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Global Post-Marketing Safety Surveillance of Tumor Treating Fields (TTFields) in Patients With High-Grade Glioma in Clinical Practice

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Purpose/Objective(s): Tumor Treating Fields (TTFields) are an anti-neoplastic treatment delivering low-intensity (1-3 V/cm), intermediate-frequency (100-500 kHz), alternating electric fields through 2 pairs of skin-affixed, locoregionally applied transducer arrays to target tumor bed. TTFields are FDA-approved for glioblastoma (GBM; 200 kHz optimal frequency) and unresectable malignant pleural mesothelioma (150 kHz). Safety and effectiveness were demonstrated in the Phase 3 EF-11 and EF-14 clinical trials in recurrent GBM (rGBM) and in newly diagnosed GBM (ndGBM), respectively. The main TTFields-related adverse event (AE) was array-associated manageable skin irritation. We report AEs from TTFields-treated patients in the real-world, clinical practice setting.

Materials/Methods: Unsolicited, global, post-market surveillance data from TTFields-treated patients (October 2011−February 2019) were retrospectively analyzed using MedDRA v21.1 preferred terms, stratified by region (US, EMEA [Europe, Middle East, Africa], or Japan), diagnosis (ndGBM, rGBM, anaplastic astrocytoma and anaplastic oligodendroglioma, or other brain tumors that includes brain metastases from different cancer types), and years of age (<18, pediatric; 18 to 64, adults; or ≥65, elderly).

Results: Of 11,029 patients, 53% had ndGBM, 39% had rGBM (at any line of recurrence), 6% had anaplastic astrocytoma and anaplastic oligodendroglioma, and 1% had other brain tumors. Most were adults (73%) and 26% were elderly (≥65 years of age). The majority of patients were males (n = 7313; 66.3%) compared to females (n = 3716; 33.7%), with a ratio representative of a typical GBM population. The most reported TTFields-related AE was array-associated local skin reaction, with an incidence of 38% in ndGBM, 29% in rGBM, 38% in anaplastic astrocytoma and anaplastic oligodendroglioma, and 31% in other brain tumors; as well as 37% in pediatric, 34% in adult, and 36% in elderly patients. Most skin AEs were mild to moderate and resolved with no treatment or over the counter topical ointments. Incidence of other TTFields-related AEs in patients with ndGBM and rGBM, respectively, included heat sensation (under-array warmth; 11%, 10%), electric sensation (under-array tingling; 11%, 9%), and headache (7%, 6%).

Conclusion: This post-marketing, retrospective, global, TTFields safety surveillance analysis revealed no new safety signals, with favorable safety and tolerability comparable to published TTFields/GBM trials. The most common TTFields-related AE was array-associated local skin reaction on the scalp. The safety profile of TTFields remained consistent among subgroups (diagnosis, age, or region) and total cohort, indicating feasibility in multiple subpopulations, including elderly patients.

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Radiation-Induced Brain Injury In Meningioma Patients Treated With Proton Or Photon Therapy

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Purpose/Objective(s): Despite the dosimetric advantages of proton beam therapy, it remains unclear if there is a difference in the rate of radiation-induced brain injury compared to the standard photon therapy. The purpose of this study is to characterize and compare brain injury as a consequence to proton or photon therapy for meningioma.

Materials/Methods: We retrospectively reviewed 38 consecutive patients treated for meningioma with proton therapy from 2014 to 2017, and 39 patients treated with photon therapy from 2008 to 2018 at two high-volume tertiary cancer centers. Patients with history of previous radiotherapy or follow up period less than 3 months were excluded. Radiation-induced brain injuries were categorized into newly detected abnormal T2 signal intensities, or newly detected abnormal T2 and T1 post-contrast signal intensities, and compared between the two groups using Pearson's chi-squared test. Follow-up imaging was reviewed by an experienced neuro-radiologist and a radiation oncologist. Abnormal MRI scans were then reviewed after fusion with initial radiation plans. Toxicity was graded as per the common terminology criteria for adverse events (CTCAE v4.03).

Results: Median follow-up time was 18 months for the proton arm and 24 months for the photon arm. There were no significant differences in WHO grade, radiation dose, or clinical target volume (CTV) between the two groups. The median dose was 54 Gy RBE (range 50.4-60 Gy RBE) in the proton group and 54 Gy (range 50.4-61.4 Gy) in the photon group. Nine of the 39 patients in the photon group received an additional 7.5-10 Gy radiosurgical boost. In the proton group, 23 of 38 patients were treated with pencil beam scanning and 15 with uniform scanning. The cumulative incidence of abnormal T2 signal intensities was 34.2% after proton and 48.7% after photon therapy (p = 0.20), and the cumulative incidence of abnormal T2 and T1 post-contrast signal intensities was 18.4% after proton and 5.1% after photon therapy (p = 0.07). In the proton group, grade ≥2 toxicity was observed in four (10.5%) patients and one (2.6%) patient developed a grade 4 event. In the photon group, grade ≥2 toxicity was observed in three (7.7%) patients and one (2.6%) patient developed a grade 4 event.

Conclusion: Though all patients have high rates of developing parenchymal T2 signal intensity abnormalities, patients treated with proton therapy were more likely to develop parenchymal T1 post-contrast abnormalities. The majority of these imaging findings were not symptomatic, and overall toxicity was similar between the groups. However, these findings highlight differences seen in imaging after proton therapy at an early timepoint. Further study on long-term effects and developing strategies to decrease the risk of brain injury is warranted to optimize treatment of meningioma.