

For your patients with newly diagnosed grade 4 glioma

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

**Proven to provide long-term quality survival
without adding systemic toxicity^{4-6,*}**

Mild to moderate skin irritation is the main side effect associated with the use of the device

Optune Gio® is a CE, Class IIb medical device. Read the instructions for use (IFU) for a complete description of the intended use, contraindications, warnings, and other important safety information.

* 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

Optune Gio® is a wearable treatment delivery system that can provide continuous anti-cancer therapy

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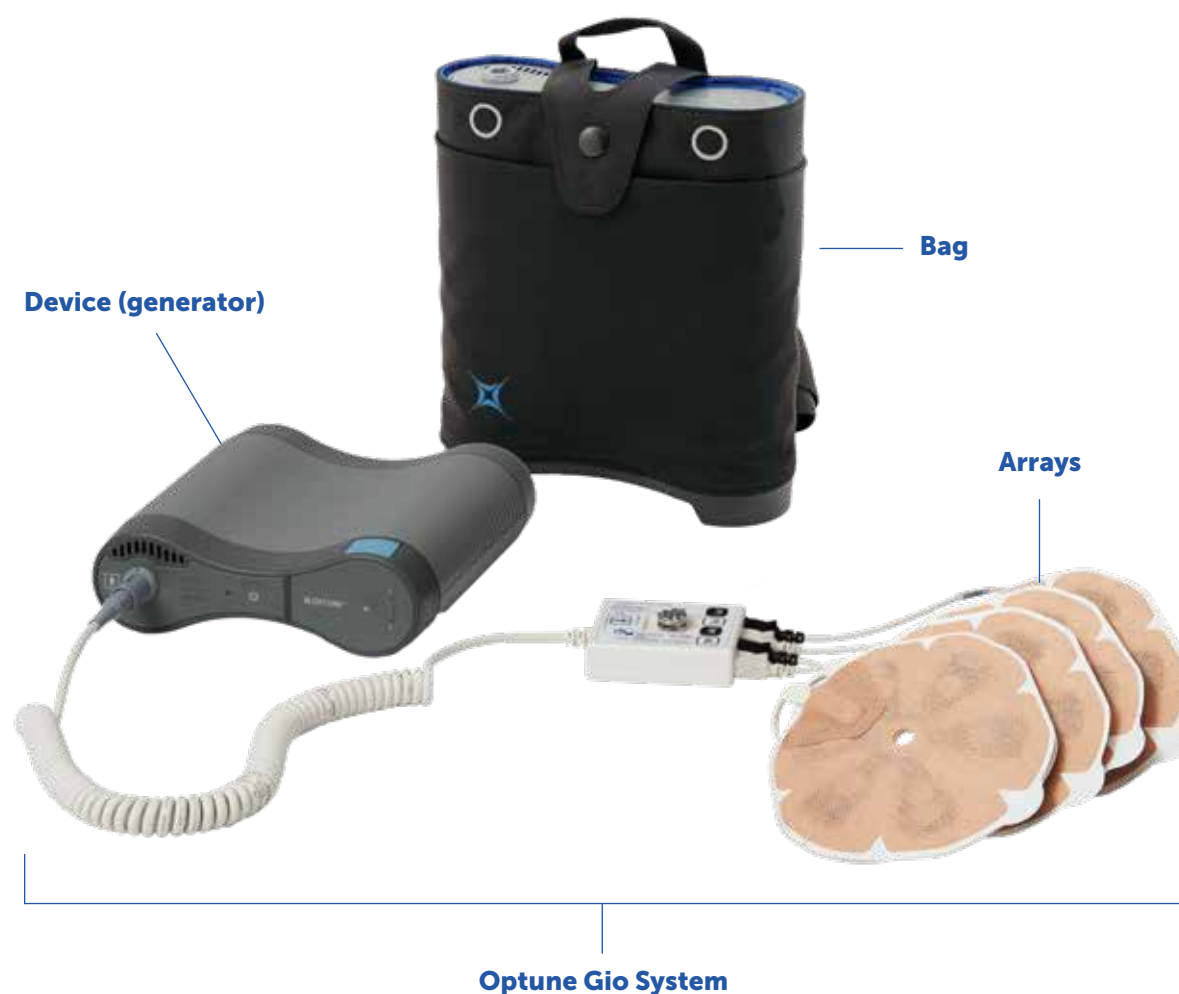
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Optune Gio® is a wearable treatment delivery system that can provide continuous anti-cancer therapy*

What is Optune Gio?⁷

- Portable, small (18 x 19 x 5 cm) and lightweight (1.2 kg) medical device, noninvasive, locally acting.
- It delivers alternating electric fields called Tumor Treating Fields (TTFields) that disrupt the division of tumor cells and can induce their death without damaging surrounding tissues.^{8,9}
- Uses 2 pairs of Arrays to be placed on the scalp.
- Designed to integrate into your patients' lives and daily activities.



Optune Gio is a CE Marked Medical Device (CE-0197).

TTFields – Mechanism of Action

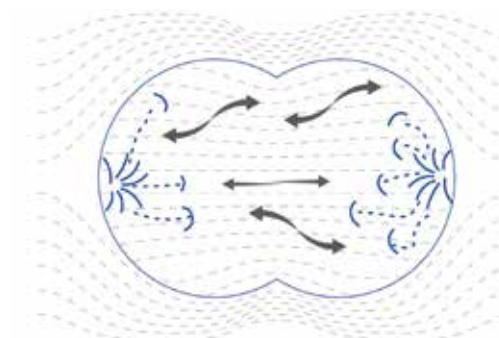
Optune Gio exploits the electrical properties of cancer cells using TTFields therapy to interfere with mitosis.^{2,7,8,9}

TTFields are delivered at a specific frequency (200kHz) to selectively disrupt the glioblastoma cell division.⁹



Metaphase^{8,9,10}

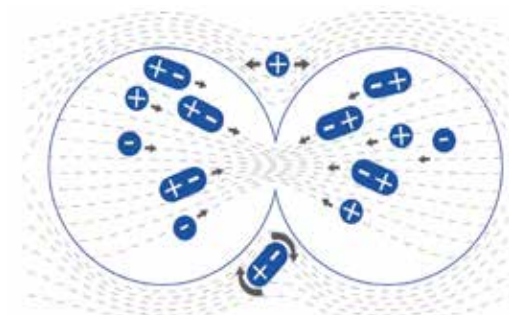
Spindle microtubule assembly is disrupted (tubulin is highly polar).



Anaphase^{8,9,10}

Disruption of the localization of contractile elements in the cleavage groove (septin is highly polar).

Asymmetric segregation of chromosomes leads to aneuploidy.



Telophase^{8,9,10}

Intracellular dielectrophoresis of polar cell components toward the cleavage furrow leads to disruption of cytokinesis.

----- Electrical fields

Scan the QR code to access a video about how TTFields work



TTFields are recommended in clinical guidelines

Efficacy results of EF-14

International guidelines:

NCCN
CATEGORY 1 PREFERRED

Alternating electric fields (Optune Gio)
for newly diagnosed GBM

The NCCN Clinical Practice Guidelines in Oncology (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 status regardless of MGMT promoter status.^{11,§}

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).¹¹

§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 ≥70.¹¹

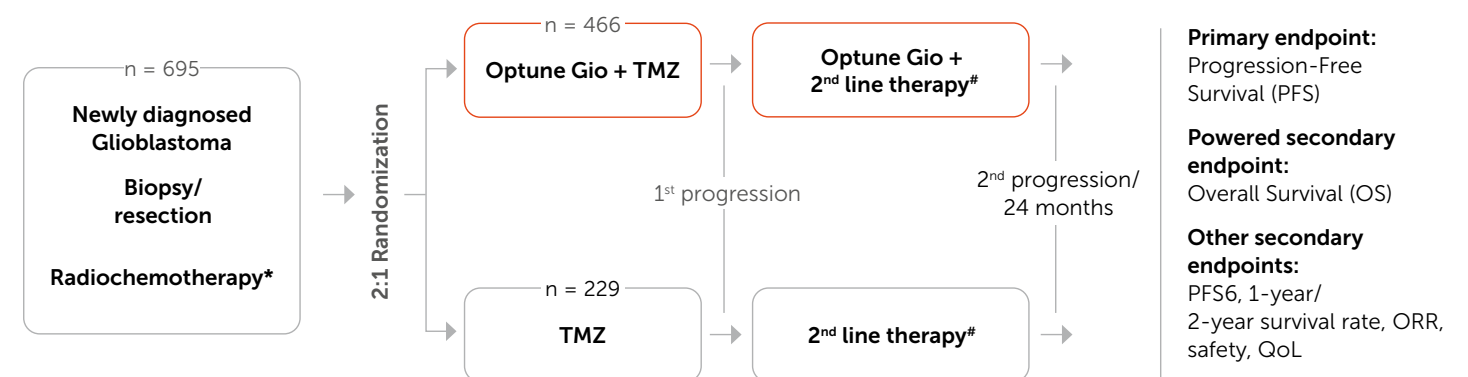
National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Local guidelines:

The SEOM-GEINO clinical guidelines for high grade gliomas of adulthood (2022) recommend that clinicians should consider treatment with TTFields and TMZ in subjects without suspected progression or pseudoprogression after chemoradiation with TMZ, if available in the center (level of recommendation: I, A)^{*12}.

EF-14 – phase III study

The EF-14 study is an international, multicenter, prospective, randomized phase 3 trial of the efficacy and safety of Optune Gio® (TTFields) + Temozolomide (TMZ) versus TMZ monotherapy in patients with newly diagnosed Grade 4 Glioma⁴



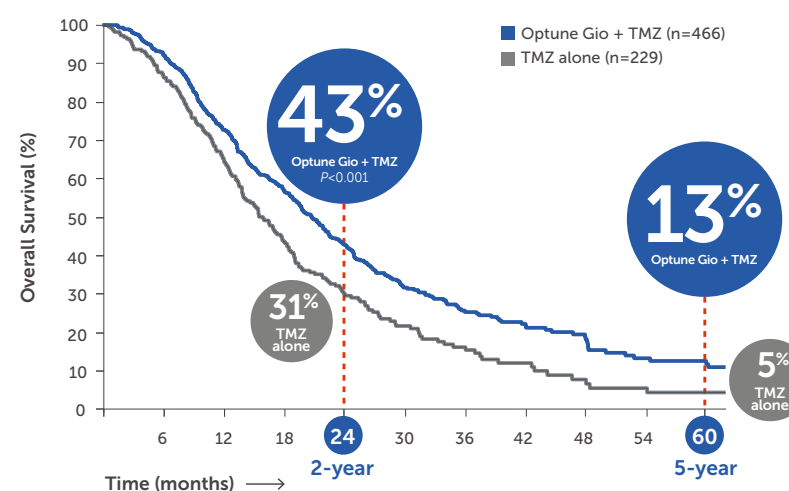
Stratified by

1. Resection (biopsy vs partial resection vs total resection)
2. MGMT promoter methylation status

* Radiochemotherapy: 45-70 Gy + TMZ. # Second line therapy: surgery, local radiotherapy, chemotherapy, or combination. MGMT, O6-methylguanine-DNA-methyl-transferase; PFS6, progression-free survival at 6 months; ORR, objective response rate; QoL, quality of life; TMZ, temozolomide

Overall survival with Optune Gio + TMZ vs TMZ alone was significantly better at the 2- and 5-year landmark analyses

Overall survival (2- and 5-year survival analysis)^{6,7}



Median OS was significantly extended with Optune Gio⁶

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

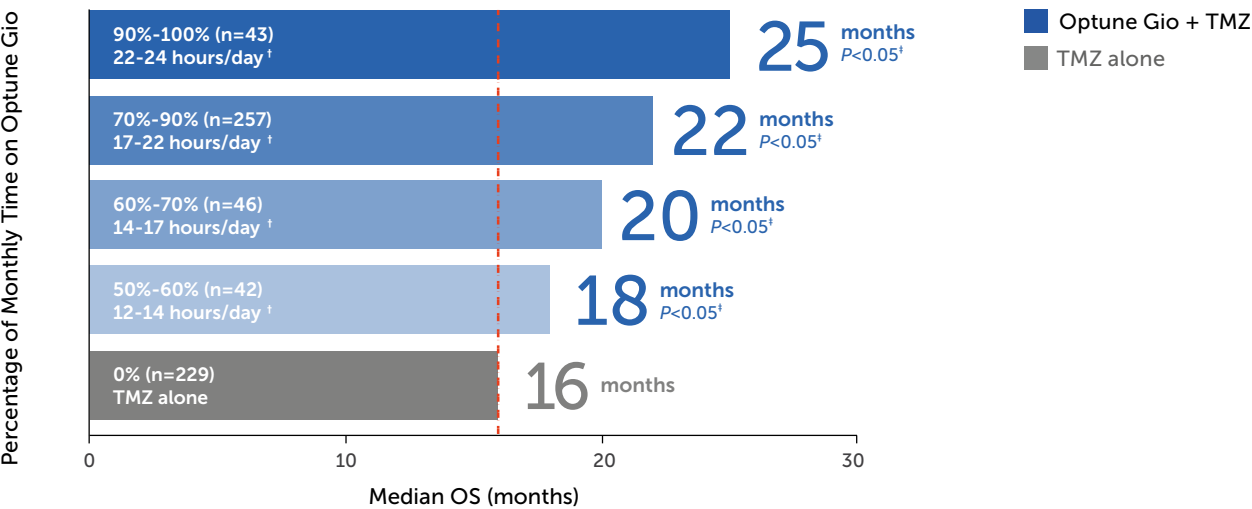
5 YEARS

Overall Survival: Optune Gio+ TMZ demonstrated greater 5-year survival compared with TMZ alone(13% vs 5%)⁶

Significantly increased survival benefit was seen with more time on Optune Gio^{®13}

EF-14 post hoc analysis by patient subgroups

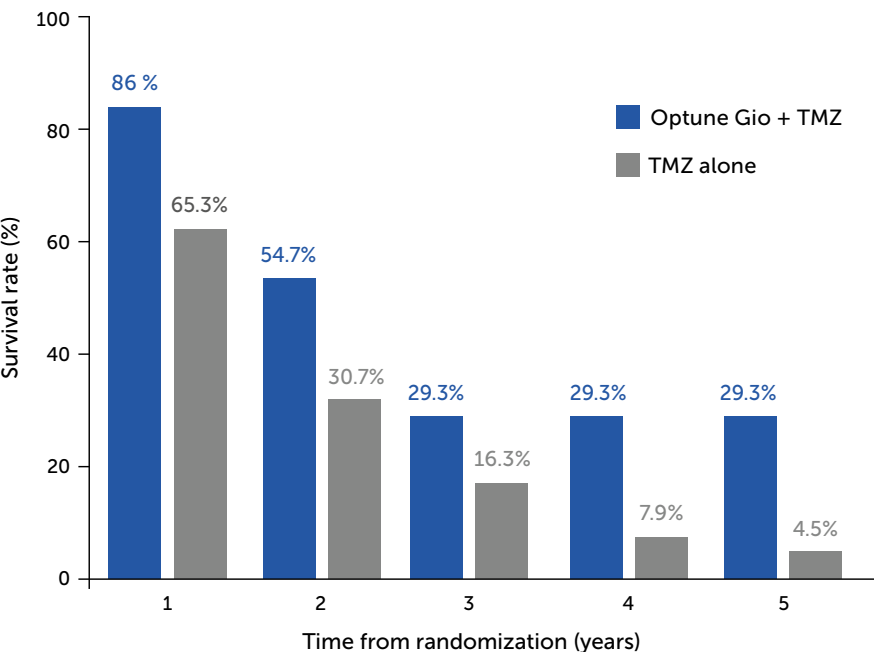
Median overall survival according to percentage of treatment time with Optune Gio¹³



Increased monthly usage[†] of Optune Gio was a predictor for improved overall survival, independent of other prognostic factors such as KPS, age or MGMT methylation status.

[†] Based on the amount of time Optune Gio was on and provided therapy over the course of a month. These data reflect the average use of patients who used Optune Gio in the first 6 months of treatment (months 1–6)¹².
[‡] Approximation, based on monthly use versus TMZ alone.

Annual survival rate of patients with highest usage¹³



**29,3%
vs 4,5%**

Probability of 5-year survival with 90 % use (N=43) vs survival with TMZ alone¹³

Overall survival according to prognostic patient subgroups⁶

Subgroup	Patients, n(%)		HR (95% CI)	Median survival (mo)	
	Optune Gio + TMZ	TMZ alone		Optune Gio + TMZ	TMZ alone
Overall	466 (100)	229 (100)		20.9	16.0
MGMT (central)					
Unmethylated	209 (45)	95 (41)		16.9	14.7
Methylated	137 (29)	77 (34)		31.6	21.2
Resection					
Biopsy	60 (13)	29 (13)		16.5	11.6
Partial	157 (34)	77 (34)		21.4	15.1
Gross total	249 (53)	123 (54)		22.6	18.5
Age					
< 65 y	377 (81)	184 (80)		21.6	17.3
≥ 65 y	89 (19)	45 (20)		17.4	13.7
KPS					
90–100	308 (66)	149 (65)		23.3	17.8
≤ 80	154 (33)	74 (32)		14.9	11.0
Sex					
Female	150 (32)	72 (31)		24.6	18.5
Male	316 (68)	157 (69)		19.1	15.5

0.1

1.0

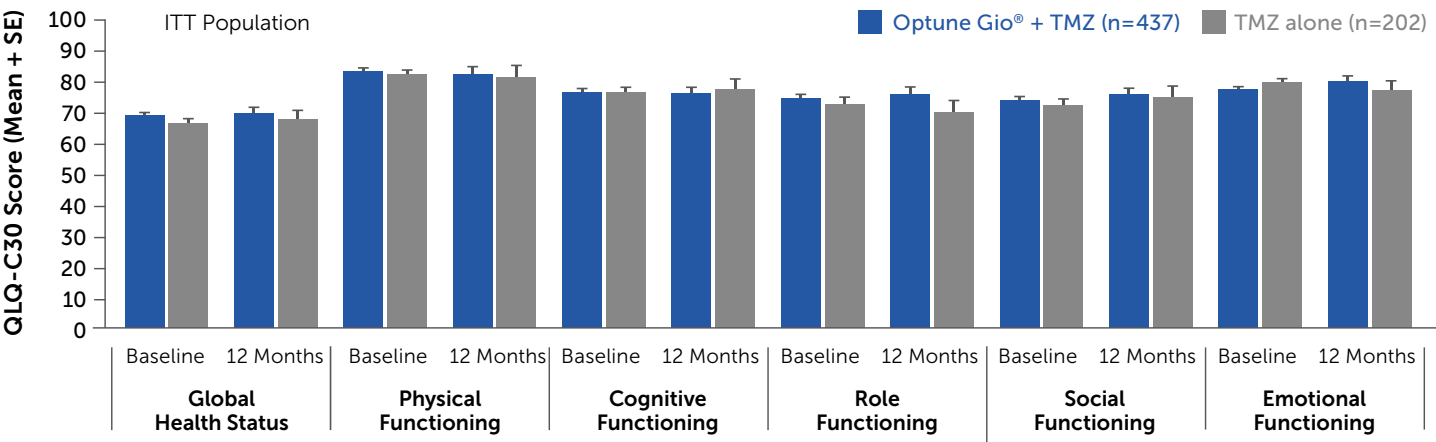
Optune Gio + TMZ better

TMZ alone better

Adapted from Stupp R, 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.
HR, hazard ratio; KPS, Karnofsky Performance Status; MGMT, O-6-methylguanine-DNA methyltransferase; OS, overall survival; TMZ, temozolomide.

QoL was maintained with TTFields + TMZ as measured up to one year^{5,14,*,†}

For the domains shown on this slide, a higher score represents a higher level of functioning



Optune Gio®: No increase in serious systemic adverse events^{6,*}

The most likely adverse events ($\geq 5\%$) involving TTFields together with TMZ were thrombocytopenia, nausea, constipation, vomiting, fatigue, headache, seizures, and depression.¹⁵

The overall incidence, distribution, and severity of adverse events were comparable to the TMZ-only arm.⁶

Incidence of grade 3/4 adverse events in $\geq 5\%$ of patients (Final Analysis)^{6,7}

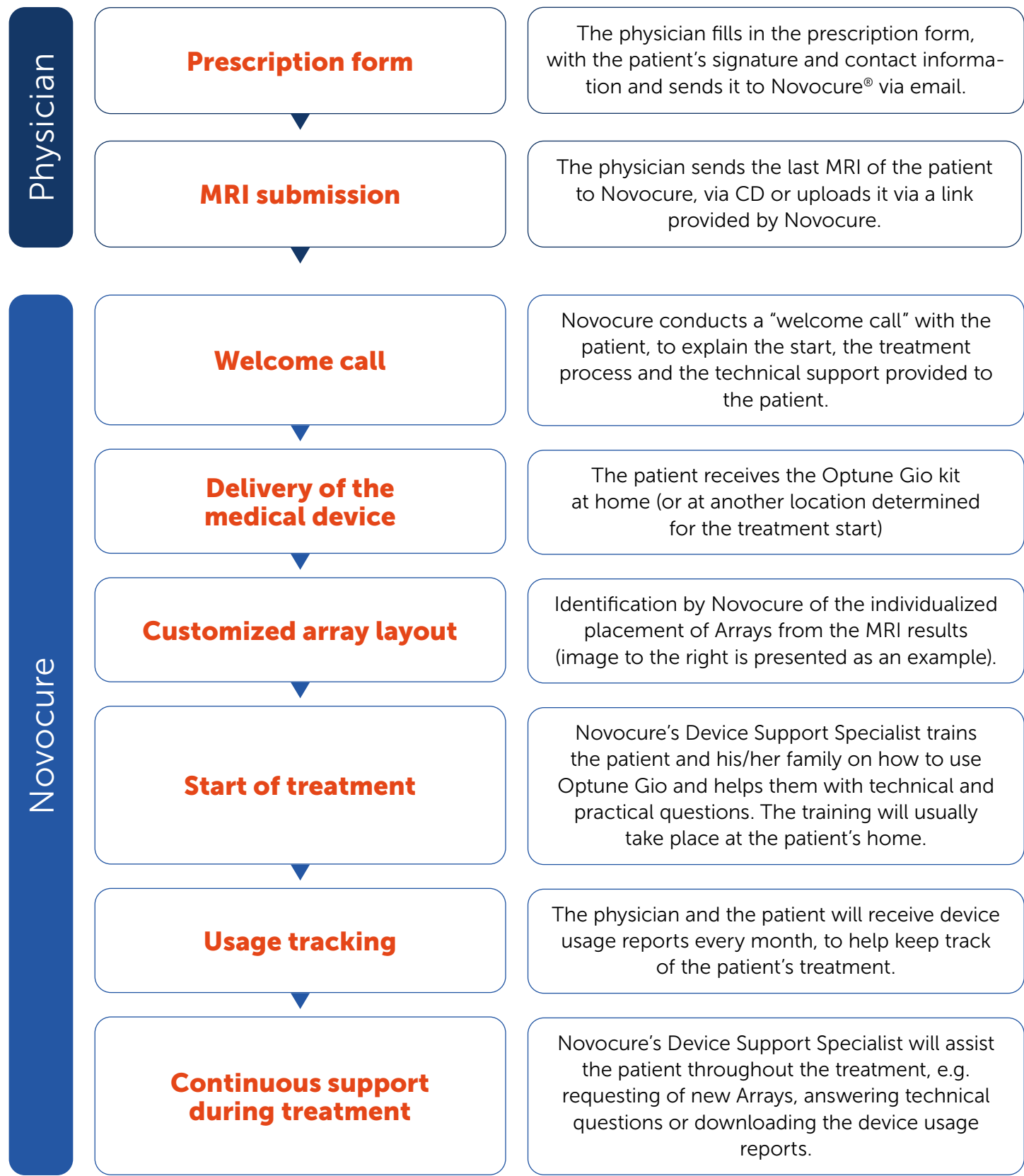
Safety Population	Optune Gio + TMZ (n=456) %	TMZ alone (n=216) %
≥ 1 Adverse event	48	44
Blood and lymphatic system disorder* Thrombocytopenia	13 9	11 5
Gastrointestinal disorders	5	4
Asthenia, fatigue, and gait disturbance	9	6
Infections	7	5
Injury, poisoning, and procedural complications (falls and 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 Seizures	24 6	20 6
Respiratory, thoracic and mediastinal disorders (pulmonary embolism, dyspnea, and aspiration pneumonia)	5	5
Incidence AE (selection)		
Grade 1–2 (grade 3)	Optune Gio+TMZ	
Skin irritation	52 % (2%)	

The most common adverse event **associated with the device** was a skin irritation observed under the Arrays. **Recorded in 52% of the patients in the study, most of the skin irritation events were mild to moderate. Severe skin irritations were found in 2% of patients.**⁶

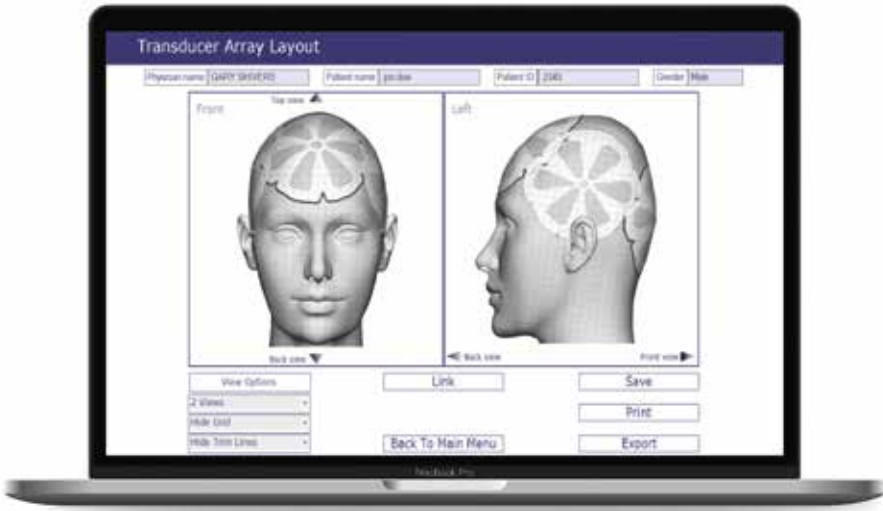
*Data collected by EORTC QLQ-C30 and QLQ-BN20 questionnaires. †Patients with newly diagnosed GBM.
EORTC, European Organisation for Research and Treatment of Cancer; GBM, glioblastoma; ITT, intent to treat; QLQ-BN20, Quality of Life Questionnaire for Brain Neoplasms; QLQ-C30, Quality of Life Core Questionnaire-C30; QoL, quality of life; SE, standard error; TMZ, temozolomide.

* The numerically slightly higher incidence of hematological toxicity, fatigue, and some other adverse effects are due to the longer treatment duration and observation time in the experimental group.TMZ, temozolomide; TTFields, Tumor Treating Fields.

Process and service provided during treatment with Optune Gio®



If patients have any medical questions about the disease or treatment, they should consult their physician. For more information about Optune Gio, please refer to the user manual: manuals.novocure.eu



Sample customized array layout report



Actress portrayals

Information your patients should know before using Optune Gio®

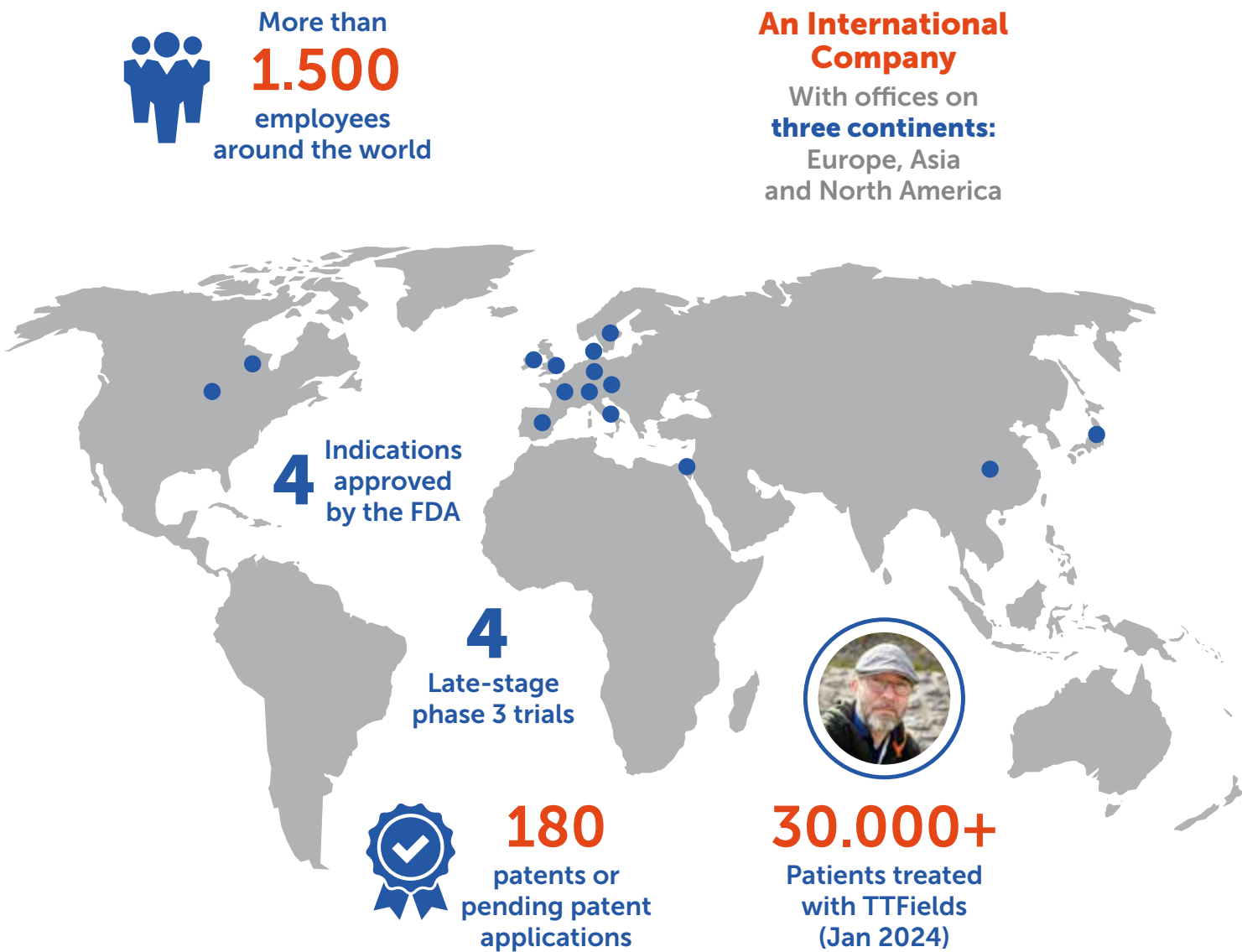
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 - Optune Gio is designed to fit into the patient's daily life routines:
 - At home
 - Outdoors
 - During daytime activities
 - While sleeping
- 
 - Optune Gio should be worn for as continuously as possible each day
- 
 - The scalp should be shaved so that the Arrays are in direct contact with the skin itself.
- 
 - The Arrays should be changed periodically (usually every 3–4 days, or at least twice a week). An assistant (family member/ friend) may facilitate the process of changing the Arrays.
- 
 - The Arrays can be covered with a breathable light cap, scarf or wig.

Travel and sport activities depend on the status of the patient and the activity done, and need to be discussed in advance with the physician

For more information about Optune Gio please read the user manual:
manuals.novocure.eu



Novocure® in numbers



novocure®



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2. Giladi M *et al.* Mitotic Spindle Disruption by Alternating Electric Fields Leads to Improper Chromosome Segregation and Mitotic Catastrophe in Cancer Cells. *Sci Rep*. 2015;5:18046.
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8. Kirson E *et al.* Disruption of Cancer Cell Replication by Alternating Electric Fields. *Cancer Research*. 2004;64(9):3288-3295.
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11. Referenced with permission from 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 30, 2023. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org).
12. Pedro Pérez Segura *et al.* Clin and Trans Oncology (2023) 25:2634-2646.
13. Toms S. A. *et al.* 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; 141:467–473
14. 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(suppl 4)
15. Novocure Data on File OPT-103.

Intended purpose

The Optune Gio treatment kit is intended for the treatment of patients with newly diagnosed WHO grade 4 glioma and for the treatment of patients with recurrent WHO grade 4 glioma.

Newly diagnosed WHO grade 4 glioma

Optune Gio is intended for the treatment of adult patients (18 years of age or older) with newly diagnosed WHO grade 4 glioma, following maximal debulking surgery or biopsy, radiation therapy and/or chemotherapy, concomitant with maintenance Temozolomide with or without Lomustine, and after systemic therapy is stopped.

Recurrent WHO grade 4 glioma

Optune Gio is intended for the treatment of patients with recurrent WHO grade 4 glioma who have progressed after surgery, radiotherapy and chemotherapy treatment for their primary disease. The treatment is intended for adult patients, 18 years of age or older.

Contraindications

Do not use the Optune Gio treatment kit if you are pregnant, think you might be pregnant, or are trying to get pregnant. If you are a woman who is able to get pregnant, you must use birth control when using the device. The Optune Gio treatment kit was not tested in pregnant women.

Do not use the Optune Gio treatment kit if you have significant additional neurological disease (primary seizure disorder, dementia, Progressive degenerative neurological disorder, Meningitis or encephalitis, Hydrocephalus associated with increased intracranial pressure).

Do not use the Optune Gio treatment kit if you are known to be sensitive to conductive hydrogels like the gel used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes. In this case, skin contact with the gel used with the Optune Gio treatment kit may commonly cause increased redness and itching, and rarely may even lead to severe allergic reactions such as shock and respiratory failure.

Do not use the Optune Gio treatment kit if you have an active implanted medical device, a skull defect (such as, missing bone with no replacement) or bullet fragments. Examples of active electronic devices include deep brain stimulators, spinal cord stimulators, vagus nerve stimulators, pacemakers and defibrillators. Use of the Optune Gio treatment kit together with implanted electronic devices has not been tested and may lead to malfunctioning of the implanted device. Use of the Optune Gio treatment kit together with skull defects or bullet fragments has not been tested and may possibly lead to tissue damage or render treatment ineffective.

For more full information about Optune Gio, please refer to the user manual: manuals.novocure.eu



Actor portrayal

Notes



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Patients treated with Optune Gio® worldwide



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Novocure Spain S.L.

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