

Effects of Tumor Treating Fields (TTFields) on Health-Related Quality of life (HRQoL) in Newly Diagnosed Glioblastoma: An Exploratory Analysis of the EF-14 Randomized Phase III Trial

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Introduction

TTFields are a novel treatment modality that continuously delivers alternating electric fields to the tumor region. TTFields interfere with the assembly of the mitotic spindle leading to apoptosis. In the EF-14 phase III study in newly diagnosed glioblastoma, TTFields plus temozolomide (TTFields/TMZ) showed significant increase in overall and 5-year survival rates compared to temozolomide. TTFields/TMZ did not negatively impact nine prespecified HRQoL scales (global health, physical, cognitive, role, social and emotional functioning, itchy skin, pain, and leg weakness) except for increased itchy skin. We present an exploratory analysis of the remaining 17 EORTC QLQ C-30 and BN-20 HRQoL scales.

Methods

HRQoL was measured by the EORTC QLQ-C30 and BN20 questionnaires at baseline and every 3 months thereafter. Mean changes from baseline as well as significant changes in scores over time (>10 points) were evaluated using a repeated measures test.

Deterioration-free survival and time-to-deterioration in HRQoL were assessed for each scale, as well as % patients with stable/improved HRQoL versus baseline.

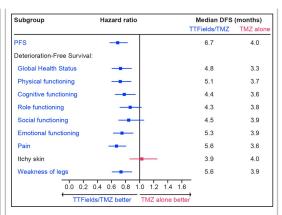


Figure 1. Effect of TTFields/TMZ on 9 pre-specified HRQoL scales in the EF 14 study in newly diagnosed glioblastoma 2.

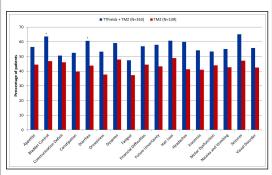


Figure 2. Proportion of the progression-free period during which patients had stable or improved HRQoL from baseline. *P<.001.

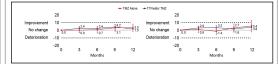


Figure 3. Mean changes in HRQoL score over time for (A) diarrhea and (B) bladder control

abgroup	Patients (%)	Median DFS (Months) TTFields/TMZ TMZ Alone				Median TTD (Months) HR TTFieldarTMZ TMZ Alcne (98% CI)				
FS	659(100)	6.7	4.0		+					
E8										
Motor dysfunction	629(91)	4.9	3.7	0.758 (0.624-0.922)		14.17	13.97	0.978 (0.716-1.336)	-	
Communication deficit	629(91)	4.9	3.9	0.816 (0.672-0.991)	-	10.60	12.13	0.962 (0.709-1.307)	-	
Patigue	629(92)	4.2	3.6	0.778 (0.644-0.943)	-	9.03	10.03	1.001 (0.752-1.332)	-	
Nausea and vomiting	635(92)	5.3	3.9	0.785 (0.647-0.952)	-	13.37	14.40	0.968 (0.696-1.347)	_	
Dysposa	635(91)	5.9	3.9	0.748 (0.615-0.908)		14.17	13.97	0.876 (0.611-1.256)		
Insomnia	635(91)	5.3	3.8	0.796 (0.657-0.996)	-	13.37	13.97	0.918 (0.676-1.247)	-	
Appetito loss	637(92)	5.4	3.9	0.815 (0.671-0.990)	-	14.17	13.97	1.064 (0.754-1.474)	-	- 1
Constipation	628(90)	4.9	3.7	0.782 (0.645-0.948)	-	13.27	12.27	0.964 (0.700-1.300)	-	
Diarrhea	637(92)	6.0	3.9	0.683 (0.563-0.829)	-	14.17	13.97	0.730 (0.508-1.050)	-	
Financial difficulties	633(91)	5.3	3.9	0.798 (0.658-0.909)	-	14.13	13.97	0.994 (0.705-1.403)		
Future uncertainty	629(91)	5,3	2.9	0.712 (0.567-0.865)		12.43	13.97	0.876 (0.632-1.213)		
Visual disorder	627(90)	5.3	3.9	0.731 (0.601-0.888)	-	14.17	14.40	0.836 (0.611-1.143)		
Headaches	628(90)	5.9	3.7	0.671 (0.553-0.815)	-	14.13	13.97	0.766 (0.543-1.080)	-	
Seizuros	624(90)	6.1	4.0	0.692 (0.567-0.845)	-	14.17	13.97	0.776 (0.512-1.175)	-	
Drovsiness	625(90)	4.9	3.9	0.739 (0.609-0.696)		14.17	11.3	0.745 (0.544-1.021)	-	
Hair loss	625(90)	6.0	4.0	0.715 (0.588-0.870)		14.17	13.97	0.758 (0.516-1.115)	-	
Bladder control	627(90)	6.1	3.9	0.746 (0.612-0.908)		14.17	13.97	0.779 (0.540-1.125)	-	
					0.0 0.5 1.0 1.8 TTF##95/TM2 Bottor TM2 Atm					1.5 2.0

Deterioration-free survival (DFS) is defined as the time to a >10 point deterioration in scores from baseline without a subsequent =10 point improvement in score compared to baseline, progressive disease. or death in the absence of a previous definitive deterioration before the next assessment. Time to deterioration (TTD) is defined similarly to DFS except for the exclusion of progressive disease as an event.

Figure 4. Evaluation of (A) deterioration-free survival and (B) time to deterioration

Results

No statistically or clinically significant decline in any of the exploratory HRQoL scales was seen in the repeated measures analysis or in time to deterioration. Significantly more patients treated with TTFields/TMZ versus TMZ reported stable/improved bladder control (63.6% versus 46.8%, p=0.001) and diarrhea (60.6% versus 43.7%, p=0.001) compared to baseline. The deterioration-free survival for diarrhea, future uncertainty and headaches was significantly delayed in TTFields/TMZ treated patients compared to TMZ alone (HR 0.68, 0.71 and 0.67, respectively, p<0.001).

Conclusions

The delay in deterioration-free survival and increase in %patients with stable/improved HRQoL in several additional HRQoL scales may be attributed in part to the longer progression-free survival observed in TTFields/TMZ treated patients in the EF-14 trial. No negative impact of HRQoL was seen in any of the exploratory scales. These results support adding TTFields to standard therapy in newly diagnosed glioblastoma.

Learning Objectives

By the conclusion of this session, participants should be able to: 1)
Describe the importance of quality of life in treatment of glioblastoma with tumor treating fields, 2) Discuss, in small groups, the effect of tumor treating fields on health related quality of life, 3) Identify an effective treatment for glioblatoma.

References

- 1. Stupp R et al. JAMA 2017;318:2306–2316.
- 2. Taphoorn J et al. JAMA Oncol.doi:10.1001/jamaoncol.2017.50 82.