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

Ram Z, Kim CY, Hottinger AF, Idbaih A, Nicholas G, Zhu JJ. *Front Oncol.* 2021;11:671972. doi:10.3389/fonc.2021.671972. Published correction appears in *Front Oncol.* 2022;12:902929. doi:10.3389/fonc.2022.902929

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.

Selected 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.

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

OPTUNE GIO™

US-OPG-00010v1.0

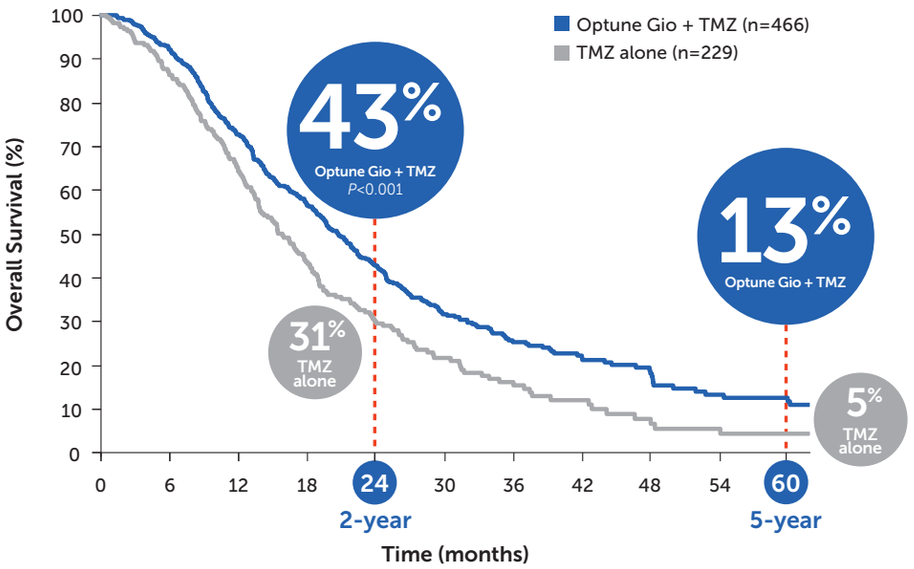
Optune Gio™ + TMZ extended OS vs TMZ alone in patients 65 years of age or older[1]

Results based on a post hoc analysis of the EF-14 phase 3 pivotal trial[1,2]

- 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 Gio + 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)



- Optune Gio + TMZ also significantly improved PFS vs TMZ alone
  - Median PFS: 6.7 months vs 4.0 months (*P*<0.001)
- Mild-to-moderate skin irritation, the most common device-related side effect with Optune Gio, was typically manageable, reversible, and did not result in treatment discontinuation[4]

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 Gio + 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, 65-83 years) and 70% were male
- The primary efficacy endpoint was PFS; the secondary endpoint was OS
- Other efficacy 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)

Important Safety Information (cont'd)

Contraindications (cont'd)

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.

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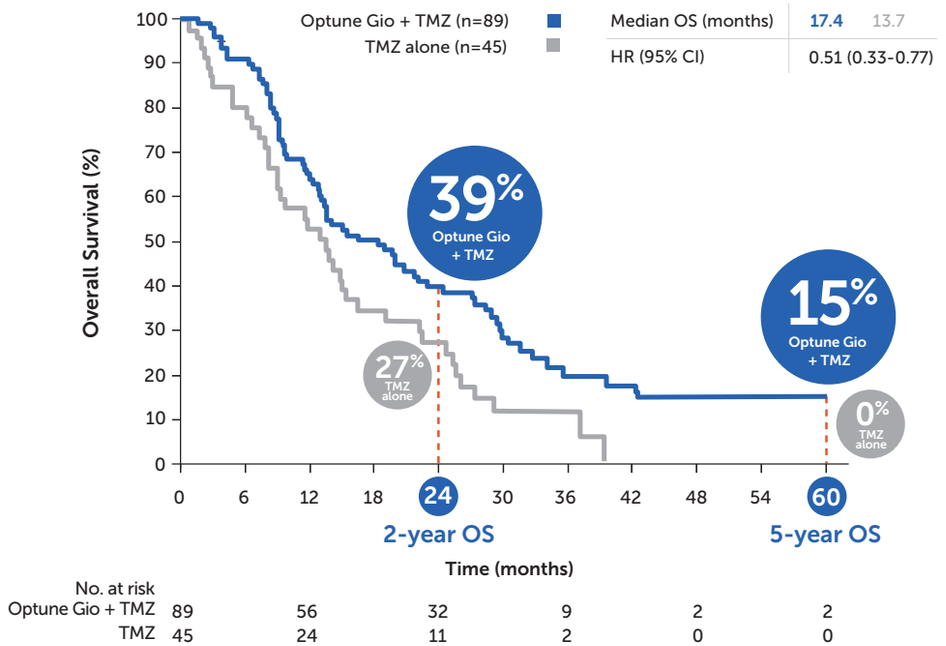
Survival with Optune Gio + TMZ vs TMZ alone was higher at the 2-year landmark analysis[1,2]

Overall Survival in Patients 65 Years of Age and Older[1]



Many elderly patients were able to use Optune Gio effectively, with more than half (57%) achieving average time on treatment of ≥75% (≥18 hours/day).[1]

- Median OS was 17.4 months with Optune Gio + TMZ vs 13.7 months with TMZ alone (HR: 0.51 [95% CI, 0.33-0.77])[1]
- Median PFS was 6.5 months with Optune Gio + TMZ vs 3.9 months with TMZ alone (HR: 0.47 [95% CI, 0.30-0.74])[1]
- Survival rates for patients 65 years of age and older were consistent with the overall trial population[1,2]

Optune Gio + TMZ in elderly patients showed no increase in AEs

- Systemic AEs were similar in patients treated with Optune + TMZ (46%) vs TMZ alone (40%)
- Serious AEs were reported in 39% of patients treated with Optune Gio + TMZ and in 33% of patients treated with TMZ alone. None were considered related to treatment with Optune Gio
- The rate of grade 1 or 2 medical device site reaction was 51% for Optune Gio + TMZ, and severe (grade 3) skin involvement occurred in 2% of patients treated with Optune Gio + TMZ

Patients treated with Optune Gio + TMZ maintained quality of life similar to those on TMZ alone, as measured up to 1 year[1]

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

Access this article within the folder, or view on your device by scanning the QR code

AE, adverse event; HCP, healthcare professional; HRQoL, health-related quality of life; OS, overall survival; PFS, progression-free survival; TMZ, temozolomide.

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Help prevent dermatologic AEs to maximize time on therapy

Scan the QR code for management guidance from Optune Gio™

A National Comprehensive Cancer Network® (NCCN®) Category 1 treatment option for GBM, for patients 70 years of age and older with a good performance score (KPS ≥60)[5,*]

NCCN
CATEGORY 1 PREFERRED
Alternating electric fields (Optune Gio) for newly diagnosed GBM

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers include alternating electric fields (Optune Gio) as a Category 1 Preferred regimen, following maximal safe resection if feasible (or else biopsy), and standard radiation therapy with concurrent and adjuvant TMZ, for patients aged ≤70 years with newly diagnosed supratentorial GBM and good performance status* regardless of MGMT promoter status.

There is uniform NCCN consensus for this recommendation based on high-level evidence (Category 1), and superior efficacy, safety, evidence, and when appropriate, affordability (Preferred).[†]

*The NCCN defines good performance as Karnofsky Performance Score (KPS) ≥60. The trial on which the IFU is based used an eligibility criterion of KPS ≥70.[2,5]

[†]NCCN 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.

GBM, glioblastoma; IFU, Instructions For Use; MGMT, O-6-methylguanine-DNA methyltransferase; NCCN, National Comprehensive Cancer Network® (NCCN®).

Important Safety Information (cont'd)

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. Ram Z, Kim CY, Hottinger AF, Idbaih A, Nicholas G, Zhu JJ. 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. *Front Oncol.* 2021;11:671972. doi:10.3389/fonc.2021.671972. Published correction appears in *Front Oncol.* 2022;12:902929 doi:10.3389/fonc.2022.902929 **2.** Stupp R, Taillibert S, Kanner A, et al. Effect of Tumor-Treating Fields plus maintenance temozolomide vs maintenance temozolomide alone on survival in patients with glioblastoma: a randomized clinical trial. *JAMA*. 2017;318(23):2306-2316. **3.** Optune Gio. Instructions For Use. Novocure; 2023. **4.** Novocure Data on File OPT-135. **5.** Referenced with permission from 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.

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