

Product Fact Sheet

Tumor Treating Fields (TTFields)

- Tumor Treating Fields (TTFields) are low-intensity alternating electric fields tuned to specific frequencies that continuously disrupt cancer cell division.
 - TTFields inhibit tumor growth and potentially cause cancer cells to die while sparing normal healthy cells.
- Optune® and Optune Lua™ are wearable and portable cancer treatments that deliver TTFields

Optune in Glioblastoma (GBM)

- Optune is an FDA-approved treatment for GBM, the most common and deadliest type of primary brain cancer.
 - Optune is the first FDA-approved treatment in more than a decade for newly diagnosed GBM.
 - Optune received FDA approval in newly diagnosed GBM in 2015. The FDA previously approved Optune in 2011 for the treatment of recurrent GBM. Optune was approved under the Premarket Approval (PMA) pathway.
 - More than 15,000 patients with GBM have started Optune.
- For patients with newly diagnosed GBM, Optune has proven to extend survival and maintain quality of life.
 - A large clinical trial showed that the survival rate with Optune + TMZ vs TMZ alone was significantly higher at the 2-year landmark analysis (43% vs 31%) and remained higher at 5 years (13% vs 5%)
 - In a 5-year follow up, people on Optune + TMZ lived longer across all groups analyzed regardless of well-being, age, gender and how much of the tumor was removed.
 - Patients using Optune + TMZ in the study were also able to maintain their mental, emotional, and physical well-being longer than those on chemotherapy alone for up to one year.
 - Mild-to moderate skin irritation was the most common device-related adverse effect reported with Optune use

Optune Lua in Unresectable Malignant Pleural Mesothelioma

- Optune Lua is FDA approved for the first-line treatment of unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM), a rare cancer with a poor prognosis.
 - Optune Lua is the first FDA-approved treatment in MPM in over 15 years.
 - Optune Lua for MPM is classified as a Humanitarian Use Device (HUD), approved under the Humanitarian Device Exemption (HDE). The HDE pathway was created to encourage companies to innovate in rare diseases with underserved patient populations.



- A clinical trial showed that Optune Lua and pemetrexed + cisplatin/carboplatin may help people with mesothelioma live longer
 - MPM patients who received Optune Lua with platinum-based chemotherapy experienced median overall survival of 18.2 months.
 - 97% of patients (n=72) with at least one follow-up CT scan had tumors that shrank (40% partial response) or stopped growing (57% stable disease)
 - More than half of patients enrolled in STELLAR trial who used Optune Lua + platinum-based chemotherapy were still alive at 1 year.
 - At year 1: 62% of patients (N=80)
 - At Year 2: 42% of patients (N=80)
 - Mild-to-moderate skin irritation was the most common device-related adverse effect reported with Optune Lua use

Additional background

- TTFields do not enter the bloodstream like a drug, so they did not significantly increase chemotherapy-related side effects.
- Optune and Optune Lua are wearable and portable so continuous treatment with both can be received almost everywhere.
- Optune and Optune Lua deliver treatment to the region of the tumor via 4 adhesive patches called transducer arrays. These arrays are applied to the shaved skin and are connected to the device and battery.
- Optune study was a prospective, randomized, open label, phase 3 clinical trial to evaluate efficacy and safety in newly diagnosed GBM patients (N=695) who after maximal debulking surgery, had completed radiation and adjuvant TMZ.
- Optune Lua study was a prospective, multicenter, single arm, phase 2 clinical trial designed to study the safety and efficacy of Optune Lua and pemetrexed + cisplatin or carboplatin first line in patients with unresectable, locally advanced or metastatic MPM.

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.

Optune Lua™ is indicated for the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma (MPM) to be used concurrently with pemetrexed and platinum-based chemotherapy.

Caution: Federal law restricts this device to sale by or on the order of a physician. Humanitarian Device. Authorized by Federal law for use in the treatment of adult patients with unresectable, locally advanced or metastatic, malignant pleural mesothelioma concurrently with pemetrexed and platinum-based chemotherapy. The effectiveness of this device for this use has not been demonstrated.

Important Safety Information

Contraindications

Do not use Optune in patients with GBM with an implanted medical device, a skull defect (such as, missing bone with no replacement), or bullet fragments. 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 Lua in patients with MPM with implantable electronic medical devices such as pacemakers or implantable automatic defibrillators, etc.

Use of Optune for GBM or Optune Lua for MPM together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device.

Do not use Optune for GBM or Optune Lua for MPM in patients known to be sensitive to conductive hydrogels. Skin contact with the gel used with Optune and Optune Lua may commonly cause increased redness and itching, and may rarely lead to severe allergic reactions such as shock and respiratory failure.

Warnings and Precautions

Optune and Optune Lua can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure®.

The most common ($\geq 10\%$) adverse events involving Optune in combination with chemotherapy in patients with GBM were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression.

The most common ($\geq 10\%$) adverse events involving Optune Lua in combination with chemotherapy in patients with MPM were anemia, constipation, nausea, asthenia, chest pain, fatigue, medical device site reaction, pruritus, and cough.

Other potential adverse effects associated with the use of Optune Lua include: treatment related skin toxicity, allergic reaction to the plaster or to the gel, electrode overheating leading to pain and/or local skin burns, infections at sites of electrode contact with the skin, local warmth and tingling sensation beneath the electrodes, muscle twitching, medical device site reaction and skin breakdown/skin ulcer.

If the patient has an underlying serious skin condition on the treated area, evaluate whether this may prevent or temporarily interfere with Optune and Optune Lua treatment.

Do not prescribe Optune or Optune Lua for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune Lua and Optune in these populations have not been established.

Please [click here](#) to see the Optune Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings and precautions.

Please [click here](#) to see the Optune Lua IFU for complete information regarding the device's indications, contraindications, warnings and precautions.

-
1. Optune Instructions For Use. Novocure 2019.
 2. Ostrom QT, Cioffi G, Gittleman H, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. *Neuro Oncol.* 2019;21(Suppl 5):v1-v100. doi:10.1093/neuonc/noz150
 3. Novocure Data on File. OPT-117.
 4. Summary of Safety and Effectiveness Data (SSED). US FDA Website. https://www.accessdata.fda.gov/cdrh_docs/pdf10/p100034s013b.pdf. Accessed April 9, 2019.
 5. Stupp R, Taillibert S, Kanner A, et al. Effect of tumor-treating fields plus maintenance temozolomide vs maintenance temozolomide alone on survival in patients with glioblastoma: a randomized clinical trial. *JAMA Oncology.* 2017;318(23):2306-2316.
 6. Taphoorn M, Dirven L, Kanner A, et al. Influence of treatment with tumor-treating fields on health-related quality of life of patients with newly diagnosed glioblastoma: a secondary analysis of a randomized clinical trial. *JAMA Oncol.* 2018 Apr 1;4(4):495-504. doi: 10.1001/jamaoncol.2017.5082. *JAMA Oncol.* 2018 Apr 1;4(4):495-504.
 7. Optune Lua. Instructions for Use for Unresectable Malignant Pleural Mesothelioma. Novocure; 2019.
 8. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol.* 2003;21(14):2636-2644.
 9. Hazarika M, White RM, Johnson JR, et al. FDA drug approval summaries: pemetrexed (Alimta®). *The Oncologist.* 2004;9(5):482-488.