

For your patients with newly diagnosed GBM,

Optune Gio™ delivers the power of TTFields to attack GBM cells where they're vulnerable¹⁻³

A standard of care proven to provide long-term quality survival without adding systemic toxicity^{4-6,*}

*Patient-reported data collected per EORTC QLQ-C30 at baseline and months 3, 6, 9, and 12. The 30-question survey covered 5 daily functioning domains (Physical, Role, Social, Emotional, and Cognitive).⁵ EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer core quality of life questionnaire; GBM, glioblastoma; TTFields, Tumor Treating Fields.

Indications for Use

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

Optune Gio 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.

Important Safety Information

Contraindications

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

Please see the Important Safety Information on page 12 and the accompanying Optune Gio™ Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions.

novocure®

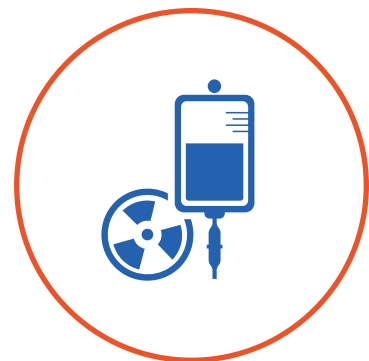
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OPTUNE
GIO™

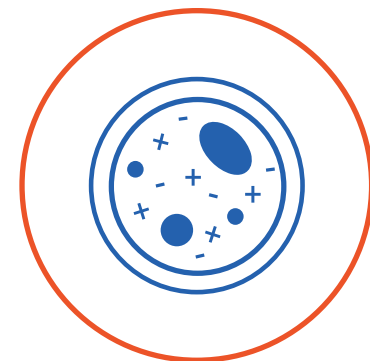


GBM: an aggressive, debilitating cancer that is challenging to control

Optune Gio™ leverages biophysical principles to disrupt tumor viability^{2,8}



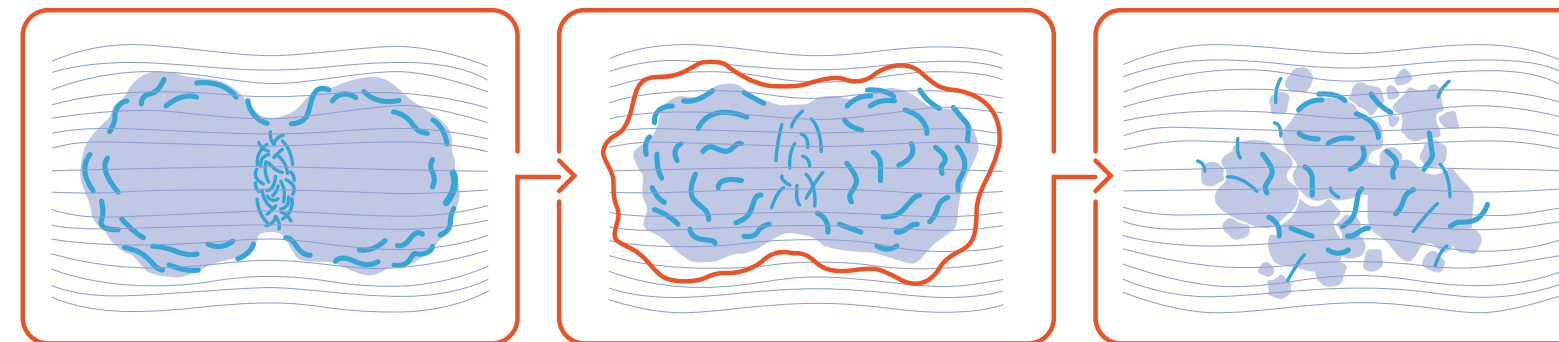
For more than a decade, the standard of care has been chemoradiation after maximal surgical resection⁷



Inherent electrical properties are a vulnerability of GBM cancer cells, which may not be addressed by current systemic or biophysical cancer-treating modalities⁸⁻¹²

Optune Gio™ is an innovative, portable treatment that can improve survival outcomes—without adding systemic toxicities—when used with SOC^{4,6}

TTFields are alternating electric fields delivered at a unique frequency that allows it to selectively disrupt GBM cell division^{8,13,14}



Optune Gio exploits cancer cells' electrical properties using TTFields to interfere with mitosis¹⁻³

Disrupts cancer cell division¹⁻³

Ultimately can destroy cancer cells¹⁻³

- Because healthy cells have different properties than cancer cells (including division rate, morphology, and electrical properties), they are spared by Optune Gio^{13,15-19}

Optune Gio delivers TTFields, which exert antitumor effects by disrupting activity of cancer cells during multiple phases of mitosis¹⁻³

Selected Safety Information

Contraindications (cont'd)

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

GBM, glioblastoma; SOC, standard of care; TTFields, Tumor Treating Fields.

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Optune Gio™ is a standard of care for newly diagnosed GBM

Including Optune Gio (which delivers TTFields therapy) as part of the treatment plan for newly diagnosed GBM gives patients every approved method to help extend survival^{6,20}

- 5-year survival results published in JAMA support an inclusion in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Central Nervous System Cancers*



The NCCN Guidelines[®] for Central Nervous System Cancers include alternating electric fields (Optune Gio) as a Category 1 Preferred regimen, following maximal safe resection if feasible (or else biopsy), and standard radiation therapy with concurrent and adjuvant TMZ, for patients aged ≤70 years with newly diagnosed supratentorial GBM and good performance score[†] regardless of MGMT promoter status.

There is uniform NCCN consensus for this recommendation based on high-level evidence (Category 1), and superior efficacy, safety, evidence, and when appropriate, affordability (Preferred).^{20,†}

*EF-14 was a prospective, randomized, open-label, phase 3 clinical trial in 695 patients with newly diagnosed glioblastoma (GBM). The trial assessed safety and demonstrated increased median PFS and OS of Optune Gio + TMZ vs TMZ alone.

[†]The NCCN defines good performance as Karnofsky Performance Score (KPS) ≥60. The trial on which the IFU is based used an eligibility criteria of KPS ≥70.^{4,20}

[‡]NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Central Nervous System Cancers V.1.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed June 19, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org.

Selected Safety Information

Warnings and Precautions

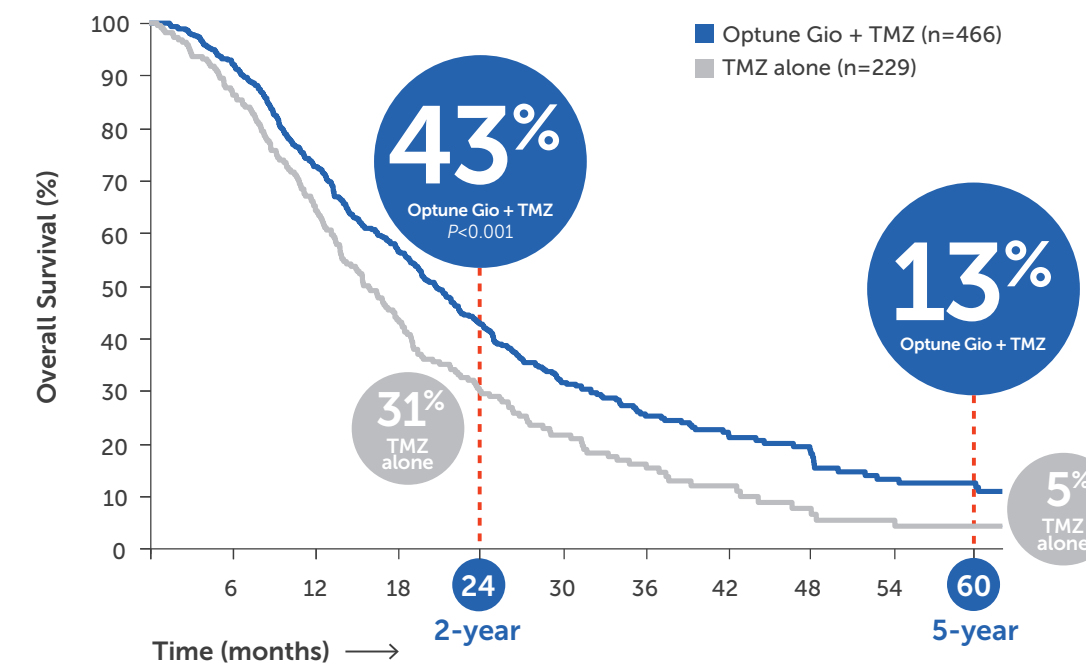
The most common (≥10%) adverse events involving Optune Gio in combination with temozolomide were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression.

In newly diagnosed GBM,

Optune Gio + TMZ provided an unprecedented long-term survival benefit^{4,6}

Survival with Optune + TMZ vs TMZ alone was significantly higher at the 2-year landmark analysis and remained higher at 5 years

Overall Survival (2- and 5-year survival analysis)^{4,6}



See study design on page 4.

GBM, glioblastoma; IFU, Instructions For Use; NCCN, National Comprehensive Cancer Network[®] (NCCN[®]); OS, overall survival; PFS, progression-free survival; TMZ, temozolomide; TTFields, Tumor Treating Fields.

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Median OS was significantly extended with Optune Gio—by nearly 5 months (P<0.001)⁴

Median OS from randomization (months)	20.9	16.0
Log-rank P value	<0.001	
HR (95% CI)	0.63 (0.55-0.76)	
Median OS from diagnosis (months)	24.5	19.8

5 YEARS
Proven to provide the best opportunity for greater overall survival at 5 years vs TMZ alone (13% vs 5%)^{4,6}

Optune Gio + TMZ also significantly improved PFS vs TMZ alone⁴

- Median PFS: 6.7 months vs 4.0 months (P<0.001)



Optune Gio™ is a wearable treatment delivery system that can provide continuous anticancer therapy^{4,*}

Significantly increased survival benefit was seen with more time on Optune Gio²²

It delivers TTFIELDS therapy locally and noninvasively, directly at the GBM tumor site via a portable device and arrays that adhere to the skin



Optune Gio is designed to fit into your patient's everyday life

- Small and lightweight, at just **2.7 pounds**²¹
- Designed for convenience, carrying comfort, and usability
- Wearable and portable for use during most normal daily activities

Recommended usage is at least **18 hours/day**, which gives patients flexibility to decide which times of day are best for use^{4,22}

MyNovocure™ is a personalized support program that can help you integrate Optune Gio into your practice and your patients' lives (See details on page 13)



Scan to see videos of patients integrating Optune Gio into daily life

Gill is an Optune Gio user and Patient Ambassador. Patient image reflects the health status of the patient at the time the photo was taken.

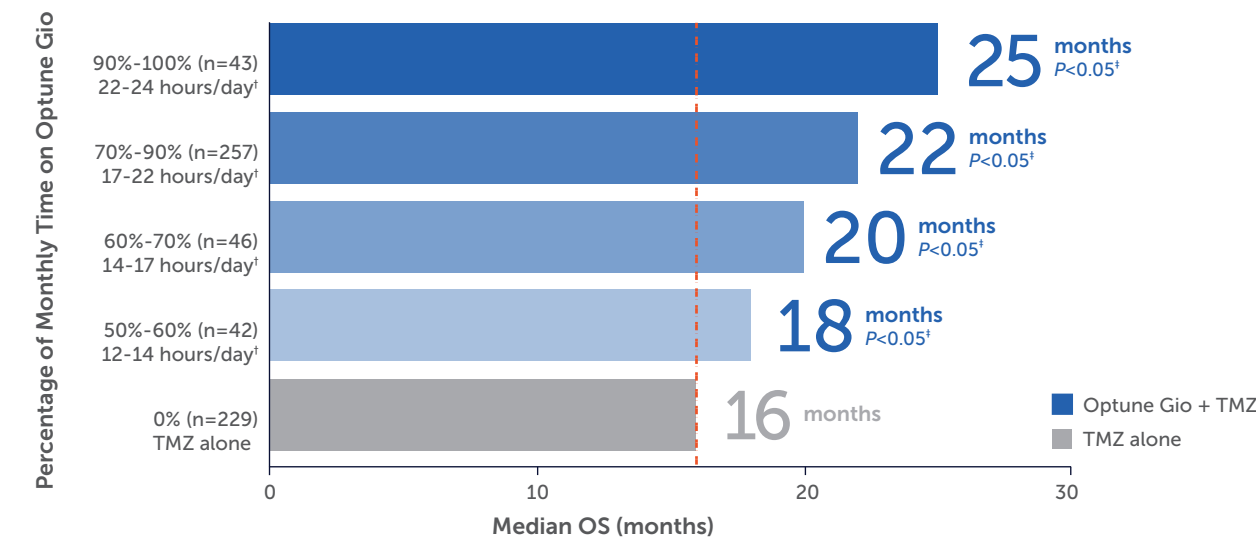
*Continuous treatment requires patient to be wearing the powered device.

Selected Safety Information

Warnings and Precautions (cont'd)

If the patient has an underlying serious skin condition on the scalp (e.g. ulcers, open wound, broken skin) evaluate whether this may prevent or temporarily interfere with Optune Gio treatment.

Median OS by Usage (Percentage of Monthly Time)



- Monthly usage was a predictor of survival benefit, independent of other prognostic factors such as KPS, age, or MGMT methylation status

[†]Based on the amount of time Optune Gio was turned on and providing therapy over the course of a month. These data reflect the average patient usage of Optune Gio for the first 6 months of treatment (months 1-6).²²

[‡]Approximation, based on monthly usage vs TMZ alone.

GBM, glioblastoma; KPS, Karnofsky Performance Score; MGMT, O-6-methylguanine-DNA methyltransferase; OS, overall survival; TMZ, temozolomide; TTFIELDS, Tumor Treating Fields.

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86%

of patients received a survival benefit from Optune Gio because they used it more than half the time (n=388/450)²²



In newly diagnosed GBM,

QoL was maintained over 12 months in patients treated with Optune Gio™ + TMZ^{5,23}

To measure QoL while using Optune Gio, patients were asked a broad range of questions from the EORTC Quality of Life survey across 5 categories related to daily living and physical-cognitive functioning²⁴



Physical

eg, carrying luggage



Role

eg, work/daily job



Social

eg, family life



Emotional

eg, level of tension



Cognitive

eg, remembering things



Patient image reflects the health status of the patient at the time the photo was taken.

“ *Optune Gio has been an excellent treatment option for me, and I have been using it for more than two years. ... It does not impede my movement.* **”**
— Scott, Optune Gio user and Patient Ambassador

Selected Safety Information

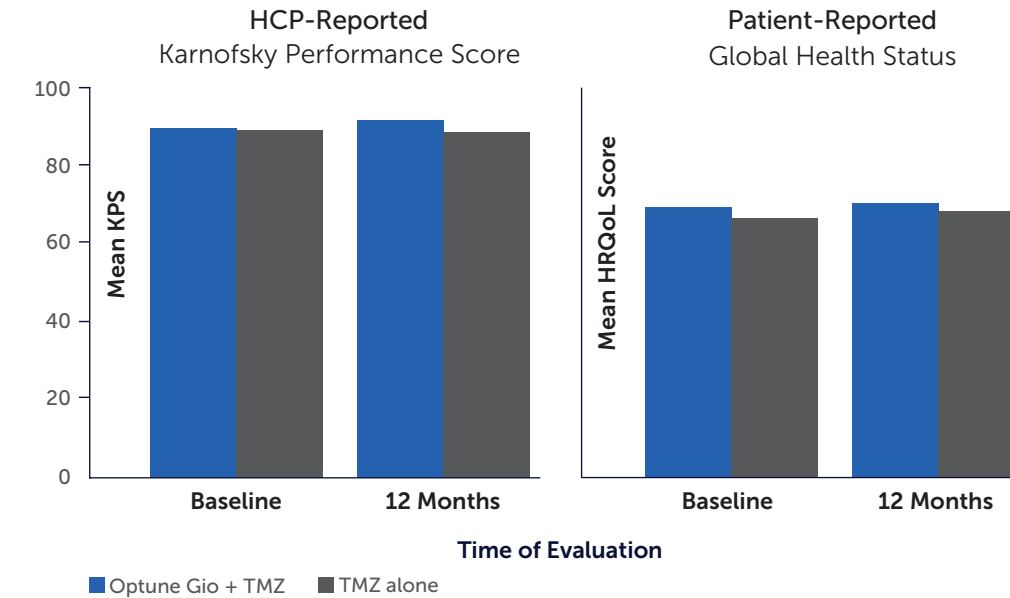
Warnings and Precautions (cont'd)

Use of Optune Gio in patients with an inactive implanted medical device in the brain has not been studied for safety and effectiveness, and use of Optune Gio in these patients could lead to tissue damage or lower the chance of Optune Gio being effective.

Optune Gio did not inhibit patients' ability to perform physical activities of daily living or cognitive function^{5,23}

Both HCPs and patients reported stable predefined daily functioning scores up to 1 year of Optune Gio use

QoL Over 12 Months



- HCP-reported KPS and patient-reported Global Health Status were
 - Maintained from baseline through 12 months of follow-up
 - Comparable with the TMZ-alone arm
- In the pivotal study, patients were treated with the first model of Optune Gio, which was twice as large in size and weight (6 lb) as the currently available device (2.7 lb)

*HCP-reported data collected per KPS assessment at baseline and then repeated monthly. Patient functional status via KPS (at multiple time points) measured patient independence in activities of daily living.^{5,23}

[†]Patient-reported data collected per EORTC QLQ-C30 at baseline and months 3, 6, 9, and 12. This 30-question survey covered 5 daily-functioning domains (Physical, Role, Social, Emotional, and Cognitive).^{5,23}

EORTC, European Organisation for Research and Treatment of Cancer; GBM, glioblastoma; KPS, Karnofsky Performance Score; QoL, quality of life; TMZ, temozolomide.

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No late-emerging serious AEs were seen in the 5-year follow-up

Incidence of grade 3/4 AEs occurring in 5% of patients during 5 years of follow-up	Optune Gio + TMZ (n=456) %	TMZ alone (n=216) %
≥1 AE	48	44
Blood and lymphatic system disorders	13	11
Thrombocytopenia	9	5
Gastrointestinal disorders	5	4
Asthenia, fatigue, and gait disturbance	9	6
Infections	7	5
Injury, poisoning, and procedural complications (falls and medical device site reaction)	5	3
Metabolism and nutrition disorders (anorexia, dehydration, and hyperglycemia)	4	5
Musculoskeletal and connective tissue disorders	5	4
Nervous system disorders	24	20
Seizures	6	6
Respiratory, thoracic, and mediastinal disorders (pulmonary embolism, dyspnea, and aspiration pneumonia)	5	5

Selected Safety Information

Warnings and Precautions (cont'd)

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

Optune Gio can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure (the device manufacturer).

No significant increase in serious AEs compared with TMZ alone^{4,25}

- The most common (≥10%) AEs involving Optune Gio in use with TMZ were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression²⁵
- A slightly higher incidence of grade 1/2 AEs was seen in some of the systems in the Optune Gio + TMZ arm of the study. This is most likely a reflection of the longer duration of TMZ treatment due to the increase in PFS seen in the treatment group⁴
- The rate of grade 1/2 medical device site reaction was 52% for Optune Gio + TMZ compared with 0% for TMZ alone, and severe (grade 3) skin involvement occurred in 2% of patients treated with Optune Gio + TMZ⁴
- Grade 3/4 AEs were well balanced between arms. None of the systemic grade 3/4 AEs were considered related to Optune Gio by any of the investigators⁴
- Mild-to-moderate skin irritation, the most common device-related side effect with Optune Gio, was typically manageable, reversible, and did not result in treatment discontinuation^{4,25}

AEs, adverse events; GBM, glioblastoma; PFS, progression-free survival; TMZ, temozolomide.

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Warnings and Precautions

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

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References: **1.** Gera N, Yang A, Holtzman TS, Lee SX, Wong ET, Swanson KD. Tumor treating fields perturb the localization of septins and cause aberrant mitotic exit. *PLoS One*. 2015;10(5):1-20. doi:10.1371/journal.pone.0125269 **2.** Giladi M, Schneiderman RS, Voloshin T, et al. Mitotic spindle disruption by alternating electric fields leads to improper chromosome segregation and mitotic catastrophe in cancer cells. *Sci Rep*. 2015;5:1-16. doi:10.1038/srep18046 **3.** Voloshin T, Kaynan N, Davidi S, et al. Tumor-treating fields (TTFields) induce immunogenic cell death resulting in enhanced antitumor efficacy when combined with anti-PD-1 therapy. *Cancer Immunol Immunother*. 2020;69(7):1191-1204. doi:10.1007/s00262-020-02534-7 **4.** Optune Gio. Instructions For Use. Novocure; 2023. **5.** Taphoorn MJB, Dirven L, Kanner AA, 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;4(4):495-504. doi:10.1001/jamaoncol.2017.5082 **6.** 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*. 2017;318(23):2306-2316. doi:10.1001/jama.2017.18718 **7.** Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med*. 2005;352:987-996. doi:10.1056/NEJMoa043330 **8.** Kirson ED, Dbalý V, Tovyřš F, et al. Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors. *Proc Natl Acad Sci U S A*. 2007;104(24):10152-10157. doi:10.1073/pnas.0702916104 **9.** Bashraheel SS, Domling A, Goda SK. 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Tumor treating fields for glioblastoma treatment: patient satisfaction and compliance with the second-generation Optune® system. *Clin Med Insights Oncol*. 2019;13:1-7. doi:10.1177/1179554918825449 **22.** Toms SA, Kim CY, Nicholas G, Ram Z. Increased compliance with tumor treating fields therapy is prognostic for improved survival in the treatment of glioblastoma: a subgroup analysis of the EF-14 phase III trial. *J Neurooncol*. 2019;141(2):467-473. doi:10.1007/s11060-018-03057-z **23.** Zhu J-J, Demireva P, Kanner AA, et al. Health-related quality of life, cognitive screening, and functional status in a randomized phase III trial (EF-14) of tumor treating fields with temozolomide compared to temozolomide alone in newly diagnosed glioblastoma. *J Neurooncol*. 2017;135(3):545-552. doi:10.1007/s11060-017-2601-y **24.** EORTC Quality of Life Group. EORTC QLQ-C30, Version 3.0. 1995. 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MyNovocure™ has your patients and practice in mind

Our goal is to provide personalized support from day 1—and every step of the way



Device training as needed (how it works, side effects, etc)



Tips for integrating Optune Gio into daily life



24/7 technical support and troubleshooting



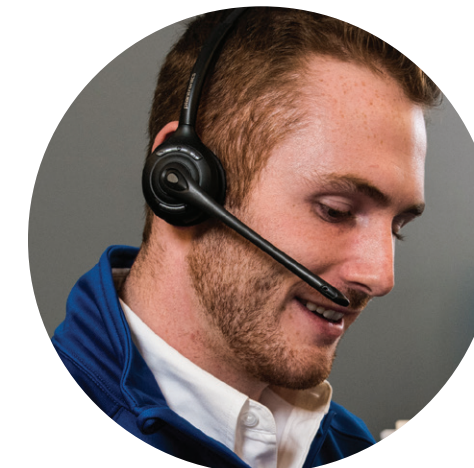
Reordering supplies (eg, arrays + batteries)



Travel support



Insurance support



Care Coordinator

Contact MyNovocure for all your practice and patient support needs



Call us any time of day:
1-855-281-9301 (toll-free)



Or email us:
support@novocure.com

MyNovocure cannot provide any medical advice. To ensure proper guidance, MyNovocure will direct your patients to ask any treatment-related questions to you

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Optune Gio™ delivers the power of TTFields to attack GBM cells where they're vulnerable¹⁻³

A standard of care that delivers TTFields and can destroy cancer cells by targeting their unique electrical properties—while sparing healthy cells^{13,15-19}

Unprecedented OS benefit with Optune Gio + TMZ^{4,6}

YEAR 2 ($P < 0.001$)

43% Optune Gio + TMZ vs 31% TMZ alone

YEAR 5

13% Optune Gio + TMZ vs 5% TMZ alone

- Significantly extended both OS (by nearly 5 months) and median PFS (6.7 months vs 4.0 months) vs TMZ alone*

* $P < 0.001$.

†QoL was measured through 12 months of follow-up.

GBM, glioblastoma; OS, overall survival; PFS, progression-free survival; QoL, quality of life; TMZ, temozolomide; TTFields, Tumor Treating Fields.



Well tolerated with no additional systemic toxicity^{4,6}



QoL maintained over time^{5,23,†}



Noninvasive, wearable treatment⁴

Optune Gio is the only treatment to be FDA-approved for newly diagnosed GBM since 2015

Please see the Important Safety Information on page 12 and the accompanying Optune Gio™ Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions.

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