ECRONICON OPEN ACCESS

EC NEUROLOGY
Mini Review

Tumor Treating Fields and New Paradigms in Glioblastoma Standard of Care

Roger Rotta*

Department of Neurosurgery, Instituto Neurológico de São Paulo, Brazil

***Corresponding Author**: Roger Rotta, Department of Neurosurgery, Instituto Neurológico de São Paulo, Brazil.

Received: January 11, 2020; **Published:** April 29, 2020

Abstract

The primary tenet of neurosurgical oncology is a survival. Glioblastoma (GBM) is the most common and deadliest primary brain tumor. With more than 14,000 new cases of GBM are diagnosed in US each year. Although new treatment paradigms with a significant impact on the outcomes of many other cancer types, treatment of malignant glioma remains a challenge. Patient survival for an average 14 months from diagnosis despite "standard of care" treatment, the survival has not changed significantly in decades.

Keywords: *Glioblastoma (GBM); Brain Tumor; Standard of Care*

Nowadays, the standard of care management of glioblastoma uses a surgery follow radiation plus chemotherapy with temozolomide. When an extent of resection starts at 78% following chemotherapy plus radiotherapy, improves OS (overall survival) and PFS (progression free survival) [1,2].

Tumor treating fields

Biological processes of cells are influenced by electrical activity, including cell division. The tumor treatment fields (TTF fields) use alternating electric fields, with low intensity and intermediate frequency in order to interrupt cell division and inhibit tumor growth.

The effect of this electric field on tumor cells is due to changes in the assembly of microtubules during mitosis, blocking the formation of the spindle's mitotic apparatus and consequently blocking the formation of 2 daughter cells. It also results in abnormal chromosomal segregation and reduced clonogenic potential of the cell's progeny.

In summary, TTFields will block the cell cycle in the mitotic phase, during metaphase, anaphase and telophase. Resulting in the interruption of the cell cycle or delaying cell division and interfering with the assembly of organelles. As a consequence, there will be inadequate cell division and inadequate chromosome distribution. Inducing cells die in apoptosis.

Glioblastoma as a proof of concept model

The initial clinical and laboratory results of this innovative cancer treatment method have been used in 2 randomized trial in recurrent and newly GBM, EF-11 and EF-14 trials respectively.

In EF-11, patients had a progressive disease even after initial treatment with radiotherapy and chemotherapy with TMZ, with an average survival of only 6.6 in cases where TTF was used, with no superiority in relation to the control group (6, 0 months), P = 0.27. After a 1-year survival rate of only 20% in both arms of the research, there was a failure to demonstrate that the use of TTF was superior to the chemotherapeutic regimens normally used. Mrugala., *et al.* summarized the experience of using TTF in 457 patients in 91 institutions in

the USA (Patient Registry Dataset; PRiDe), found a mean global survival of 9.6 months and in the subgroup of patients treated during the first recurrence (n = 152) this median survival was 20 months.

In the phase 3 EF-14 study, patients with newly diagnosed GBM were randomized only after completing the first cycle of chemoradiotherapy concomitant with TMZ. The 2 arms of the study consisted of chemotherapy with standard maintenance TMZ (for 6 to 12 cycles) with or without concomitant administration of TTFields. A follow-up of the first 315 randomized patients was performed for a minimum period of 18 months, with a significant improvement in progression-free survival and overall survival; consequently, the study was terminated, so that all patients were transferred to the TTFields arm. The median PFS increased by 3.1 months in the TTFields group with a median PFS of 7.1 months (95% CI, 5.9 - 8.2 months) compared to 4.0 months (95% CI, 3.3 -5.2 months) in the control group (HR, 0.62 [98.7% CI, 0.43 - 0.89]; P = 0.001). The mean OR of randomization (ITT) was 19.6 months (95% CI, 16.6 - 24.4 months) in the TTFields plus TMZ group compared to 16.6 months (95% CI, 13.6 - 19, 2 months) in the TMZ control group (HR: 0.74 [95% CI, 0.56 - 0.98]; P = 0.03). The percentage of patients alive at 2 years after enrollment was 43% in the TTFields/TMZ group and 29% in the isolated TMZ group (P = 0.006) (Figure 1).

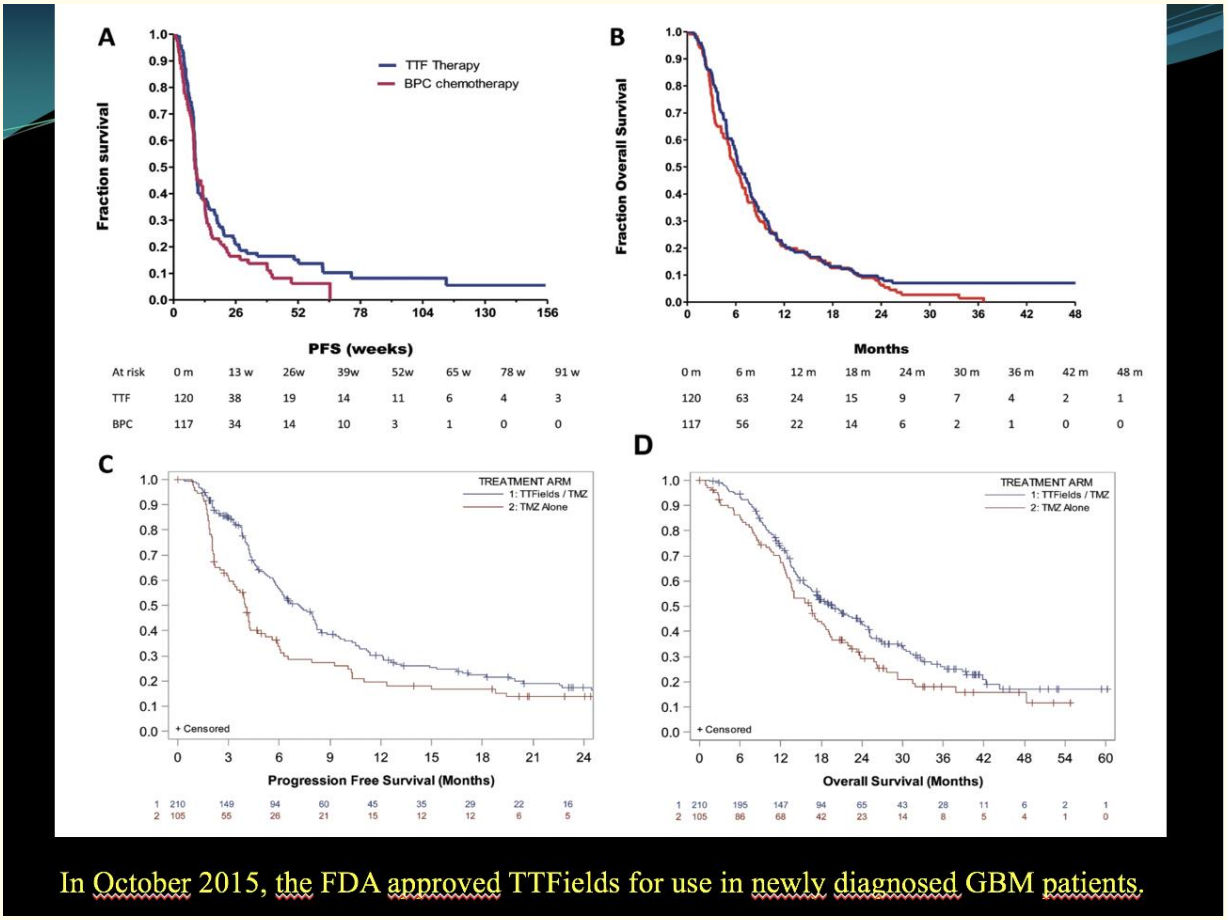

Figure 1

Conclusion

Based on the principles of physics and the respective cellular biophysical effects, TTF therapy has a well-established mechanism for cancer therapy.

TTF is a new modality to complement and add to the treatment of GBM. This new technique through the use of low intensity electric fields interrupts several cellular processes, mainly during its active division, especially in mitosis, and thus inhibiting the growth of the tumor.

A Level 1 evidence provided by the EF-14 study showed a positive impact on tumor growth control and, consequently, a significant improvement in progression-free survival and overall survival of patients with GBM.

Bibliography

1. N Sanai., *et al*. "An extent of resection threshold for newly diagnosed glioblastomas". *Journal of Neurosurgery* 115 (2011): 3-8.

2. R Stupp., *et al*. "Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma". *New England Journal of Medicine* 352 (2005): 987-996.

Volume 12 Issue 5 May 2020