

Novocure, Inc.

www.novocure.com

novocure™

# TTFields: a radical new approach to cancer treatment using electric fields

**Tumor-treating fields (TTFields) use electric fields tuned to specific frequencies to disrupt the division of solid tumor cancer cells. Novocure has launched Optune, its first TTFields delivery system, for the treatment of glioblastoma multiforme and potentially other solid tumor indications.**

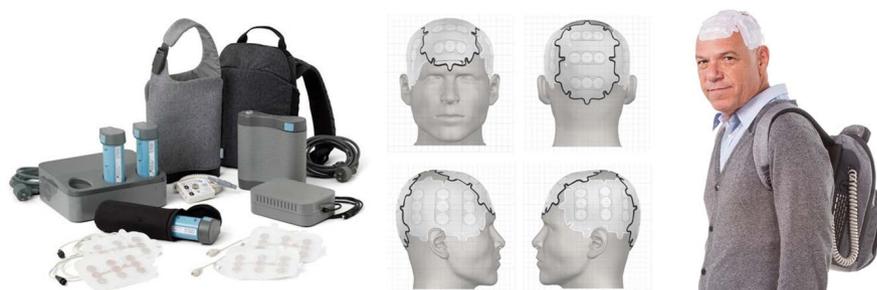
For over 100 years, surgery, radiation, and pharmacological treatment have been the main pillars of cancer therapy. These modalities, used alone or in combination, have greatly improved therapeutic outcomes for patients with a range of solid and dispersed cancers, but a significant unmet need for improved survival and quality of life remains.

Since 2000, cancer company Novocure has been developing an alternative therapeutic modality specifically for solid cancers: TTFields. The TTFields therapy consists of low-intensity, alternating electric fields that slow and reverse tumor growth by interfering with the mitotic process of cancer cells. The therapy is administered via a noninvasive portable device that delivers continuous electric fields to the patient through transducer arrays placed on the skin in the region of the tumor (Fig. 1). TTFields therapy has a mild side effect profile, and no cumulative systemic toxicity. Novocure's device, Optune, was approved by the US Food and Drug Administration (FDA) in 2011 to treat recurrent glioblastoma multiforme (GBM), and in 2015 to treat newly diagnosed GBM in combination with Temozolomide (TMZ). Novocure is now advancing its clinical trial pipeline to expand the application of TTFields therapy to other solid tumor indications. After obtaining positive results that showed significant extension of progression-free and overall survival in newly diagnosed GBM patients treated with Optune in combination with TMZ versus TMZ alone, Novocure has undertaken ongoing or planned phase 3 pivotal trials in brain metastases, in non-small-cell lung cancer (NSCLC), and in pancreatic cancer, as well as a phase 2 pilot trial in mesothelioma. A pilot trial in ovarian cancer has been completed.

According to Eilon Kirson, Novocure's CSO and head of R&D, "we believe our preclinical and clinical research demonstrates that TTFields' mechanism of action affects fundamental aspects of cancer cell division and may have broad applicability across a variety of solid tumors."

## TTFields

Electric fields are characterized by their ability to exert force on charged molecules. Novocure founder Yoram Palti hypothesized that at particular frequencies and intensities, electric fields can potentially have an antimetabolic effect on cells by interacting with polar molecules such as tubulin and thus disrupting the mitotic spindle, which would slow or completely stop cell proliferation. On the basis of this concept and preliminary *in vitro* experiments, Palti founded Novocure in 2000.



**Figure 1: The Novocure Optune system.** Optune is a noninvasive portable device that delivers continuous electric fields through transducer arrays. Transducers are placed on the glioblastoma patient's scalp.

Pioneering work at the company showed that inhibition of cell proliferation and accelerated cell death by TTFields are optimal at intensities of 1–5V cm<sup>-1</sup> and frequencies between 100 and 500 kHz, depending on the cell type—the mitotic spindle is best disrupted at 150 kHz in pancreatic cancer and NSCLC, and at 200 kHz in ovarian cancer and GBM. Mitosis in non-cancerous cells is typically disrupted at frequencies of about 50 kHz, which minimizes the potential side effects of TTFields on nonproliferating cell types. Additionally, no tissue heating occurs after TTFields treatment because the applied frequencies are well below the 1,000-kHz threshold above which tissue temperature is affected.

TTFields therapy is applied with a battery-powered or wall-powered electric field generator that produces the alternating electric fields. Transducer arrays connected to the generator and placed on the patient's skin direct the fields to the desired region of the body. The patient carries an over-the-shoulder bag or a backpack containing the generator to receive continuous treatment without having to change his or her daily routine. For optimal outcomes, TTFields should be applied for a minimum of 18 h per day. No systemic toxicities have been reported, and only mild skin reactions to the placement of transducer arrays have been observed.

"We believe the mechanism of action of TTFields can have broad applicability to a variety of solid tumors, and the fourth quarter of 2016 was marked by multiple clinical milestones," added William Doyle, Novocure's executive chairman.

## GBM breakthroughs

Novocure developed a prototype device designed to deliver TTFields directly and continuously to the brain. The company's first target indication was GBM, an aggressive type of brain cancer that is treated first

with maximal safe resection, and then with radiation and TMZ.

Novocure launched its first clinical trials for GBM in 2009. These efforts culminated recently in the release of long-term survival data from a 695-patient, phase 3 pivotal trial of Optune in combination with TMZ for the treatment of newly diagnosed GBM, which showed significant extension of both progression-free survival ( $P=0.00005$ ) and overall survival ( $P=0.00006$ ) in patients who received the combination therapy.

"Optune plus TMZ is the first treatment in more than a decade to significantly improve outcomes for patients with newly diagnosed GBM. We are committed to bringing our profoundly different approach to cancer treatment to as many patients as possible," said Asaf Danziger, Novocure's CEO.

Optune is now approved by the US FDA, the Japan Pharmaceuticals and Medical Devices Agency and CE marked in the European Union for therapeutic use in both recurrent GBM and newly diagnosed GBM.

## An expanding field

Novocure has ongoing clinical pipelines to treat brain metastases, NSCLC, ovarian cancer, pancreatic cancer, and mesothelioma. The preclinical R&D program includes breast cancer, cervical cancer, colorectal carcinoma, gastric adenocarcinoma, hepatocellular carcinoma, malignant melanoma, renal adenocarcinoma, urinary transitional-cell carcinoma, and small-cell lung cancer.

contact

Eilon Kirson, CSO & Head of R&D  
Novocure, Inc.  
Haifa, Israel  
Tel: +1-212-767-7530  
Email: generalinfo@novocure.com