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OPTUNE EDUCATIONAL PROGRAM

Tumor Treating Fields for Glioblastoma
Disclaimer

- Novocure and its employees are not acting as health care professionals and cannot provide medical advice to patients
Learning Objectives

Optune Educational Program

Goal: Provide an overview of Optune (TTFields) for the management of patients with GBM

- Optune Mechanism of Action
- Optune Clinical Data
- Optune Patient Selection and Management
- Integrating Optune into the treatment plan for GBM

Discussing Optune with Patients and Caregivers

TTFields, Tumor Treating Fields; GBM, glioblastoma multiforme.
Overview of Glioblastoma
Glioblastoma

- Most prevalent and aggressive central nervous system cancer in adults\(^1\)
  - Disease prognosis depends on
    - Age\(^1-3\)
    - Extent of surgical resection\(^2,3\)
    - Tumor location\(^1,3\)
    - Genetics\(^4,5\)
    - Functional status\(^2,3\)

- Historically poor prognosis has been due to limited treatment options\(^6\)

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Optune Indications for Use and Important Safety Information
Optune Indications for Use and Important Safety Information

INDICATIONS

• 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.

• For the treatment of recurrent GBM, Optune is indicated following histologically-or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

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.

Please see the Optune Instructions for Use (IFU) for complete information regarding the device’s indications, contraindications, warnings and precautions at http://www.optune.com/hcp/instructions-for-use.aspx.
Important Safety Information

WARNINGS AND PRECAUTIONS

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

- 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.

- 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.

- The most common (≥10%) adverse events seen with Optune monotherapy were medical device site reaction and headache.

- The following adverse reactions were considered related to Optune when used as monotherapy: medical device site reaction, headache, malaise, muscle twitching, fall and skin ulcer.

- 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.

- If the patient has an underlying serious skin condition on the scalp, evaluate whether this may prevent or temporarily interfere with Optune treatment.

Please see the Optune Instructions for Use (IFU) for complete information regarding the device’s indications, contraindications, warnings and precautions at http://www.optune.com/hcp/instructions-for-use.aspx.
Understanding Optune
What is Optune?

- Optune is a wearable, FDA-approved device\(^1\)
  - Noninvasive and portable
  - Classified as durable medical equipment
- Complete system includes\(^2\)
  - Electric field generator
  - Connection cable and box
  - 4 transducer arrays
  - 4 batteries and a charger
  - Plug-in power supply
  - Carrying bag

To date, >10,000 patients with GBM treated with Optune\(^3\)

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How Does Optune Work?

- Optune has been shown in clinical trials to safely deliver continuous therapy to the area of the brain where the GBM tumor is located.\(^1\)
- Optune delivers therapy through the 4 adhesive patches, called transducer arrays, that are applied to the scalp and are connected to the device and battery.\(^1,2\)
- When Optune is turned on, it creates low-intensity, wave-like electric fields called TTFields.\(^1\)
- TTFields may interfere with GBM cancer cell division. This action slows or stops GBM cancer cells from dividing, and may cause them to die.\(^1\)

GBM, glioblastoma multiforme; TTFields, Tumor Treating Fields.
Glioblastoma (GBM)
Cancer Cell Division
and
Tumor Treating Fields (TTFields)
Clinical Data in Newly Diagnosed Glioblastoma
Primary endpoint (ITT population): PFS
Secondary endpoint (PP population): OS
Additional secondary endpoints: PFS6, 1-y/2-y survival, ORR, safety, QoL

Stratification by
1. Resection (biopsy vs partial vs gross total)
2. MGMT promoter methylation status

*Treatment with Optune was continued for 24 months or until second progression, whichever occurred first unless prohibited by the patient’s clinical condition.¹,²

GBM, glioblastoma multiforme; TMZ, temozolomide; RT, radiation therapy; 2L, second-line; SRS, stereotactic radiosurgery; ITT, intent-to-treat; PFS, progression-free survival; PP, per-protocol; OS, overall survival; PFS6, the percentage of patients alive and progression-free at 6 months; ORR, objective response rate; QoL, quality of life; MGMT, O6-methylguanine-DNA methyltransferase.

EF-14: Progression-Free Survival¹

All patients included in the EF-14 analysis had a minimum follow-up of 24 months.¹

ITT, intent to treat; TMZ, temozolomide; PFS, progression-free survival; CI, confidence interval; HR, hazard ratio.

EF-14: Overall Survival

### ITT Population

<table>
<thead>
<tr>
<th></th>
<th>Optune + TMZ (n=466)</th>
<th>TMZ Alone (n=229)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS from randomization, mo$^1$</td>
<td>20.9</td>
<td>16.0</td>
</tr>
<tr>
<td>95% CI, mo$^1$</td>
<td>19.1-22.6</td>
<td>13.9-18.2</td>
</tr>
<tr>
<td>Stratified log-rank$^1$</td>
<td>$P&lt;0.001$</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)$^1$</td>
<td>0.63 (0.53-0.76)</td>
<td></td>
</tr>
<tr>
<td>Median OS from diagnosis, mo$^2$</td>
<td>24.5</td>
<td>19.8</td>
</tr>
<tr>
<td>2-year OS$^1$</td>
<td>43%</td>
<td>31%</td>
</tr>
</tbody>
</table>

**Notes:**


**Legend:**

- ITT, intent to treat; TMZ, temozolomide; CI, confidence interval; HR, hazard ratio; OS, overall survival.
- Overall Survival (months) vs. Fraction Survival
- Median OS from randomization and diagnosis with 95% CI
- Stratified log-rank test with P-value
- Hazard ratio with 95% CI
EF-14: Long-Term Survival Rates

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

**Year From Randomization**

<table>
<thead>
<tr>
<th>Year</th>
<th>Survival Rate Optune + TMZ</th>
<th>Survival Rate TMZ Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73%</td>
<td>65%</td>
</tr>
<tr>
<td>2</td>
<td>43%</td>
<td>31%</td>
</tr>
<tr>
<td>3</td>
<td>26%</td>
<td>16%</td>
</tr>
<tr>
<td>4</td>
<td>20%</td>
<td>8%</td>
</tr>
<tr>
<td>5</td>
<td>13%</td>
<td>5%</td>
</tr>
</tbody>
</table>

TMZ, temozolomide.
EF-14: Monthly Time on Optune Impacts Overall Survival

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Optune + TMZ</th>
<th>TMZ Alone</th>
<th>Hazard Ratio</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>450 (100)</td>
<td>229 (100)</td>
<td></td>
<td>20.9/16.0</td>
</tr>
<tr>
<td>% of monthly time on Optune</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;90†</td>
<td>43 (10)</td>
<td></td>
<td></td>
<td>24.9/16.0</td>
</tr>
<tr>
<td>80–90†</td>
<td>166 (37)</td>
<td></td>
<td></td>
<td>21.5/16.0</td>
</tr>
<tr>
<td>70–80†</td>
<td>91 (20)</td>
<td></td>
<td></td>
<td>21.7/16.0</td>
</tr>
<tr>
<td>60–70†</td>
<td>46 (10)</td>
<td></td>
<td></td>
<td>19.9/16.0</td>
</tr>
<tr>
<td>50–60†</td>
<td>42 (9)</td>
<td></td>
<td></td>
<td>18.0/16.0</td>
</tr>
<tr>
<td>30–50</td>
<td>40 (9)</td>
<td></td>
<td></td>
<td>17.9/16.0</td>
</tr>
<tr>
<td>≤30</td>
<td>22 (5)</td>
<td></td>
<td></td>
<td>18.2/16.0</td>
</tr>
</tbody>
</table>

Optune should be used at least 75% of the time or ≥18 hours per day. Monthly time on Optune was an independent predictor of improved overall survival with Optune.

*From a post hoc analysis. †P <0.05 for Optune + TMZ compared to TMZ alone.
TMZ, temozolomide.
EF-14: HCP- and Patient-Reported Quality of Life

**QoL over 12 months**

<table>
<thead>
<tr>
<th>Time of Evaluation</th>
<th>HCP-Reported</th>
<th>Patient-Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Karnofsky Performance Score¹,*</td>
<td>Global Health Status²,†</td>
</tr>
<tr>
<td>Baseline</td>
<td>100</td>
<td>Baseline</td>
</tr>
<tr>
<td>12 Months</td>
<td>100</td>
<td>12 Months</td>
</tr>
</tbody>
</table>

**Mean KPS**

- Optune + TMZ
- TMZ Alone

**Mean HRQoL Score**

Both HCPs and patients reported stable QoL evaluation scores up to 1 year of Optune use

*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.¹ 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).²

HCP, healthcare provider; QoL, quality of life; TMZ, temozolomide; KPS, Karnofsky Performance Score; HRQoL, health-related quality of life; EORTC, European Organisation for Research and Treatment of Cancer; QLQ-C30, Quality of Life Core Questionnaire-C30.

**EF-14 Safety Summary: Incidence of Grade 3/4 Adverse Events in ≥5% of Patients¹,²**

<table>
<thead>
<tr>
<th>Safety Population</th>
<th>Optune + TMZ (n=456) %</th>
<th>TMZ Alone (n=216) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 Adverse event</td>
<td>48</td>
<td>44</td>
</tr>
<tr>
<td>Blood and lymphatic system disorder*</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Asthenia, fatigue, and gait disturbance</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Infections</td>
<td>7</td>
<td>5</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>24</td>
<td>20</td>
</tr>
<tr>
<td>Seizures</td>
<td>6</td>
<td>6</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>

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

*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. The differences disappear when data are normalized to treatment duration.

TMZ, temozolomide.

## EF-14: Summary of Outcomes for Optune + TMZ Compared With TMZ Alone

<table>
<thead>
<tr>
<th><strong>Significantly improved PFS</strong>(^1)</th>
<th>• Median PFS: 6.7 months vs 4.0 months ((P &lt; 0.001))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long-term survival benefit</strong>&lt;br&gt;that increased with more time on Optune(^{1,2})</td>
<td>• Median OS: 20.9 months vs 16.0 months ((P &lt; 0.001))&lt;br&gt;• Percentage of monthly time on Optune was an independent predictor of improved OS</td>
</tr>
<tr>
<td><strong>Maintained QoL over time</strong>&lt;br&gt;and across predefined daily-functioning domains(^3)</td>
<td>• Patients in the study were able to maintain their mental, emotional, and physical well-being longer as measured up to 1 year</td>
</tr>
<tr>
<td><strong>Optune + TMZ have been safely combined</strong>(^1)</td>
<td>• The most common device-related side effect with Optune was mild-to-moderate skin irritation&lt;br&gt;• No significant increase in serious AEs or systemic side effects was seen when Optune was added to TMZ</td>
</tr>
</tbody>
</table>

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TMZ, temozolomide; PFS: progression-free survival; OS, overall survival; QoL, quality of life; AE, adverse event.
Resources and Additional Information
Primary Optune Patient Resources

- **Diagnosis**
  - *First Glance at Optune*

- **Treatment Consideration**
  - *Understanding Optune*

- **Monthly Usage & Self-Management**
  - *Patient Scalp Care Guidelines*
Additional Resources For Your Patients

- Buddy Program
- Optune Insights
- nCompass Brochure
- nCompass Travel Support Brochure
- Patient Video Library DVD
- Optune.com
- Optune Facebook Page
- Optune YouTube Channel
- Patient MOA Video
Additional Resources For Your Practice

Optune Practice Resource Kit

Optune.com/hcp

Optune Exchange
Optune Resources Are Available at Optune.com