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Title: Tumor Treating Fields (TTFields) Combined with Temozolomide in Elderly Glioblastoma Patients: Extended Survival Analysis

Publication Type

Clinical Trial (Phase III Extension Study)

Year of Publication

2025

Patient Demographics

- **Age Group**: 65-79 years (median age: 70 years)
- **Sample Size**: 98 patients
- **Condition**: Newly diagnosed glioblastoma following maximal safe resection
- **Gender Distribution**: 54% male, 46% female
- **ECOG Performance Status**: 0-2
- **Geographic Distribution**: Multi-national (United States, Europe, Canada)
- **Minimum Skin Coverage Area**: Adequate for transducer array placement

Disease Focus

Glioblastoma multiforme with focus on non-invasive device-based therapy combined with chemotherapy in geriatric population

Treatment Discussed

Tumor Treating Fields (TTFields) - Optune Device: Non-invasive, portable medical device delivering alternating electric fields (200 kHz frequency) via transducer arrays applied to the scalp. Arrays repositioned every 3 days to cover tumor location based on MRI-guided planning.

Treatment Protocol: - TTFields: Minimum 18 hours daily usage (goal: ≥22 hours/day) - Concurrent maintenance temozolomide: 150-200 mg/m², days 1-5 of 28-day cycles - Treatment duration: Until disease progression (up to 24 months protocol) - Transducer array placement: Optimized based on tumor location mapping

Device Compliance Monitoring: Daily usage recorded electronically. Median compliance: 20.3 hours/day (range: 12.1-24 hours). 71.4% of patients achieved ≥18 hours daily usage threshold.

Study Outcome Summary

Primary Endpoints: - Median overall survival: 20.7 months (95% CI: 18.1-23.8) - Comparison to temozolomide-alone historical control: HR 0.69 (p=0.006) - Median progression-free survival: 8.9 months (95% CI: 7.5-10.4) - 24-month survival rate: 43.9% - 36-month survival rate: 28.6% - 60-month survival rate: 13.3%

Compliance-Outcome Relationship: - High compliance (≥22 hrs/day): median OS 24.1 months - Medium compliance (18-22 hrs/day): median OS 19.8 months - Low compliance (<18 hrs/day): median OS 14.7 months - Compliance significantly correlated with survival (p<0.001)

Response Assessment: - 6-month PFS rate: 68.4% (vs 56% in TMZ-alone historical controls) - 12-month PFS rate: 34.7% - Radiographic response rate: 28.6% (CR + PR) - Stable disease: 44.9%

Quality of Life: EORTC QLQ-C30 scores remained stable during treatment. Minor decrements in role functioning related to device burden, but global health status maintained. Social functioning scores impacted by visible transducer arrays (cosmetic concerns).

Safety and Tolerability: TTFields device-related adverse events: - Skin irritation beneath arrays (Grade 1/2: 87.8%, Grade 3: 16.3%) - Contact dermatitis (52.0%) - Scalp pruritus (43.9%) - Local infection requiring antibiotics (8.2%) - Ulceration (Grade 3: 3.1%)

Systemic chemotherapy toxicity similar to standard TMZ: - Hematologic toxicity (Grade 3/4: 19.4%) - Fatigue (Grade 3: 12.2%) - Nausea/vomiting (Grade 1/2: 61.2%)

Treatment Discontinuation: - Disease progression: 67.3% - Device-related issues (compliance/tolerance): 18.4% - Chemotherapy toxicity: 9.2% - Patient preference: 5.1%

Elderly-Specific Findings: No increased toxicity observed in patients ≥70 years compared to 65-69 age group. Compliance rates were similar across age strata. Cognitive function preservation comparable to standard therapy alone.

FDA Approval Status

Approved - Tumor Treating Fields (Optune device) received FDA approval in 2011 for recurrent glioblastoma and expanded approval in 2015 for newly diagnosed glioblastoma in combination with temozolomide based on the pivotal EF-14 trial. The device is approved for adult patients (22+ years) with histologically confirmed supratentorial glioblastoma.

Key Findings

Addition of Tumor Treating Fields to standard temozolomide therapy in elderly glioblastoma patients demonstrated significant survival benefit, extending median overall survival by approximately 4-5 months compared to historical controls. The benefit was most pronounced in patients maintaining high device compliance (≥22 hours/day).

TTFields represent a unique therapeutic modality with a distinct mechanism of action (disruption of mitotic spindle formation during cell division) and non-overlapping toxicity profile with chemotherapy. The device was generally well-tolerated in the elderly population, with dermatologic effects being the primary adverse event.

Key challenges in elderly patients included device compliance due to lifestyle restrictions, skin fragility requiring careful transducer management, and cosmetic concerns affecting social functioning. However, motivated patients who achieved high compliance derived substantial clinical benefit.

The non-invasive nature of TTFields makes it particularly attractive for elderly patients who may not tolerate additional systemic chemotherapy. The technology represents an important addition to the limited therapeutic armamentarium for glioblastoma.

Patient education, skin care protocols, and close monitoring of compliance are essential for maximizing benefit. Cost-effectiveness and insurance coverage remain important considerations for elderly patients on fixed incomes.

Citations

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