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TRANSLATIONAL RESEARCH

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patientforward

TTFields' mechanism of action hinders cells' ability to develop resistance

Research

JAMA | Original Investigation

Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma

A Randomized Clinical Trial

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IMPORTANCE Tumor-treating fields (TTFields) is an antimitotic treatment modality that interferes with glioblastoma cell division and organelle assembly by delivering low-intensity alternating electric fields to the tumor.

OBJECTIVE To investigate whether TTFields improves progression-free and overall survival of patients with glioblastoma, a fatal disease that commonly recurs at the initial tumor site or in the central nervous system.

DESIGN, SETTING, AND PARTICIPANTS In this randomized, open-label trial, 695 patients with glioblastoma whose tumor was resected or biopsied and had completed concomitant radiochemotherapy (median time from diagnosis to randomization, 3.8 months) were enrolled at 83 centers (July 2009-2014) and followed up through December 2016. A preliminary report from this trial was published in 2015; this report describes the final analysis.

INTERVENTIONS Patients were randomized 2:1 to TTFields plus maintenance temozolomide chemotherapy (n = 466) or temozolomide alone (n = 229). The TTFields, consisting of low-intensity, 200 kHz frequency, alternating electric fields, was delivered (≥ 18 hours/d) via 4 transducer arrays on the shaved scalp and connected to a portable device. Temozolomide was administered to both groups (150-200 mg/m^2) for 5 days per 28-day cycle (6-12 cycles).

MAIN OUTCOMES AND MEASURES Progression-free survival (tested at $\alpha = .046$). The secondary end point was overall survival (tested hierarchically at $\alpha = .048$). Analyses were performed for the intent-to-treat population. Adverse events were compared by group.

RESULTS Of the 695 randomized patients (median age, 56 years; IQR, 48-63; 473 men [68%]), 637 (92%) completed the trial. Median progression-free survival from randomization was 6.7 months in the TTFields-temozolomide group and 4.0 months in the temozolomide-alone group (HR, 0.63; 95% CI, 0.52-0.76; P < .001). Median overall survival was 20.9 months in the TTFields-temozolomide group vs 16.0 months in the temozolomide-alone group (HR, 0.63; 95% CI, 0.53-0.76; P < .001). Systemic adverse event frequency was 48% in the TTFields-temozolomide group and 44% in the temozolomide-alone group. Mild to moderate skin toxicity underneath the transducer arrays occurred in 52% of patients who received TTFields-temozolomide vs no patients who received temozolomide alone.

CONCLUSIONS AND RELEVANCE In the final analysis of this randomized clinical trial of patients with glioblastoma who had received standard radiochemotherapy, the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival. These results are consistent with the previous interim analysis.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00916409

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Summary Video
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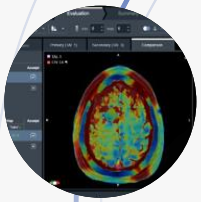
radiation oncologists engage in developing a new anti-mitotic therapy

surgeon

introduces the need for multidisciplinary care including Tumor Treating Fields



radiation oncologist

maps the array layout

patient

wears a portable, noninvasive device that provides localized treatment with TTFields

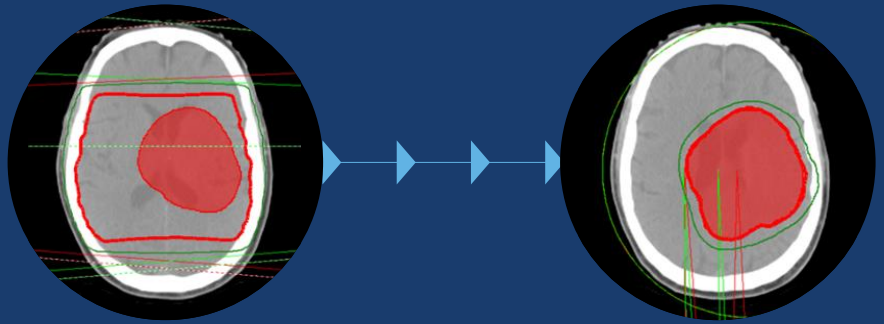
neuro-oncologist

writes the order for Optune®

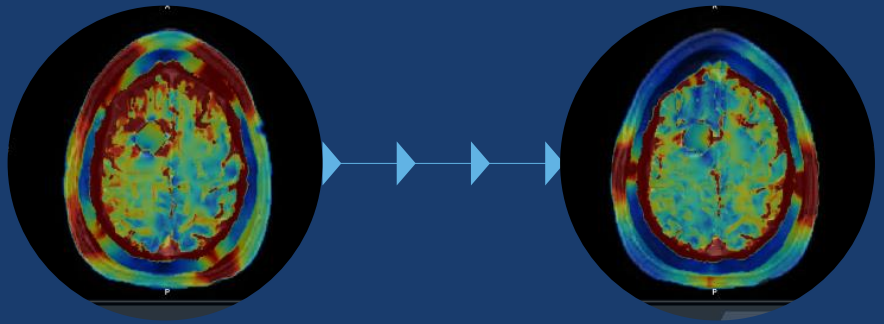
patientforward

TTFields provides basis for multidisciplinary activities

ionizing radiation dose distributions are routinely improved using sophisticated planning software



MAXPOINT™ treatment planning software visualizes the spatial distribution of Tumor Treating Fields



1 estimate field intensity delivered to tumor

2 optimize TTFields dose delivered to tumor

3 provide framework for managing patient's device usage

MAXPOINT™ is an investigational product that has not been approved by the FDA

MAXPOINT™ treatment planning software beta testing underway