In a Post Hoc Analysis, Optune® + TMZ Was Associated With Improved Clinical Outcomes vs TMZ Alone When Tumor Resection Is Not Feasible[1]

Not every patient with GBM is a candidate for gross total or partial resection—some may only have a biopsy[2]

Actor portrayals.

- **Based on multidisciplinary input, if feasible, for treatment planning:[2]**
  - 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[2]**
  - Subtotal resection with MRI after resection
  - Biopsy (stereotactic or open)

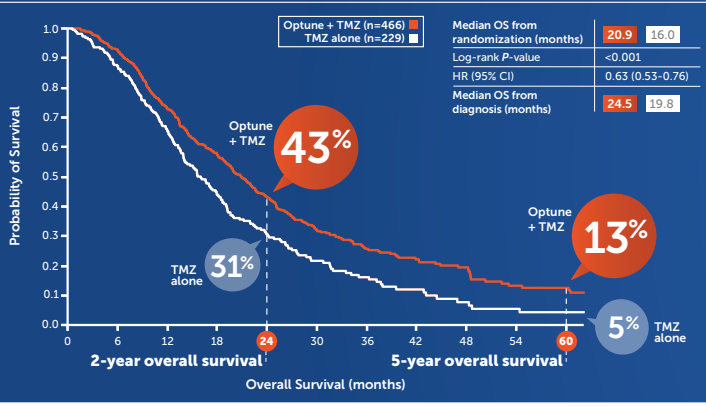
Please see the Important Safety Information for Optune on back cover and the accompanying Optune Instructions For Use (IFU) for complete information regarding the device's indications, contraindications, warnings, and precautions.

OPTUNE®

Optune® + TMZ Provided an Unprecedented Long-Term Survival Benefit[3]

- Survival with Optune + TMZ vs TMZ alone was significantly higher at the 2-year landmark analysis and remained higher at 5 years[3]
- Median OS was significantly extended with Optune—by nearly 5 months (*P* <0.001)[3]

Overall survival (5-year survival analysis)[3,4]



Proven to provide the best opportunity for greater OS at 5 years vs TMZ alone (13% vs 5%)[3]

Optune + TMZ also significantly improved PFS vs TMZ alone[3]

- Median PFS: 6.7 months vs 4.0 months (*P* <0.001)[3]
- 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)[3]
  - PFS, primary endpoint
  - OS, secondary endpoint
- Key inclusion criteria:[3]
  - 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[1,3]

No significant increase in serious AEs compared with TMZ alone[1,3]

Incidence of grade 3/4 AEs occurring in ≥5% of patients during 5 years of follow-up[1,3]	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[5]
- 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[3]
- 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[1]
- 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[3]
- 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[5]

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]

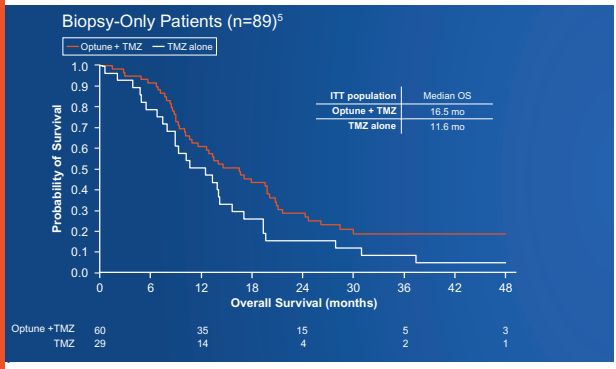
The EF-14 pivotal phase 3 trial included patients with newly diagnosed GBM who only had a biopsy[1]

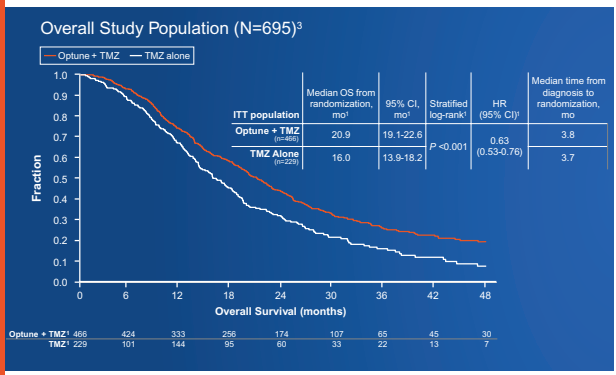
- Patients who did not have a resection had a biopsy[5]

Extent of Resection Was Consistent Across Both Study Arms[1]

	Optune + TMZ % (n)	TMZ alone % (n)
Biopsy only	13% (60)	13% (29)
Partial resection	34% (157)	33% (77)
Gross total resection	53% (249)	54% (123)
Total (N=695)	100% (466)	100% (229)

The study protocol defined surgery as surgical resection to the extent safely feasible or biopsy.[1]





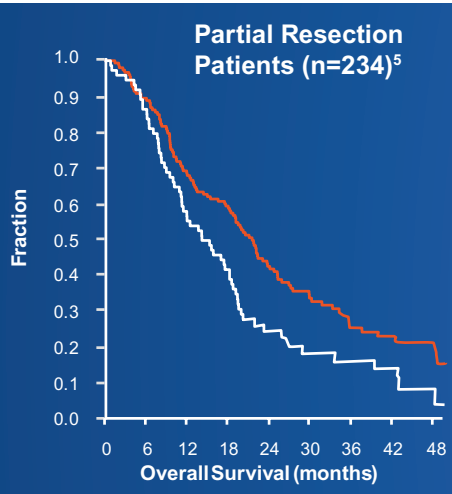
Biopsy-only patients using Optune + TMZ had longer median OS (16.5 months) vs those using TMZ alone (11.6 months)[1]

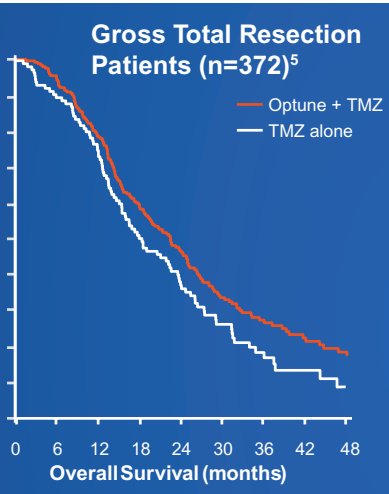
- In the EF-14 trial[1]
  - 13% of patients in each study arm only had a biopsy
- The biopsy-only subgroup analysis suggests OS was maintained with Optune + TMZ in the long-term analysis[5]
  - 8% (n=3) of patients treated with Optune + TMZ were alive at study end vs 0% (n=1) in the TMZ alone group

In a Post Hoc Analysis, Extension of OS Was Observed With Optune® + TMZ Across All Patient Subgroups vs TMZ Alone[1,*]

- 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)[1]
- 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)[1]

Optune + TMZ Improved Median Survival vs TMZ Alone Regardless of Extent of Resection





Optune+TMZ	157	105	58	22	8	249	193	101	38	19
TMZ	77	42	16	7	2	123	88	40	13	4

ITT population	Median OS, mo
Optune + TMZ	21.4
TMZ alone	15.1

ITT population	Median OS, mo
Optune + TMZ	22.6
TMZ alone	18.5

*A randomized, open-label trial in 695 patients with newly diagnosed GBM whose tumor was resected or biopsied and had completed concomitant radiochemotherapy were randomized 2:1 to TTFields plus maintenance TMZ or TMZ alone.

GBM, glioblastoma; OS, overall survival; TMZ, temozolomide.

REFERENCES

1. Stupp R, et al. *JAMA*. 2017;318(23):2306-2316. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers. V.3.2020. ©2020 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed September 29, 2020. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way. **3.** Optune. Instructions for Use. Novocure; 2019. **4.** Stupp R, et al. *Cancer Res*. 2017;77(suppl 13). American Association for Cancer Research abstract CT007. doi:10.1158/1538-7445.AM2017-CT007. **5.** 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.

US-OPT-03914 Released October 2020