A Post Hoc Analysis

Efficacy and Safety of Tumor Treating Fields (TTFields) in Elderly Patients with Newly Diagnosed Glioblastoma: Subgroup Analysis of the Phase 3 EF-14 Clinical Trial


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.

Selected 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.

Please see Important Safety Information throughout and the Instructions for Use (IFU) at Optune.com/IFU.
Results based on a post hoc analysis of the EF-14 phase 3 pivotal trial\(^1,^2\)

- 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 + TMZ vs TMZ alone.

Survival results in the EF-14 trial in the intent-to-treat population\(^2,^3\)

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

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<th>Time (months)</th>
<th>Overall Survival (%)</th>
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<td>6</td>
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- Median OS from diagnosis: 20.9 months
- Median OS from restenosis: 16.0 months
- HR (95% CI): 0.63 (0.53-0.76)
- Log-rank P value: <0.001

A post hoc analysis of the EF-14 trial measured PFS and OS in all elderly patients\(^1\)

- Post hoc analysis included all 134 patients from the phase 3 EF-14 trial who were 65 years of age and older (Optune + TMZ, n=89; TMZ alone, n=45).
- Patient baseline characteristics and known prognostic factors were balanced between the 2 treatment groups.
- Median age was 69 years (range, 65-80 years) and 70% were male.
- The primary efficacy endpoint was PFS; the secondary endpoint was OS.
- Other endpoints included PFS at 6 months (PFS-6), annual survival rates, and HRQoL. The PFS and OS were also evaluated in the smaller cohort of patients who were 70 years of age and older (n=59).

Optune® + TMZ extended OS vs TMZ alone in patients 65 years of age or older\(^1\)

Results based on a post hoc analysis of the EF-14 phase 3 pivotal trial\(^1,^2\)

- First patients were enrolled in 2015. The study was completed in 2017; patients were followed up to 2 years post-treatment.
- Median OS was 17.4 months with Optune + TMZ versus 13.7 months with TMZ alone (HR: 0.51 [95% CI, 0.33-0.77]).

Survival with Optune + TMZ vs TMZ alone was higher at the 2-year landmark analysis\(^1,^2\)

- Median OS: 27% for TMZ alone vs 39% for Optune + TMZ
- Median OS at 5 years: 15% for TMZ alone vs 24% for Optune + TMZ

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\(^2\)

Optune + TMZ also significantly improved PFS vs TMZ alone
- Median PFS: 6.7 months vs 4.0 months (P<0.001)
- Survival rates for patients 65 years of age and older were consistent with the overall trial population\(^2,^3\)

Optune + TMZ in elderly patients showed no significant increase in AEs\(^4\)

- No significant increase in systemic AEs in patients treated with Optune + TMZ (46%) vs TMZ alone (40%).
- Serious AEs were reported in 39% of patients treated with Optune + TMZ and in 33% of patients treated with TMZ alone.
- The rate of grade 1 or 2 medical device site reaction was 5% for Optune + TMZ, and severe (grade 3) skin involvement occurred in 2% of patients treated with Optune + TMZ.

Patients treated with Optune + TMZ maintained quality of life similar to those on TMZ alone, as measured up to 1 year\(^2\)

- Both HCPs and patients reported stable evaluation scores across predetermined daily function domains, such as physical, cognitive, and emotional functioning.

Important Safety Information (cont’d)

**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.
An NCCN Category 1 treatment option for GBM, for patients 70 years of age and older with good performance status (KPS ≥60)*

*NCCN Clinical Practice Guidelines in Oncology (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 glioblastoma (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).

Important Safety Information (cont’d)

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: