**Tumor Treating Fields (TTFields) A Novel Cancer Treatment Modality: Translating Preclinical Evidence and Engineering Into a Survival Benefit with Delayed Decline in Quality of Life**

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**Purpose/Objective(s):** Tumor treating fields (TTFields) is a novel non-ionizing radiation cancer treatment modality using a patient-operated home-use device that delivers 200 kHz alternating electrical fields to the brain. TTFields interfere with cell division and selectively disrupt mitosis by interfering with the spatial alignment of polar macromolecules within the cell. TTFields also inhibit DNA damage repair of double strand breaks. Maintenance of quality of life during therapy with TTFields was compared to standard therapy alone.

**Materials/Methods:** TTFields were tested in a large phase 3 trial in patients with newly diagnosed GBM (EF-14; n=695). Patients who had completed radiochemotherapy were randomized to either standard temozolomide (TMZ) chemotherapy alone, or to TTFields and TMZ. Progression-free and overall survival were the main endpoints, with quality of life (QoL) as a predefined and important secondary endpoint. QoL was assessed longitudinally using the EORTC QLQ C-30 with brain cancer module (BN-20) questionnaires.

**Results:** TTFields added to standard adjuvant temozolomide (TMZ) chemotherapy led to a significant prolongation of both progression-free and overall survival (HR 0.63 [CI 0.53-0.76]; P= .000059). Toxicity was comparable between the two treatment arms with the exception of the expected mild-moderate skin toxicity due to the electrode placement on the TTFields treated patients. All predefined clinical and molecular subgroups benefitted from TTFields. More TTFields patients reported stable or improved scores on global health status, pain, physical functioning, and leg weakness (all P .01), while the area under the curve for improvement or stability over time was not significantly different between groups. Deterioration-free survival was significantly longer with TTFields for global health, physical and emotional functioning, pain, and leg weakness (all P<.01). Time to deterioration was shorter for itchy skin and longer for pain (both P<.001).

**Conclusion:** TTFields are an effective non-ionizing radiation treatment for GBM with a novel mechanism of action and unique delivery method. Patients become rapidly independent in handling the device allowing patients to control their treatment at home. Deterioration of key QOL scales is delayed in patients treated with TTFields.