Optune® + TMZ has been proven to provide long-term quality survival to patients with newly diagnosed GBM¹²,*

*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).
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer core quality of life questionnaire; GBM, glioblastoma; TMZ, temozolomide.

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.

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Please see the Important Safety Information for Optune on page 10 and the accompanying Optune Instructions for Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.
GBM: an aggressive disease that is challenging to control

GBM is always present and continually proliferating\(^3\)

- The continuous division, migration, and invasion of GBM has been difficult to control over time\(^4,5\)

With a high risk of GBM recurrence, every appropriate treatment available should be used to combat this persistent threat

- For more than a decade, post-surgery radiation and chemotherapy have been the standard of care\(^6\)
Optune®: a well-suited part of the treatment plan for newly diagnosed GBM

Optune provides continuous action against GBM progression

- Optune delivers TTFields to selectively and continuously disrupt mitosis for as long as it is worn7,8

Including Alternating Electric Field Therapy (Optune) as part of the treatment plan for newly diagnosed GBM gives patients every approved method to prevent progression

- 5-year survival results published in JAMA9 support an update to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers10

The NCCN Guidelines® for Central Nervous System Cancers include alternating electric field therapy (Optune) together with temozolomide (TMZ) following maximal safe resection and standard brain radiation therapy with concurrent TMZ as a Category 1 recommended treatment option for patients with newly diagnosed supratentorial GBM and good performance status. The NCCN-preferred adjuvant treatment regimen is radiation therapy with concurrent and adjuvant TMZ +/- Optune. There is uniform NCCN consensus for this recommendation based on high-level evidence (Category 1).*

*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.

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GBM, glioblastoma; TTFields, Tumor Treating Fields.

Please see the accompanying Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.

*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.
In newly diagnosed GBM, Optune® + TMZ provided an unprecedented long-term survival benefit that increased with more time on Optune.

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

### Overall Survival (5-year survival analysis)

- **Optune + TMZ (n=466)**
- **TMZ alone (n=229)**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Optune + TMZ</th>
<th>TMZ alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-year</td>
<td>20.9</td>
<td>16.0</td>
</tr>
<tr>
<td>Median OS from randomization (months)</td>
<td>20.9</td>
<td>16.0</td>
</tr>
<tr>
<td>Log-rank P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.63 (0.53-0.76)</td>
<td>1.00 (0.80-1.26)</td>
</tr>
<tr>
<td>Median OS from diagnosis (months)</td>
<td>24.5</td>
<td>19.8</td>
</tr>
</tbody>
</table>

Proven to provide the best opportunity for Greater Overall Survival At 5 Years vs TMZ alone (13% vs 5%).

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

Optune + TMZ also significantly improved PFS vs TMZ alone

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

Selected Safety Information

**Contraindications (cont’d)**

Do not use Optune in patients that 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.
More time on Optune predicted increased significant survival benefit

Median OS by Percentage of Monthly Time on Optune*

- 90%-100% (n=43) 22-24 hours/day†
- 70%-90% (n=257) 17-22 hours/day†
- 60%-70% (n=46) 14-17 hours/day†
- 50%-60% (n=42) 12-14 hours/day†
- 0% (n=229) TMZ alone

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

86% of patients received a survival benefit from Optune because they used it more than half the time (n=388/450)‡

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

‡vs TMZ alone.

GBM, glioblastoma; KPS, Karnofsky Performance Score; MGMT, O-6-methylguanine–DNA methyltransferase; OS, overall survival; PFS, progression-free survival; TMZ, temozolomide.

Please see the accompanying Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.
In newly diagnosed GBM,

Patients treated with Optune® + TMZ maintained QoL over time across predefined daily-functioning domains

Both HCPs and patients reported stable predefined daily functioning scores up to 1 year of Optune use²,¹⁴.⁺,†

QoL Over 12 Months²,¹⁴

- 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, which was twice as large in size and weight (6 lb) than 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.

†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).

Selected Safety Information

Warnings and Precautions
The most common (≥10%) adverse events involving Optune in combination with temozolomide were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression.
Physical, Role, Social, Emotional, and Cognitive Functioning for patients treated with Optune + TMZ all remained stable and comparable with the TMZ alone arm²

<table>
<thead>
<tr>
<th>Functioning domain</th>
<th>Sample questions from the EORTC QLQ-C30 core questionnaire¹⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?</td>
</tr>
<tr>
<td>Role</td>
<td>During the past week, were you limited in doing either your work or other daily activities?</td>
</tr>
<tr>
<td>Social</td>
<td>During the past week, has your physical condition or medical treatment interfered with your social activities?</td>
</tr>
<tr>
<td>Emotional</td>
<td>During the past week, did you feel tense?</td>
</tr>
<tr>
<td>Cognitive</td>
<td>During the past week, have you had difficulty remembering things?</td>
</tr>
</tbody>
</table>

“Getting used to Optune took a village—Cecil, Ben, me, and my doctors. But I refuse to sit down and give up when it comes to my care. A positive attitude means so much.”

-Kim, Optune user and Patient Ambassador

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer core quality of life questionnaire; GBM, glioblastoma; HCPs, healthcare professionals; HRQoL, health-related quality of life; KPS, Karnofsky Performance Score; QoL, quality of life; TMZ, temozolomide.

Please see the accompanying Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.
In newly diagnosed GBM, Optune® was safely used together with TMZ

No late-emerging serious AEs were seen in the 5-year follow-up\textsuperscript{1,9}

<table>
<thead>
<tr>
<th>Incidence of grade 3/4 AEs occurring in $\geq$5% of patients during 5 years of follow-up</th>
<th>Optune + TMZ (n=456) %</th>
<th>TMZ alone (n=216) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq$1 AE</td>
<td>48</td>
<td>44</td>
</tr>
</tbody>
</table>
| Blood and lymphatic system disorders
  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 |  |
No significant increase in serious AEs compared with TMZ alone

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

• A slightly higher incidence of grade 1/2 AEs was seen in some of the systems in the Optune + 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 group.

• The rate of grade 1/2 medical device site reaction was 52% for Optune + TMZ compared with 0% for TMZ alone, and severe (grade 3) skin involvement occurred in 2% of patients treated with Optune + TMZ.

• Grade 3/4 AEs were well balanced between arms. None of the systemic grade 3/4 AEs were considered related to Optune by any of the investigators.

• Mild-to-moderate skin irritation, the most common device-related side effect with Optune, was typically manageable, reversible, and did not result in treatment discontinuation.

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

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Important Safety Information

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

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Do not use Optune in patients that 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
The most common (>10%) adverse events involving Optune in combination with temozolomide were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression.

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 treatment.

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

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

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

References:
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Partnering with your patients and your practice at every step of the journey

nCompass®: an award-winning support program with comprehensive services for your patients using Optune

Reimbursement assistance
• Supports your patients and your practice through the reimbursement process, starting with an investigation of benefits

Customized support based on patient or caregiver needs, including
• In-person device education
• Resources and tips for using Optune
• Technical support via phone
• Reordering supplies

Contact nCompass for all your patients’ Optune support needs

Call us any time of day: 1-855-281-9301 (toll-free)
Or email us: support@novocure.com

Novocure is NOT permitted to provide medical advice to patients. All patients with medical questions will be referred back to their healthcare provider.

Please see the accompanying Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.
For your next patient with newly diagnosed GBM,

**PUT GBM ON PAUSE.**

**PUT LIFE ON PLAY.**

Optune® + TMZ has been proven to provide long-term quality survival\(^1,2\)

<table>
<thead>
<tr>
<th>Unprecedented long-term survival significantly increased with more time on Optune(^1,12)</th>
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<td>• OS was significantly higher at the 2-year landmark analysis and remained higher at 5 years</td>
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<td>– Median OS was significantly extended with Optune—by nearly 5 months ((P &lt; 0.001))</td>
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<th>Patients treated with Optune + TMZ maintained QoL over time across predefined daily-functioning domains(^2,14)</th>
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<td>• Both HCPs and patients reported stable predefined daily functioning scores up to 1 year of Optune use, as defined inside</td>
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<th>Optune + TMZ have been safely used together for 5 years(^1,9)</th>
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<tr>
<td>• No significant increase in serious AEs compared with TMZ alone</td>
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<tr>
<td>• The most common side effect was mild-to-moderate skin irritation</td>
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AEs, adverse events; GBM, glioblastoma; HCP, healthcare professional; OS, overall survival; QoL, quality of life; TMZ, temozolomide.

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