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Tumor Treating Fields Therapy in Patients With Newly Diagnosed Glioblastoma: Long-Term Survival Results From TTFields in Germany in Routine Clinical Care (TIGER) Study

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Background

- Glioblastoma (GBM) is the most frequent primary malignant brain tumor.[1] Prognosis is poor, with a median survival of 8 months and 5-year survival rate of 6.9%[2]
- Effective treatment options for GBM remain limited despite many clinical trials conducted over the past 20 years to improve survival outcomes[3]
- Tumor Treating Fields (TTFields) therapy concomitant with maintenance chemotherapy has demonstrated efficacy while maintaining quality of life in trials and real-world settings[4-7]
  - TTFields demonstrated significant improvements in overall survival (OS) and progression-free survival (PFS) when applied with adjuvant temozolomide (TMZ) compared to TMZ alone in patients with newly diagnosed GBM (ndGBM)[4]
  - In a global, post-marketing surveillance analysis of >25,000 patients treated with TTFields therapy, mild to moderate skin reactions were the most common treatment-related adverse event (AE) and no systemic toxicities were reported; however, data were limited to safety outcomes[7]
- TTFields therapy delivers electric fields, through scalp-placed arrays, that disrupt cellular processes critical for cancer cell viability[8-10]
- TTFields therapy is approved for GBM by the US Food and Drug Administration and Conformité Européenne (CE)-marked for World Health Organization (WHO) grade 4 glioma[11,12]
- The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include TTFields therapy as a NCCN Category 1 option with radiation therapy and TMZ (preferred for age ≤70 years) and a Category 2B option for recurrent GBM[13]

Objective

- To evaluate the safety and efficacy of TTFields therapy during routine clinical care in patients with ndGBM in Germany

Methods

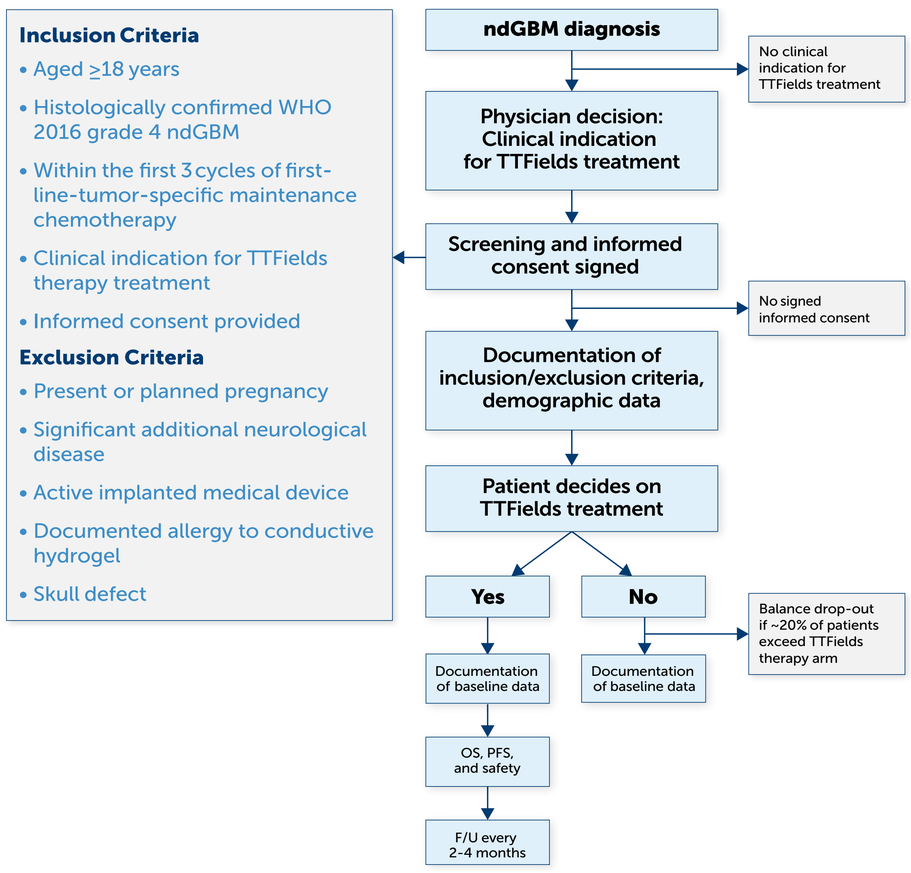
Participants and Study Design

- TIGER (NCT03258021) is a prospective, noninterventional, multicenter, medical device study that enrolled patients from August 2017 to November 2019 in 81 participating centers in Germany (**Figure 1**)

Assessments

- Endpoints included OS, PFS, and safety in patients who initiated TTFields therapy
  - OS: time of death from any cause after diagnosis
  - PFS: time to first progression of GBM by radiologic and/or clinical or neurologic assessment
  - Serious AEs (SAEs) after initiation of TTFields therapy
- The intent-to-treat (ITT) population included all enrolled patients who initiated TTFields therapy

Figure 1. Study Design



F/U, follow-up; ndGBM, newly diagnosed glioblastoma; OS, overall survival; PFS, progression-free survival; TTFields, Tumor Treating Fields; WHO, World Health Organization.

Results

Baseline Patient Characteristics and Demographics

- Of the 710 patients who agreed to participate in the study, 583 (82%) patients opted for TTFields therapy, and 429 received treatment (ITT population, **Table 1**)

Table 1. Patient Baseline Characteristics and Demographics

	ITT (n=429)
Age, median (range), y	58 (19–82)
Sex, n (%)	
Male	275 (64.1)
Female	154 (35.9)
KPS, n (%)	
70%	47 (11.0)
80%	73 (17.0)
90%	159 (37.1)
100%	83 (19.3)
MGMT status, n (%)	
Methylated	199 (46.4)
Unmethylated	186 (43.4)
Extent of resection, n (%)	
Biopsy	65 (15.2)
Gross total resection	226 (52.7)
Partial/subtotal resection	134 (31.2)
IDH1 status, n (%)	
Mutated	55 (12.8)
Wild-type	369 (86.0)
LOH 1p/19q status, n (%)	
Mutated	11 (2.6)
Wild-type	78 (18.2)
Skin status, n (%)	
Normal	364 (84.8)
Abnormal	18 (4.2)
Time from diagnoses to study enrollment, median (range), d*	83 (–6 to 582)

*ITT, n=425. IDH1, isocitrate dehydrogenase 1; ITT, intent-to-treat; KPS, Karnofsky Performance Scale; LOH, loss of heterozygosity; MGMT, O6-methylguanine-DNA methyltransferase.

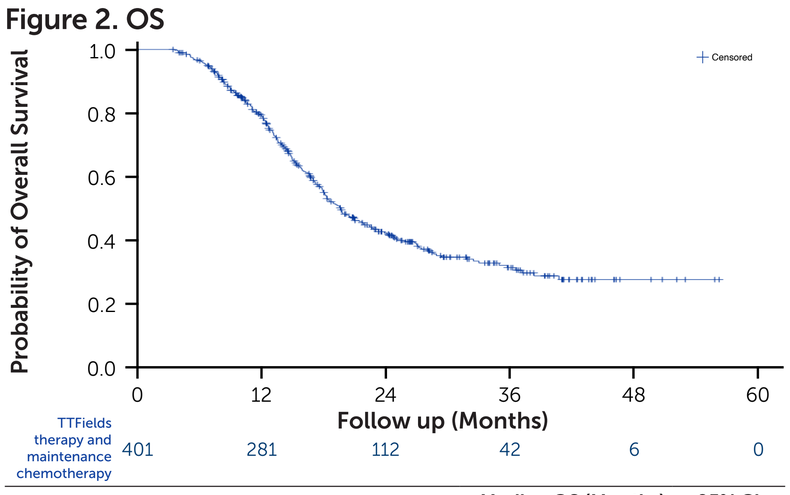
Efficacy Analyses (ITT Population)

- Median follow-up duration was 56.2 months

Overall Survival

- Median OS was 19.6 months (95% CI, 17.9–22.4; **Figure 2**)
- OS rates at years 1, 2, 3, and 4 were 79.2%, 42.4%, 31.5%, and 27.7%, respectively (**Table 2**)

Figure 2. OS



	Median OS (Months)	95% CI
TTFields therapy and maintenance chemotherapy	19.6	17.9–22.4

OS, overall survival; TTFields, Tumor Treating Fields.

Table 2. OS Rates With TTFields Therapy and Maintenance Chemotherapy

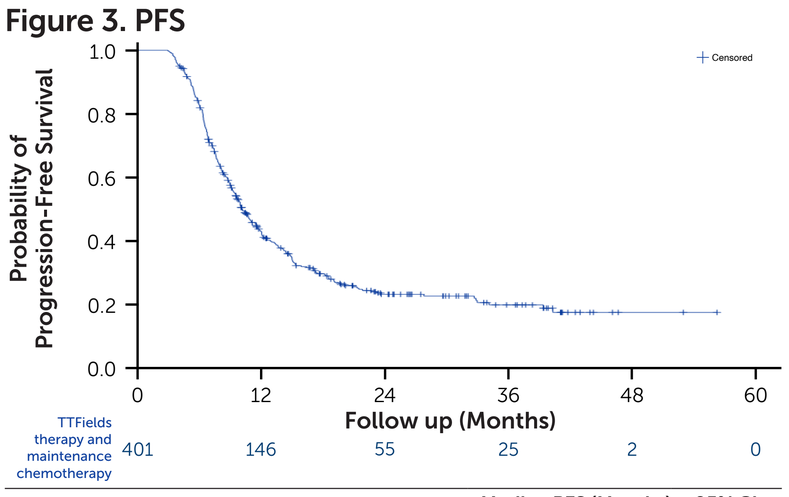
OS rates, % (95% CI)	ITT (n=401)
12 months	79.2 (74.7–83.0)
24 months	42.4 (37.0–47.7)
36 months	31.5 (25.8–37.2)
48 months	27.7 (21.8–33.9)

ITT, intent-to-treat; OS, overall survival; TTFields, Tumor Treating Fields.

Progression-Free Survival

- Median PFS was 10.2 months (95% CI, 9.4–11.4; **Figure 3**)
- PFS rates at years 1, 2, 3, and 4 were 42.0%, 23.2%, 19.9%, and 17.6%, respectively (**Table 3**)

Figure 3. PFS



	Median PFS (Months)	95% CI
TTFields therapy and maintenance chemotherapy	10.2	9.4–11.4

PFS, progression-free survival; TTFields, Tumor Treating Fields.

Table 3. PFS Rates With TTFields Therapy and Maintenance Chemotherapy

PFS rates, % (95% CI)	ITT (n=401)
12 months	42.0 (37.0–47.0)
24 months	23.2 (18.8–28.0)
36 months	19.9 (15.4–24.9)
48 months	17.6 (12.7–23.1)

ITT, intent-to-treat; PFS, progression-free survival; TTFields, Tumor Treating Fields.

Safety (ITT Population)

- Median therapy exposure (range) was as follows:
  - 5.9 (0.1–64.3) months with TMZ
  - 3.7 (0–28.4) months with lomustin
  - 5.7 (0–43.4) months with TTFields therapy
- SAEs were observed in 77% of patients, with only 0.7% being attributed to TTFields therapy (by clinical endpoint committee [CEC] adjudication; **Table 4**)

Table 4. SAEs by CEC Adjudication

	ITT (n=427)
SAEs after TTFields therapy start, n (%)	
Death as primary SAE*	194 (45)
Other SAEs	250 (58)
Total SAEs	329 (77)
TTFields-related SAEs, n (%)	
Death as primary SAE*	0
Other SAEs†	3 (0.7)
Total SAEs	3 (0.7)

*Not death as an outcome of another event. †All TTFields-related SAEs were mild to moderate in severity.
CEC, clinical endpoint committee; ITT, intent-to-treat; SAE, serious adverse event; TTFields, Tumor Treating Fields.

Conclusions

- TIGER is the largest prospective study to date on routine clinical practice in ndGBM
- TIGER reaffirms TTFields therapy's positive safety profile, and its OS and PFS results are consistent with prior studies[4,5]
- Treatment with TTFields therapy demonstrates promising long-term survival rates in patients with ndGBM

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