In a post hoc analysis, Optune Gio™ + TMZ was associated with improved clinical outcomes vs TMZ alone when tumor resection was not feasible[1,2]

Not every patient with GBM is a candidate for gross total or partial resection—some may only have a biopsy[3]

Actor portrayals.

- **Based on multidisciplinary input, if feasible[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[3]**
  - Subtotal resection with MRI after resection
  - Biopsy (stereotactic or open)

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

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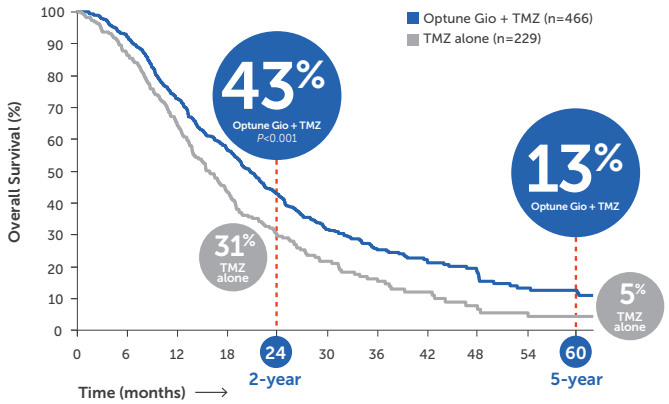
OPTUNE GIO™

IN NEWLY DIAGNOSED GBM,

Optune Gio™ + TMZ provided an unprecedented long-term survival benefit[4]

- Survival with Optune Gio + TMZ vs TMZ alone was significantly higher at the 2-year landmark analysis and remained higher at 5 years[4]
- Median OS was significantly extended with Optune Gio—by nearly 5 months (*P*<0.001)[4]

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



Proven to provide the best opportunity for greater OS at 5 years vs TMZ alone (13% vs 5%)[4]

Optune Gio + TMZ also significantly improved median PFS vs TMZ alone (6.7 months vs 4.0 months, *P*<0.001)[4]

- 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 Gio + TMZ vs those treated with TMZ alone (N=695)[4]
  - PFS, primary endpoint
  - OS, secondary endpoint
- Key inclusion criteria[4]:
  - 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; GBM, glioblastoma; Gy, gray; HR, hazard ratio; KPS, Karnofsky Performance Score; MRI, magnetic resonance imaging; OS, overall survival; PFS, progression-free survival; TMZ, temozolomide; WHO, World Health Organization.

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IN NEWLY DIAGNOSED GBM,

Optune Gio™ was safely used together with TMZ[1,4]

No significant increase in serious AEs compared with TMZ alone[1,4]

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

- The most common (≥10%) AEs involving Optune Gio together 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 Gio + TMZ arm of the study. This most likely reflects the longer duration of TMZ treatment in these patients[4]
- The rate of grade 1/2 medical device site reaction was 52% for Optune Gio + TMZ compared with 0% for TMZ alone and severe (grade 3) skin involvement occurred in 2% for Optune Gio + TMZ[1]
- Grade 3/4 AEs were well balanced between arms. None of the systemic grade 3/4 AEs were considered related to Optune Gio by any of the investigators[4]
- Mild-to-moderate skin irritation, the most common device-related side effect observed with Optune Gio, was typically manageable, reversible, and did not result in treatment discontinuation[5]

IN NEWLY DIAGNOSED GBM,

Results of a post hoc analysis showed Optune Gio™ + TMZ was associated with increased median OS vs TMZ alone in patients ineligible for surgical resection[1,2]

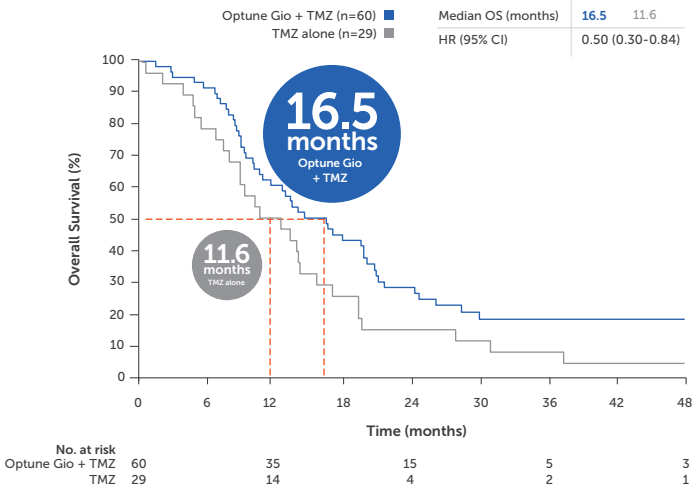
The EF-14 pivotal phase 3 trial included patients with newly diagnosed GBM who only had a biopsy[1]

- 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]

	Optune Gio + 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)

Overall Survival in Biopsy-Only Patients (n=89)[2]



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

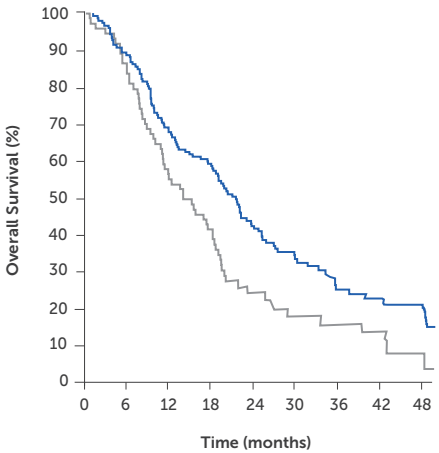
- In the EF-14 trial, 13% of patients in each study arm only had a biopsy[1,2]
- The biopsy-only subgroup analysis suggests OS was maintained with Optune Gio + TMZ in the long-term analysis[2]

IN NEWLY DIAGNOSED GBM,

In a post hoc analysis, Optune Gio™ + 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 Gio + 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 Gio + TMZ (n=249) compared with 18.5 months with TMZ alone (n=123) (HR: 0.70; 95% CI, 0.54-0.91)[1,2]

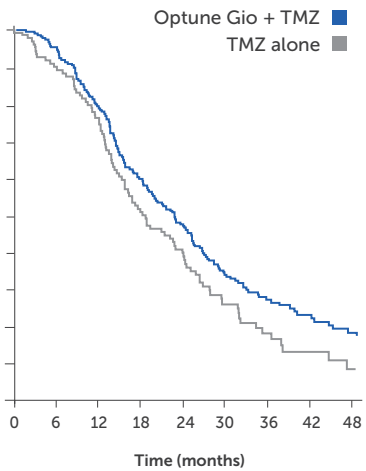
Partial Resection Patients (n=234)[2]



No. at risk					
Optune Gio + TMZ	157	105	58	22	8
TMZ	77	42	16	7	2

ITT population	Median OS, mo
Optune Gio + TMZ	21.4
TMZ alone	15.1
HR (95% CI)	0.56 (0.41-0.77)

Gross Total Resection Patients (n=372)[2]



249	193	101	38	19
123	88	40	13	4

ITT population	Median OS, mo
Optune Gio + TMZ	22.6
TMZ alone	18.5
HR (95% CI)	0.70 (0.54-0.91)

*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; ITT, intent to treat; OS, overall survival; TMZ, temozolomide; TTFields, Tumor Treating Fields.

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Regardless of extent of surgical resection, consider if Optune Gio™ is a viable treatment choice for your patients with newly diagnosed GBM

Indications for Use

Optune Gio™ is intended as a treatment for adult patients (22 years of age or older) with histologically confirmed glioblastoma multiforme (GBM).

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

Do not use Optune Gio in patients that are known to be sensitive to conductive hydrogels. In this case, skin contact with the gel used with Optune Gio 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 Gio 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 Gio treatment.

Use of Optune Gio in patients with an inactive implanted medical device in the brain has not been studied for safety and effectiveness, and use of Optune Gio in these patients could lead to tissue damage or lower the chance of Optune Gio being effective.

Do not prescribe Optune Gio for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune Gio in these populations have not been established.

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

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References: 1. Stupp R, Taillibert S, Kanner A, et al. *JAMA*. 2017;318(23):2306-2316. **2.** Stupp R, Hegi ME, Idbaih A, et al. *Cancer Res*. 2017;77(suppl 13). American Association for Cancer Research abstract CT007. doi:10.1158/1538-7445.AM2017-CT007 **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers V.1.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed June 30, 2023. To view the most recent and complete version of the guideline, 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. **4.** Optune Gio. Instructions For Use. Novocure; 2023. **5.** Novocure Data on File OPT-103.