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FRONTIER

STUDY

A guide to help you learn about the FRONTIER study and the use of TheraSphere™ GBM Y-90 Glass Microspheres for patients with recurrent glioblastoma

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A Patient's Guide to the FRONTIER Study

You are considering enrollment in the FRONTIER study which will use TheraSphere™ GBM Y-90 Glass Microspheres to treat recurrent glioblastoma (GBM). This booklet contains information to help you learn about the FRONTIER study design, the TheraSphere technology, and what to expect with the procedures and follow-up visits. It also contains some helpful information with medical terms found in the glossary.

You should have a detailed discussion with your doctor about potential risks covered in the Informed Consent and to address any questions you may have regarding participation in the study.

Glossary

Blood Vessel: part of the circulatory system which carries blood throughout the body.

Clinical Trial: research study that tests new medical treatments and evaluates their effects on human volunteers (participants) to advance medical knowledge.

Early Feasibility Study: clinical trial with a small number of patients using a device early in development to evaluate the initial clinical safety and functionality.

Informed Consent: written agreement to participate in the study with knowledge of potential consequences regarding risks and benefits of the treatment.

Microcatheter: thin, flexible tube introduced through a blood vessel to access the treatment region to inject fluids or implant TheraSphere glass microspheres.

TheraSphere: a treatment for hepatocellular carcinoma (liver cancer) that is made up of tiny glass microspheres (beads) containing radioactive Yttrium-90.

Yttrium-90 (Y-90): the radioactive material inside the glass microspheres that emits radiation into the area surrounding the microspheres; when Yttrium-90 (radioactive material) emits its radiation, it turns into Zirconium-90 (non-radioactive material).

Glioblastoma

Glioblastoma (GBM) is an aggressive form of brain cancer and is the most common type of cancer that begins in the brain. GBM is difficult to treat because tumor cells extend beyond what can be seen on clinical imaging. About 12,000 patients are diagnosed every year with GBM in the United States[1].

Treatment Options

Standard treatment for GBM typically includes a combination of surgery, external radiation therapy, and chemotherapy.

If the tumor is in an area of the brain which can be operated on, surgery is performed where the surgeon removes as much of the tumor as possible while trying to minimize removing healthy brain tissue. Following a surgery recovery period, patients typically undergo both external radiation therapy and chemotherapy for six weeks to treat tumor cells that could not be removed by surgery. Chemotherapy is often continued for six months after the radiation therapy has finished.

For GBM that has recurred (the cancer has come back), there is no standard treatment considered by medical professionals as best practice. Treatment varies with individual patient conditions. Current treatment options for recurrent GBM patients include additional surgery, external radiation, chemotherapy and tumor treating fields (TTF). Some patients may also be eligible for investigational treatment options in clinical trials such as the FRONTIER study.

You should talk with your doctor regarding treatment goals, quality of life, benefits and risks of treatments to determine the right treatment option for you.

[1] Ostrom, QT, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. Neuro-Oncology. (2019)

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The FRONTIER study is a first-in-human early feasibility study assessing the use of TheraSphere™ GBM Y-90 Glass Microspheres in patients with recurrent GBM. The purpose of the study is to evaluate the safety of using this therapy in the brain. Additionally, the study will evaluate the accuracy and effectiveness of the therapy. The study sponsor, Boston Scientific, has obtained approval from the FDA to conduct this study.

The FRONTIER study will enroll up to 12 patients at up to 5 hospitals in the United States.

If you agree to participate in the study by providing informed consent, you will visit the hospital on separate occasions for imaging and treatment planning which will not require a hospital stay. You will return to the hospital on the day of the procedure to administer the TheraSphere GBM Y-90 Glass Microspheres and will stay in the hospital until the following day discharge. You will return to the hospital for follow-up visits at the following intervals post-treatment:

- 7, 14, 21 days
- Monthly through 6 months
- Post 6 months visits will be based on your health status and the hospital's standard of care visit frequency

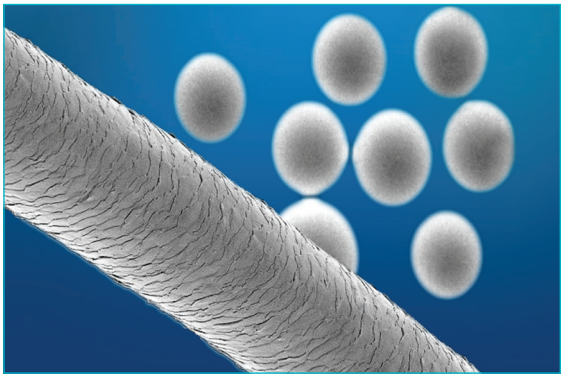
More information on the pre-procedural visits, the administration procedure, and follow-up visits is provided in the following sections.

What is TheraSphere™ and How Does it Work?

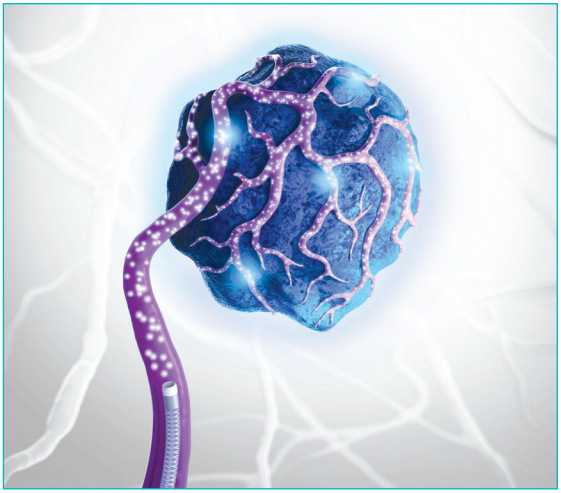
TheraSphere Y-90 Glass Microspheres is a targeted cancer therapy consisting of tiny glass microspheres containing radioactive Yttrium-90 (Y-90). The glass microspheres are approximately 0.001 inches in diameter – about a third of the width of a human hair. The glass microspheres are injected directly into the blood vessel feeding the tumor through a small flexible tube called a microcatheter. The glass microspheres enter the tumor's blood supply, lodge within tumor micro blood vessels, and release radiation to the tumor.

This process is referred to as selective internal radiation therapy (SIRT) where the radiation works to destroy the tumor cells from within the tumor. The intention of SIRT is to limit radiation exposure to surrounding healthy tissue. The glass microspheres will deliver most of the radiation (>95%) to the tumor in the first two weeks following the TheraSphere administration procedure. Although the amount of radiation released decreases over time, the glass microspheres will remain permanently implanted.

TheraSphere Y-90 Glass Microspheres have been used to treat hepatocellular carcinoma (liver cancer) in the United States for over 20 years. The purpose of the FRONTIER study is to determine the ability to safely use the technology in the treatment of patients with recurrent GBM.



TheraSphere microspheres next to human hair.



TheraSphere microspheres are delivered through a microcatheter to the blood vessel feeding the tumor where they become lodged and release radiation to the tumor

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Before the Administration Procedure

Prior to the TheraSphere™ GBM administration procedure, diagnostic imaging will be conducted to assess tumor characteristics, blood vessel anatomy in the brain, and blood flow. This will help the doctor care team in navigating the microcatheter to reach the tumor and identify the treatment volume to determine the amount of TheraSphere GBM to administer. These visits will not require a hospital stay.

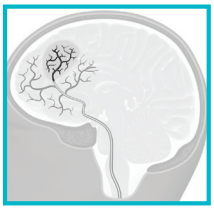
Visit #1: Pre-Procedural Diagnostic Imaging

TUMOR ON MRI

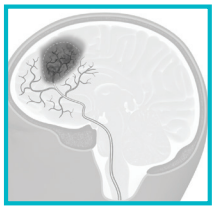
- Images acquired: MRI and CT Perfusion
- **MRI (magnetic resonance imaging):** provides clear images of soft tissue such as the brain, tumor, and can detect inflammation and swelling via magnetic fields and intravenous (IV) contrast injection
- **CT (computed tomography) Perfusion:** provides detailed information about blood flow to the brain via x-ray and intravenous (IV) contrast injection
- Purpose: Used to assess baseline tumor size, location and blood flow
- Timing: within 21 days prior to TheraSphere GBM administration procedure

Visit #2: Treatment Planning

VESSELS TO THE BRAIN / TUMOR



VESSELS TO THE TUMOR



BLOOD FLOW VOLUME TO TISSUE

- Images acquired: Angiography and Cone-Beam CT (CBCT)
  - A microcatheter will be navigated into the brain to the blood vessels supplying the tumor to acquire angiography and CBCT
- **Cerebral Angiography:** provides images of blood vessels in the brain via x-ray and a microcatheter contrast injection to areas being examined.
- **CBCT (cone-beam computed tomography):** provides 3D images of the treatment volume via x-ray and microcatheter contrast injection to areas being examined
- Purpose: Used to determine the blood vessels supplying the tumor and the volume of tissue that will be treated
- Timing: 7-14 days prior to TheraSphere GBM administration procedure

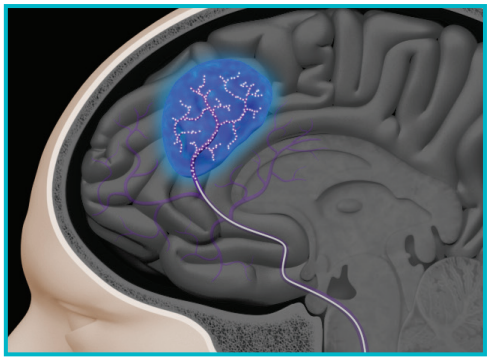
After treatment planning, the medical team will combine images to ensure the volume of tissue identified on CBCT covers the recurrent tumor shown on MRI. These images will also be used to calculate the volume of tissue to be treated and determine the amount of TheraSphere GBM radiation dose. Each dose is made uniquely for the patient being treated.

TheraSphere™ GBM Administration Procedure

Microcatheter navigated to the treatment location and repeat treatment planning imaging

On the day of the TheraSphere GBM administration procedure, the doctor will insert a microcatheter into the femoral artery and navigate to the brain vessels using imaging guidance.

Another CBCT and angiography will be taken to replicate the microcatheter tip position from the treatment planning and verify the treatment volume.



TheraSphere GBM Y-90 Glass Microspheres are delivered through the microcatheter to the tumor

TheraSphere GBM Y-90 Glass Microspheres will be delivered to the tumor through the microcatheter that is placed in a vessel that supplies blood to the tumor.

The glass microspheres will be trapped in the tumor and deliver radiation from within the tumor. The maximum radiation penetration depth of Y-90 glass microspheres is 0.5 inches, therefore, the treatment intent is to provide radiation to the tumor while limiting radiation exposure to nearby healthy brain tissue.

Post-procedure Imaging and Monitoring

Following the TheraSphere™ GBM administration procedure, you will have an MRI and will be monitored with neurological assessments until time of hospital discharge (24 to 36 hours post-treatment). A PET (positron emission tomography) image will be acquired and will show the Y-90 radiation activity. This image confirms that the glass microspheres were delivered to and are irradiating the intended location. The doctor will evaluate the imaging and neurological assessments prior to your discharge from the hospital to return home.

Because the radiation produced by the glass microspheres have a very small range of action, the radioactive energy outside your body is very low and is not a safety issue. The hospital may give you instructions when you leave the hospital, as a precaution. No safety restrictions are required for visitors, family, or caregivers.

PET image to identify the Y-90 radiation activity

Follow-up Visits

For on-going evaluation of the therapy, you will return to the hospital where treatment was received for FRONTIER study-required follow-up office visits at the following intervals:

- Weekly for the first month post-procedure (no imaging acquired unless clinically indicated)
- Monthly through 6 months post-procedure (includes monthly MRI)
- After 6 months, hospital standard of care visit schedule

None of the planned follow-up visits will require a surgical procedure or hospital stay. The follow-up visits will include physical exams, neurological assessments including NIHSS (National Institutes of Health Stroke Scale), and adverse events assessments.

MRI is to be acquired, at minimum, every month through the 6-month visit and is recommended to be acquired at a minimum of every 2-3 months thereafter during standard of care visits.

Potential Risks and Informed Consent

Participation in the FRONTIER study is voluntary. Your study doctor will discuss potential risks to participating in this study. You should refer to the Informed Consent for a list of potential risks.

There may be additional risks linked to the investigational procedure and follow-up testing that are unknown.

Contact Information and Notes

HEALTH CARE TEAM	
NAME	
POSITION	
ADDRESS	
PHONE #	
E-MAIL	

NAME	
POSITION	
ADDRESS	
PHONE #	
E-MAIL	

SUPPORT TEAM/OTHER	
NAME	
POSITION	
ADDRESS	
PHONE #	
E-MAIL	

NAME	
POSITION	
ADDRESS	
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NOTES

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