In a post hoc analysis, Optune® + TMZ was associated with improved clinical outcomes vs TMZ alone when tumor resection is not feasible\textsuperscript{1,2}

Not every patient with GBM is a candidate for gross total or partial resection—some may only have a biopsy\textsuperscript{3}

• Based on multidisciplinary input, if feasible, for treatment planning\textsuperscript{3}:
  – Patients will undergo maximal debulking surgery with a goal of image-verified complete resection
  – Curative resection in GBM, however, is very rare

• If maximal, safe resection is not feasible, patients may undergo\textsuperscript{3}
  – Subtotal resection with MRI after resection
  – Biopsy (stereotactic or open)

Please see the Important Safety Information for Optune on back cover and the accompanying Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions.
Optune® + TMZ provided an unprecedented long-term survival benefit

- Survival with Optune + TMZ vs TMZ alone was significantly higher at the 2-year landmark analysis and remained higher at 5 years
- Median OS was significantly extended with Optune—by nearly 5 months (P<0.001)

EF-14 was a prospective, randomized, open-label, active, parallel-control trial to compare the effectiveness and safety outcomes of patients with newly diagnosed GBM treated with Optune + TMZ vs those treated with TMZ alone (N=695)

- PFS, primary endpoint
- OS, secondary endpoint

Key inclusion criteria:
- Pathological evidence of GBM using WHO classification criteria
- Age ≥18 years
- KPS ≥70
- Life expectancy of at least 3 months
- Treatment start date at least 4 weeks out from surgery
- Treatment start date at least 4 weeks out but not more than 7 weeks from the latest dose of concomitant TMZ or radiotherapy
- Had undergone maximal debulking surgery or biopsy, and radiotherapy concomitant with TMZ (45-70 Gy)

Optune + TMZ also significantly improved median PFS vs TMZ alone (6.7 months vs 4.0 months, P<0.001)

- The most common (≥10%) AEs involving Optune together 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 patients in the Optune + TMZ arm of the study. This most likely reflects the longer duration of TMZ treatment in these patients
- 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% for 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 observed with Optune, was typically manageable, reversible, and did not result in treatment discontinuation

No significant increase in serious AEs compared with TMZ alone

### Overall Survival (5-year survival analysis)²,⁴

Optune + TMZ (n=466)

- Median OS from randomization (months)
- Log-rank P value
- HR (95% CI)
- Median OS from diagnosis (months)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Survival (%)</td>
<td>0</td>
<td>10</td>
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Optune + TMZ (n=466) vs TMZ alone (n=229)

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<th>Time (months)</th>
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<th>5-yr</th>
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<td>Survival (%)</td>
<td>24%</td>
<td>60%</td>
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Proven to provide the best opportunity for greater OS at 5 years vs TMZ alone (13% vs 5%)

### Overall Survival (5-year survival analysis)²,⁴

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Proven to provide the best opportunity for greater OS at 5 years vs TMZ alone (13% vs 5%)

IN NEWLY DIAGNOSED GBM, Optune® was safely used together with TMZ¹,⁴

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IN NEWLY DIAGNOSED GBM, Optune® was safely used together with TMZ¹,⁴

No significant increase in serious AEs compared with TMZ alone¹,⁴

<table>
<thead>
<tr>
<th>Incidence of grade 3/4 AEs occurring in ≥15% of patients during 5 years of follow-up¹,⁴</th>
<th>Optune + TMZ (n=456)</th>
<th>TMZ alone (n=216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 AE</td>
<td>48%</td>
<td>44%</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenia, fatigue, and gait disturbance</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury, poisoning, and procedural complications (falls and medical device site reaction)</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders (anorexia, dehydration, and hyperglycemia)</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>24%</td>
<td>20%</td>
</tr>
<tr>
<td>Respiratory, thoracic, and mediastinal disorders (pulmonary embolism, dyspnea, and aspiration pneumonia)</td>
<td>5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

AEs, adverse events; GBM, glioblastoma; Gy, gray; HR, hazard ratio; KPS, Karnofsky Performance Score; OS, overall survival; PFS, progression-free survival; TMZ, temozolomide; WHO, World Health Organization.

Please see Important Safety Information throughout and the Instructions for Use (IFU) at Optune.com/IFU.
Results of a post hoc analysis showed Optune® + TMZ was associated with increased median OS vs TMZ alone in patients ineligible for surgical resection.1,2

The EF-14 pivotal phase 3 trial included patients with newly diagnosed GBM who only had a biopsy:1

- The study protocol defined surgery as surgical resection to the extent safely feasible or biopsy.1
- Patients who did not have a resection had a biopsy.5

Extent of resection was consistent across both study arms.1

<table>
<thead>
<tr>
<th>Extent of resection</th>
<th>Optune + TMZ % (n)</th>
<th>TMZ alone % (n)</th>
</tr>
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<tbody>
<tr>
<td>Biopsy only</td>
<td>13% (60)</td>
<td>13% (29)</td>
</tr>
<tr>
<td>Partial resection</td>
<td>34% (157)</td>
<td>33% (77)</td>
</tr>
<tr>
<td>Gross total resection</td>
<td>53% (249)</td>
<td>54% (123)</td>
</tr>
<tr>
<td>Total (N=695)</td>
<td>100% (466)</td>
<td>100% (229)</td>
</tr>
</tbody>
</table>

Biopsy-Only Patients (n=89)2

- Biopsy-only patients using Optune + TMZ had longer median OS (16.5 months) vs those using TMZ alone (11.6 months).1,2

Gabriel et al.2

In a post hoc analysis, Optune® + TMZ improved median OS vs TMZ alone regardless of extent of resection.1,2,*

- In patients who had a partial resection, median OS was 21.4 months with Optune + TMZ (n=157) compared with 15.1 months with TMZ alone (n=77) (HR: 0.56; 95% CI, 0.41-0.77).1,2
- In patients who had a gross total resection, median OS was 22.6 months with Optune + TMZ (n=249) compared with 18.5 months with TMZ alone (n=123) (HR: 0.70; 95% CI, 0.54-0.91).1,2

GBM, glioblastoma; ITT, intent to treat; OS, overall survival; TMZ, temozolomide; TTFields, Tumor Treating Fields.
Regardless of extent of surgical resection, consider if Optune® is a viable treatment choice for your patients with newly diagnosed GBM

**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.

**Important Safety Information**

**Contraindications**

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

Please see Important Safety Information throughout and the Instructions for Use (IFU) at Optune.com/IFU.

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