for 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.

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

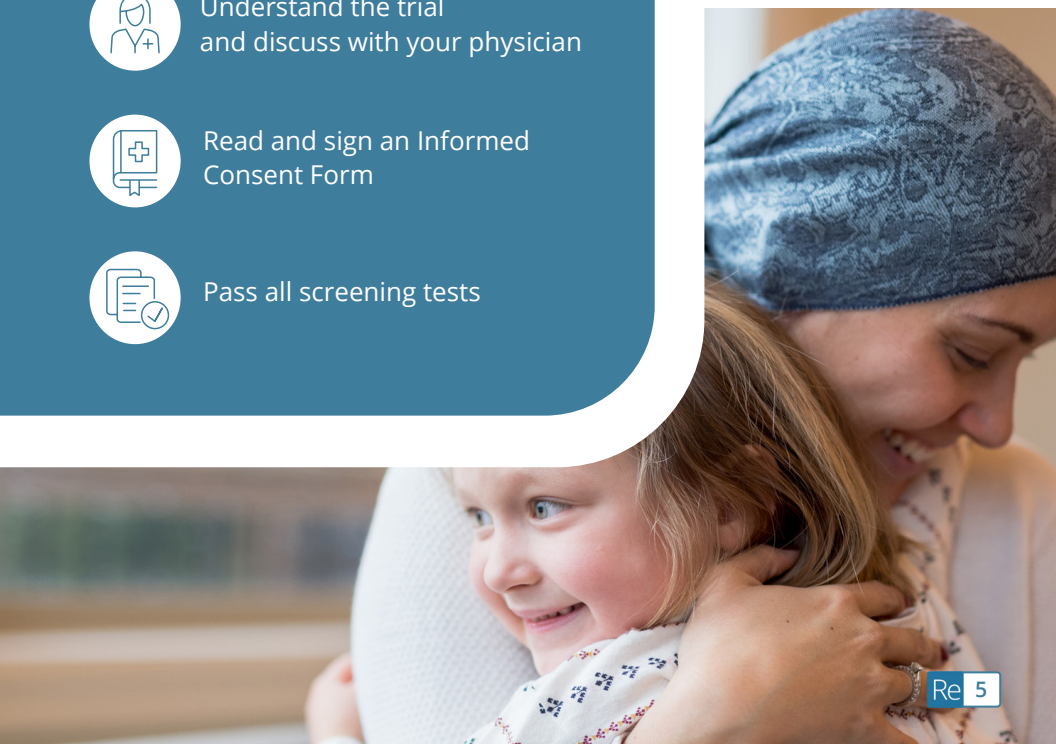
Study Qualifications

You may qualify if you meet the following criteria:

- Diagnosed with leptomeningeal metastases
- Able to undergo an MRI scan
- 18 years old or older, any gender
- Available for screening, treatment, and follow-up visits for up to 12 months
- Able to walk about, capable of self-care (Karnofsky Performance Status ≥ 60)
- No prior whole brain or spinal cord radiation therapy

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



Summary Of Visits

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

- Screening period (up to 5 weeks)
- Treatment Period and Follow-up (up to 8 weeks, through Day 56)
- 4-week evaluation periods

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-Treatment Visit

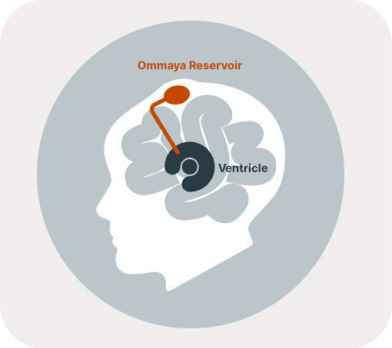
May be repeated within 7 days before study treatment if initial screen visit was more than 21 days from Day 1 (Treatment Day).

- Physical examination
- Review of your medications
- Neurological exam
- Blood draw (about 2 teaspoons)
- Urine collection
- Implanting of Ommaya reservoir (if you don't already have one) by neurosurgeon

What is the Surgical Implantation of an Ommaya Reservoir?

- The Ommaya Reservoir is a device placed during surgery on your Pre-Treatment Visit where one end of the device is under your scalp, and the other part connects to a ventricle in your brain. This implantation is done under general anesthesia and typically takes about one hour.

- Your ventricles make cerebrospinal fluid (CSF), a liquid flowing in and around your brain and spinal cord. This device will allow samples of your CSF to be taken and medications to be given.



***Note:** if you already have an Ommaya Reservoir in place, you will not need a replacement or second one. We will use the one you currently have implanted.*

CSF (Cerebrospinal Fluid) **Flow Study Visit**

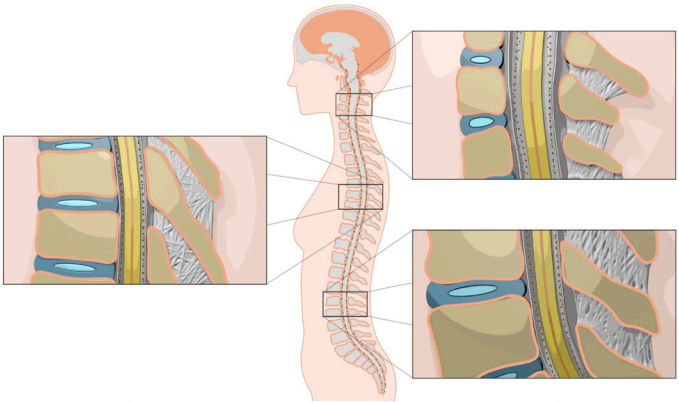
(2 - 4 Days Before Treatment Day)

We will ask you about the medications you are taking, and you will have your vital signs taken (e.g., blood pressure, pulse, respiration, temperature).

- You'll receive an intravenous (IV) infusion into a vein in your arm which will be used during the imaging step.
- Imaging will be performed at the end of the infusion, 4 hours, 12 hours, and 24 hours after infusion, including the lumbar, thoracic, and cervical subarachnoid spaces.

Imaging is performed using a dual-detector 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.

***Note:** Abnormal CSF flow will result in screen failure and discontinuation of the study.*



CSF flow study: checks for flow of fluid, blockage, and characteristics of the space; uses an imaging agent (Indium-111 diethylenetriamine-pentaacetic acid) which will be given via the Ommaya Reservoir (from your Pre-Study visit).

What to Expect on Treatment Day

Treatment Day: Day 1

- Physical and neurological exams.
- An ECG.
- 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 Ommaya Reservoir. This process takes about 5 minutes and is performed in an out-patient setting.

After Administration:

- Blood (about 2 teaspoons) will be collected for radioactivity testing at 1, 2, and 3.5 hours after you receive Rhenium (^{186}Re) Obisbemeda.
  Radioactivity testing measures the amount of study drug in the body at different time points.
- CSF (about 2 teaspoons) will be collected from your Ommaya before imaging and at 5-hrs post-dose for further analysis.
  The tests will look at the radioactivity in your CSF, the number of tumor cells in your CSF, and various biomarkers that may or may not be present in your CSF over different time points.
- You will remain under observation by the nuclear medicine department for about 4 hours for post-dose safety.

The Next Days: Day 2 and Day 3

- 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.
- CSF (about 2 teaspoons) will be collected from your Ommaya reservoir for further analysis **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.

Your healthcare provider can answer any questions you may have about the trial and your specific type of cancer.

Day 7 and Day 14/21 Visits

Day 7 Visit

- Imaging similar to **Day 2** and **Day 3**
- Review of any side effects and medications
- Physical and neurological exams
- ECG
- Blood draw (about 2 teaspoons)

Day 14 / 21 Visit

- Review any side effects and medications
- Physical and neurological exams
- Blood draw (about 2 teaspoons)

Day 28 Visit

and Every 28 Days Thereafter

- Review any side effects and medications
- Physical and neurological exams
- Blood draw (about 2 teaspoons)
- CSF (about 2 teaspoons) will be collected from your Ommaya Reservoir for additional analysis (tumor cells and other biomarkers)

End-of-Study Visit

- Review any side effects and medications
- Physical and neurological exams
- ECG
- Blood draw (about 2 teaspoons)
- An MRI to check the status of the disease (if you have not had one within the past 4 weeks)

You will have an MRI of the brain at Day 28 (+/-1 day), Day 56 (+/-3 days), and then every 56 days starting at Day 56 during standard of care clinic follow-up visits.

Study Follow-Up

Long Term Follow-Up Visits (every 3 months)

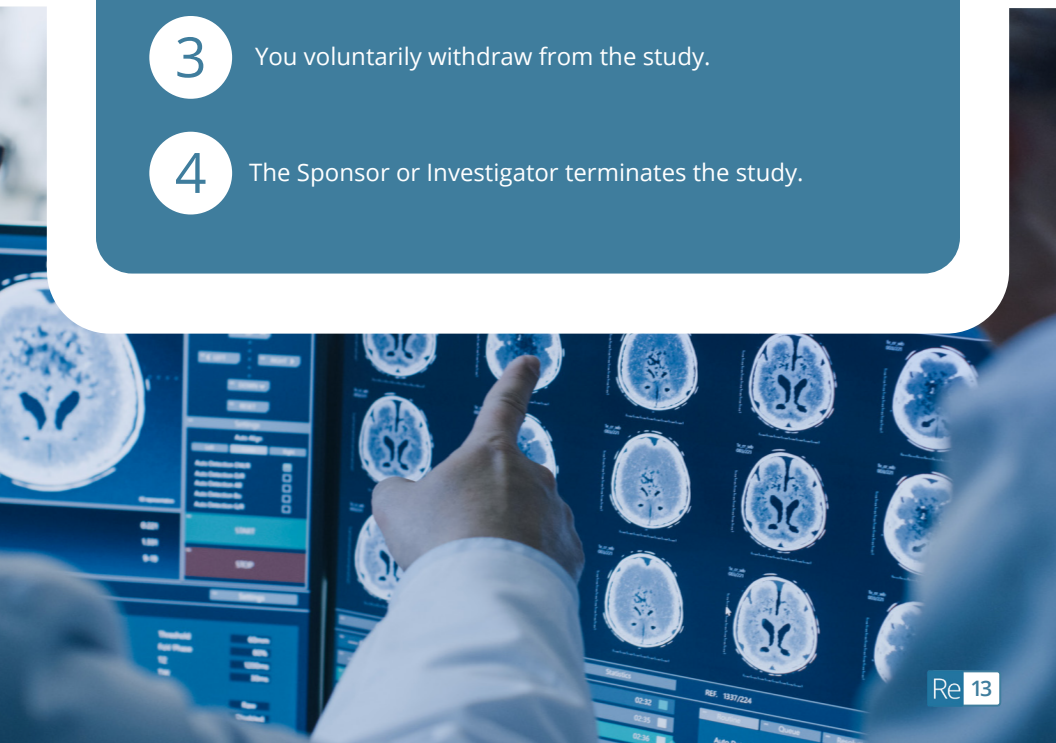
You may be seen in a clinic visit or contacted by phone every 3 months and review the following:

- Any side effects and medications
- 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 hearing

This study may result in symptomatic relief and/or improved survival depending on the individual. You will be given a gift card with a total of $300.00 for your time and travel for taking part in this study at the completion of Day 28.

Resources

Visit ReSPECT-Trials.com to Learn More.

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To learn more about Leptomeningeal Metastases, check out our patient guide of the cancer at **ReSPECT-Trials.com/Patient-Guide-LM**

Notes