In a Post Hoc Analysis, Optune® + TMZ Was Associated With Improved Clinical Outcomes in Elderly Patients With Histologically-Confirmed, Newly Diagnosed Glioblastoma (GBM)[1]

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GBM IS A CHALLENGING DISEASE WITH UNMET NEEDS, ESPECIALLY FOR ELDERLY PATIENTS.[2]

- **In 2019, 52.6% of new GBM diagnoses occurred in patients 65 years of age and older, and the incidence in this age group is increasing[3]**
  - Of the 12,900 patients of all ages in the US diagnosed with GBM, 6780 of them were 65 years of age and older[3]
  - Patients between the ages of 75 and 84 years have the highest incidence of GBM, and the incidence in this age group is increasing[3]
- **Treating GBM in patients 65 years of age or older requires careful consideration[2]**
  - 1-year survival rate is 31% in elderly patients with GBM 65-74 years of age[3]

With a high risk of disease recurrence, every appropriate treatment available should be considered to treat GBM[4]

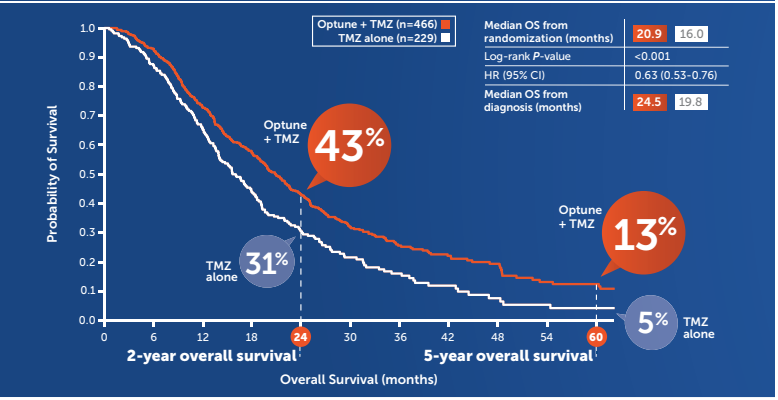
Please see the Important Safety Information for Optune on the back cover and the accompanying Optune Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions.

OPTUNE®

Optune® + TMZ Provided an Unprecedented Long-Term Survival Benefit[5]

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

Overall survival (5-year survival analysis)[5,6]



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

Optune + TMZ also significantly improved PFS vs TMZ alone[5]

- Median PFS: 6.7 months vs 4.0 months (*P* <0.001)[5]
- 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)[5]
  - PFS, primary endpoint
  - OS, secondary endpoint
- Key inclusion criteria:[5]
  - 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)

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

Optune® Was Safely Combined With TMZ[5,7]

No significant increase in serious AEs compared with TMZ alone[5,7]

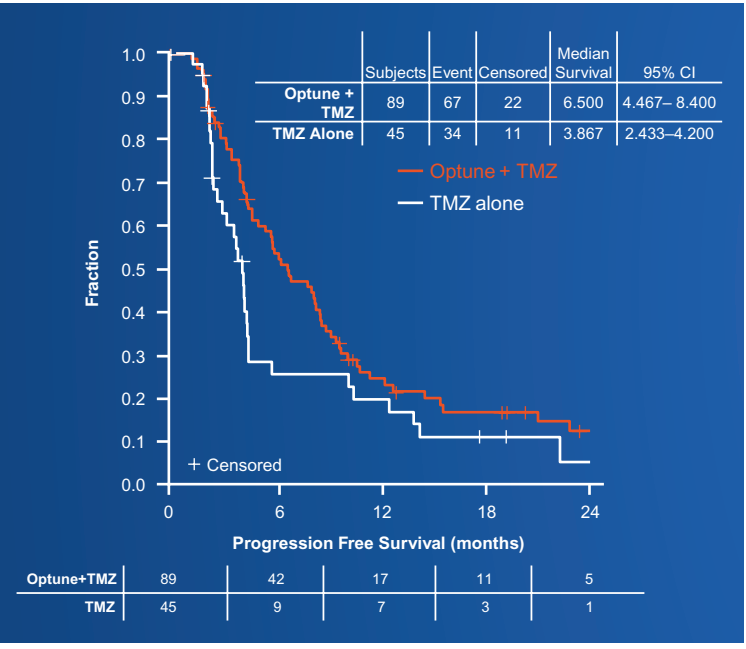
Incidence of grade 3/4 AEs occurring in ≥5% of patients during 5 years of follow-up[5,7]	Optune + TMZ (n=456) %	TMZ alone (n=216) %
≥1 AE	48	44
Blood and lymphatic system disorders	13	11
Thrombocytopenia	9	5
Gastrointestinal disorders	5	4
Asthenia, fatigue, and gait disturbance	9	6
Infections	7	5
Injury, 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	24	20
Seizures	6	6
Respiratory, thoracic, and mediastinal disorders (pulmonary embolism, dyspnea, and aspiration pneumonia)	5	5

- 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[8]
- 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[5]
- 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[7]
- 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[5]
- Mild-to-moderate skin irritation, the most common device-related side effect observed with Optune, was easily manageable, reversible, and did not result in treatment discontinuation[8]

In a Post Hoc Analysis of the EF-14 Study, Optune® + TMZ Was Associated With Increased Progression-Free Survival Vs TMZ Alone in Patients 65 Years of Age and Older[1]

- This subgroup analysis included data from all 134 patients 65 years of age and older in the intent-to-treat population[1]
- The analysis compared overall survival, progression-free survival, and safety between the two treatment arms: Optune + TMZ (n=89) vs TMZ (n=45)[1]
- Median patient age and KPS were 69 years and 90%, respectively[1]

PFS in Patients 65 years of age and older[1]

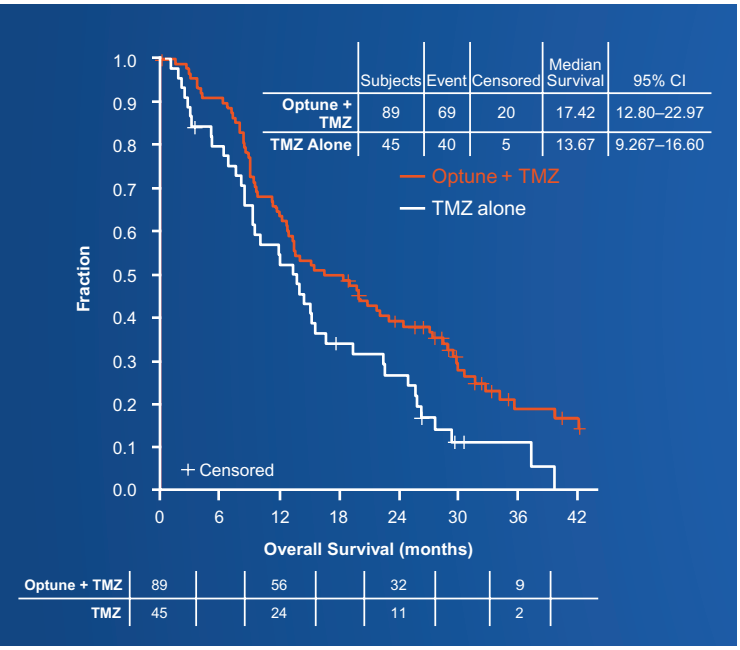


Median PFS was 6.5 months for patients using Optune + TMZ vs 3.9 months for those using TMZ alone over a 24-month period (HR=0.47)[1]

In a Post Hoc Analysis, Optune® + TMZ Was Associated With Improved OS Vs TMZ Alone in Patients 65 Years of Age and Older[1]

- Elderly patients treated with Optune + TMZ experienced longer median OS (17.4 months) vs those using TMZ alone (13.7 months)[1]
- OS with Optune + TMZ vs TMZ alone was higher at the 1-year analysis and remained higher at 2 years[1]

OS in Patients 65 years of age and older[1]



Medium OS was extended with Optune + TMZ by 3.7 months vs TMZ alone[1]

Safety Data in Patients 65 Years of Age and Older

- No significant increase in systemic AEs in patients treated with Optune + TMZ (46%) vs TMZ alone (40%)[1]
- SAEs were reported in 39% of patients treated with Optune + TMZ and in 33% of patients treated with TMZ alone[1]
- None were considered related to treatment with Optune[1]
- Grades 1 to 2 skin AEs were observed in 51% of patients using Optune[1]

AEs, adverse events; CI, confidence interval; GBM, glioblastoma; HR, hazard ratio; OS, overall survival; SAEs, serious adverse events; TMZ, temozolomide; TTFields, Tumor Treating Fields.

REFERENCES

1. Ram Z, Zhu JJ. Poster presented at the American Association for Cancer Research (AACR) Virtual Annual Meeting II; June 22-29, 2020; Abstract 10636. **2.** Wick A, et al. *Neuro Oncol*. 2018;20(2):174–183. **3.** Ostrom QT, et al. *Neuro Oncol*. 2019;21(S5):1–100. **4.** Xie Q, et al. *Neuro Oncol*. 2014;16:1575-1584. **5.** Optune. Instructions for Use. Novocure; 2019. **6.** Stupp R, et al. *Cancer Res*. 2017;77(suppl 13). American Association for Cancer Research abstract CT007. doi:10.1158/1538-7445.AM2017-CT007. **7.** Stupp R, et al. *JAMA*. 2017;318(23):2306-2316. **8.** Novocure Data on File OPT-103.

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).

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

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.

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.

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