Fighting Glioblastoma Brain Cancer with Tumor Treating Fields

A primary brain tumor is a growth of abnormal cells that originates in the brain and can be **benign** (non-cancerous) or **malignant** (cancerous).

Glioblastoma (GBM) represents about:

17% of all primary brain tumors[1] **&** **46%** of all malignant brain tumors[2]

making it the most prevalent type of brain cancer in adults.

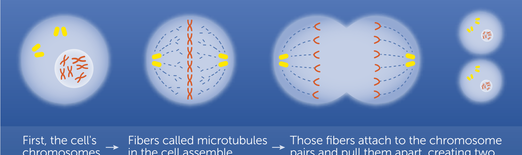
~12,500

new cases of GBM tumors, or other brain tumors that may eventually transform into GBM, may be diagnosed in the United States each year[3]

GBM is the most aggressive type of primary brain tumor.[4] Even with treatment, GBM typically comes back. This is known as recurrent GBM.[5]

- Glioblastomas can be difficult to remove completely during surgery, due to their finger-like tentacles.[6]
- Glioblastoma cells left behind quickly replicate, and many may not respond to medical therapies.[7]

In the human body, cells regularly divide and copy themselves. This process, called mitosis, helps the body grow, repair damaged tissues and replace worn-out cells.



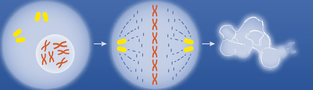
First, the cell's chromosomes duplicate → Fibers called microtubules in the cell assemble → Those fibers attach to the chromosome pairs and pull them apart, creating two identical new cells (daughter cells)

Malignant brain tumors, including GBM, grow by rapidly dividing in an uncontrolled way.

Treatments such as chemotherapy are aimed at killing these fast-growing cells.[8] Unfortunately, many chemotherapies are not effective in treating GBM because they have no or limited ability to cross the blood-brain barrier.[9]

Optune™ is the only non-invasive FDA-approved medical device for treating newly diagnosed and recurrent GBM by producing alternating electric fields (called **Tumor Treating Fields or TTFields**) that may slow or stop cancer cell division.[10]

Tumor Treating Fields interfere with mitosis, especially in rapidly dividing cells by interrupting microtubule assembly, which can lead to unsuccessful division (mitotic arrest) and cell death (apoptosis).



Tumor Treating Fields are precisely frequency-tuned to target the rapidly dividing GBM cells in the brain, and generally do not harm healthy cells.

Actor Portrayal

Tumor Treating Fields are delivered by Optune through four transducer arrays placed directly on the scalp.

Array placement is determined based on each patient's MRI measurements to maximize Tumor Treating Field intensity at the tumor.

The system is recommended to be worn for 18+ hours per day and includes battery packs so patients can be mobile and engage in daily activities.

Optune is the first therapy approved for newly diagnosed GBM in more than 10 years. A large clinical study in patients newly diagnosed with GBM showed Optune along with standard of care chemotherapy temozolomide significantly improved progression-free survival, overall survival and 2-year survival compared to temozolomide alone. Additionally, in a separate, large clinical study, Optune, when used alone, was as effective as chemotherapy in treating recurrent GBM.

- Please refer to the Instructions for Use for further clinical data on Optune.

In clinical trials, the most common adverse reaction from Optune treatment was mild to moderate skin irritation beneath the transducer arrays. There was no significant increase in serious adverse events from Optune in combination with temozolomide versus temozolomide alone.

Indications For Use

Optune is intended as a treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM).

Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery and completion of radiation therapy together with concomitant standard of care chemotherapy.

For the treatment of recurrent GBM, Optune is indicated following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

Summary of Important Safety Information

Contraindications

Do not use Optune if you have an active implanted medical device, a skull defect (such as, missing bone with no replacement), or bullet fragments. Use of Optune together with implanted electronic devices has not been tested and may theoretically lead to malfunctioning of the implanted device. Use of Optune together with skull defects or bullet fragments has not been tested and may possibly lead to tissue damage or render Optune ineffective.

Do not use Optune if you are known to be sensitive to conductive hydrogels. In this case, skin contact with the gel used with Optune may commonly cause increased redness and itching, and rarely may even lead to severe allergic reactions such as shock and respiratory failure.

Warnings and Precautions

Use Optune only after receiving training from qualified personnel, such as your doctor, a nurse, or other medical personnel who have completed a training course given by Novocure (the device manufacturer).

Do not use Optune if you are pregnant, you think you might be pregnant or are trying to get pregnant. It is not known if Optune is safe or effective in these populations.

The most common (≥10%) adverse events involving Optune in combination with temozolomide were low blood platelet count, nausea, constipation, vomiting, fatigue, scalp irritation from device use, headache, convulsions, and depression.

The most common (≥10%) adverse events seen when using Optune alone were scalp irritation from device use and headache.

The following adverse reactions were considered related to Optune when using the device alone: scalp irritation from device use, headache, malaise, muscle twitching, fall and skin ulcer.

All servicing procedures must be performed by qualified and trained personnel.

Do not use any parts that do not come with the Optune Treatment Kit, or that were not sent to you by the device manufacturer or given to you by your doctor.

Do not wet the device or transducer arrays.

If you have an underlying serious skin condition on the scalp, discuss with your doctor whether this may prevent or temporarily interfere with Optune treatment.

Please visit http://www.optune.com/instructions-for-use.aspx to see Optune Instructions for Use (IFU) for complete information regarding the device's indications, contraindications, warnings and precautions.

References

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10. Optune. Instructions for Use. Novocure. October 2015.

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