

Perampanel in add-on: effect on EEG background activity and efficacy on seizure control in patients with Brain Tumor-related Epilepsy. Preliminary data

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Objective:

Patients with brain tumor-related epilepsy (BTRE) present difficulties regarding the simultaneous management of two challenging pathologies: epilepsy and brain tumor (BT).

Patients are often forced to take polytherapy because in many cases, seizures are drug resistant.

Perampanel is a new antiepileptic drug (AED) used as adjunctive therapy in patients with partial seizures with or without secondary generalization.

The aim of this open pilot study was 1) to evaluate the effect of perampanel on EEG background activity using computerized EEG analysis and 2) to evaluate the efficacy of perampanel, as add-on during six months of treatment, in patients with uncontrolled partial-onset seizures related to BT.

Methods:

At first visit and after 6 months of therapy, patients underwent neurological examination (KPS and BI) and were evaluated according to: seizure frequency (using seizure diary), adverse events (using AEP), spontaneous reports of adverse events and Quantitative EEG.

The starting dosage of perampanel was 2 mg/die with a weekly increase of 2 mg/day.

The patients underwent 21-channel EEG recordings carried out by placing the electrodes according to International System 10-20: electrocardiogram was recorded via additional skin surface electrodes.

Recording sessions: 10 minutes at rest with eyes closed (REST), 5 minutes during hyperpnoea (HP), 5 minutes during opening and closing eyes (BR), 5 minutes during mental arithmetic task (MA), of continuous subtraction of same digit from an initial starting number. Off-line spectral analysis was performed using Fast Fourier Transform on 5-10 min of EEG signal, manually segmented into > 2 seconds epochs, after visual elimination of interictal epileptiform activity and artifacts.

These epochs were collected for each frequency band: delta (1-3.5) Hz; theta (4-7) Hz; alpha (8-12.5) Hz and beta (13-30) Hz. Relative power values were considered due to their lower inter-subject variability.

Results:

•To date, we have recruited five patients (4 M, 1 F; mean age 48.4 years), followed for at least three months (mean 4.8 months): two high-grade gliomas, two low grade gliomas and one metastasis.

•Three patients were in chemotherapy.

•Two patients have simple partial seizures and three have secondary generalized seizures.

•All patients were in AED polytherapy.

•Mean dosage of perampanel was 6 mg/die.

Mean seizure number in the month prior to administration of perampanel was 9.8

At three months the mean seizure number was 0.7

✓1 patient was seizure-free

✓4 patients have a significant reduction of seizures (> 50%)

————— **Responder rate = 100%**

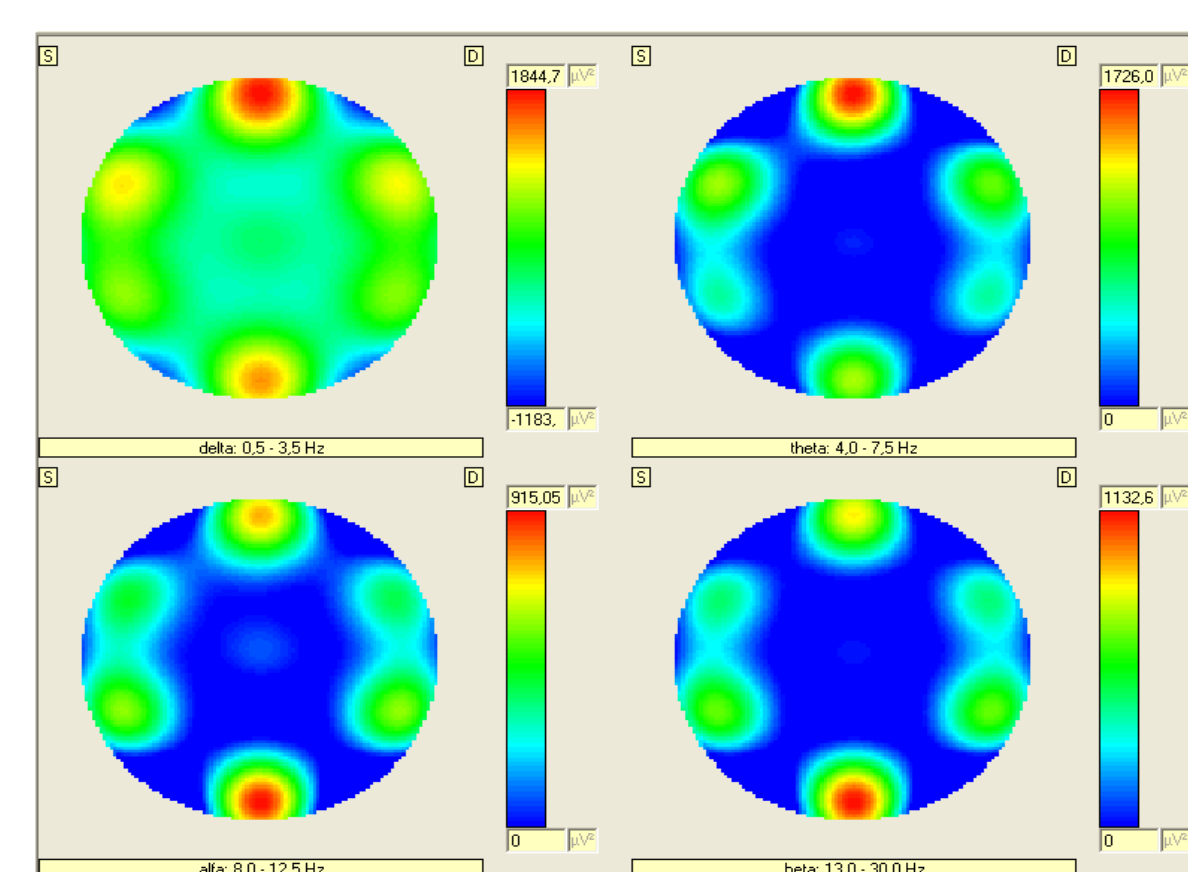
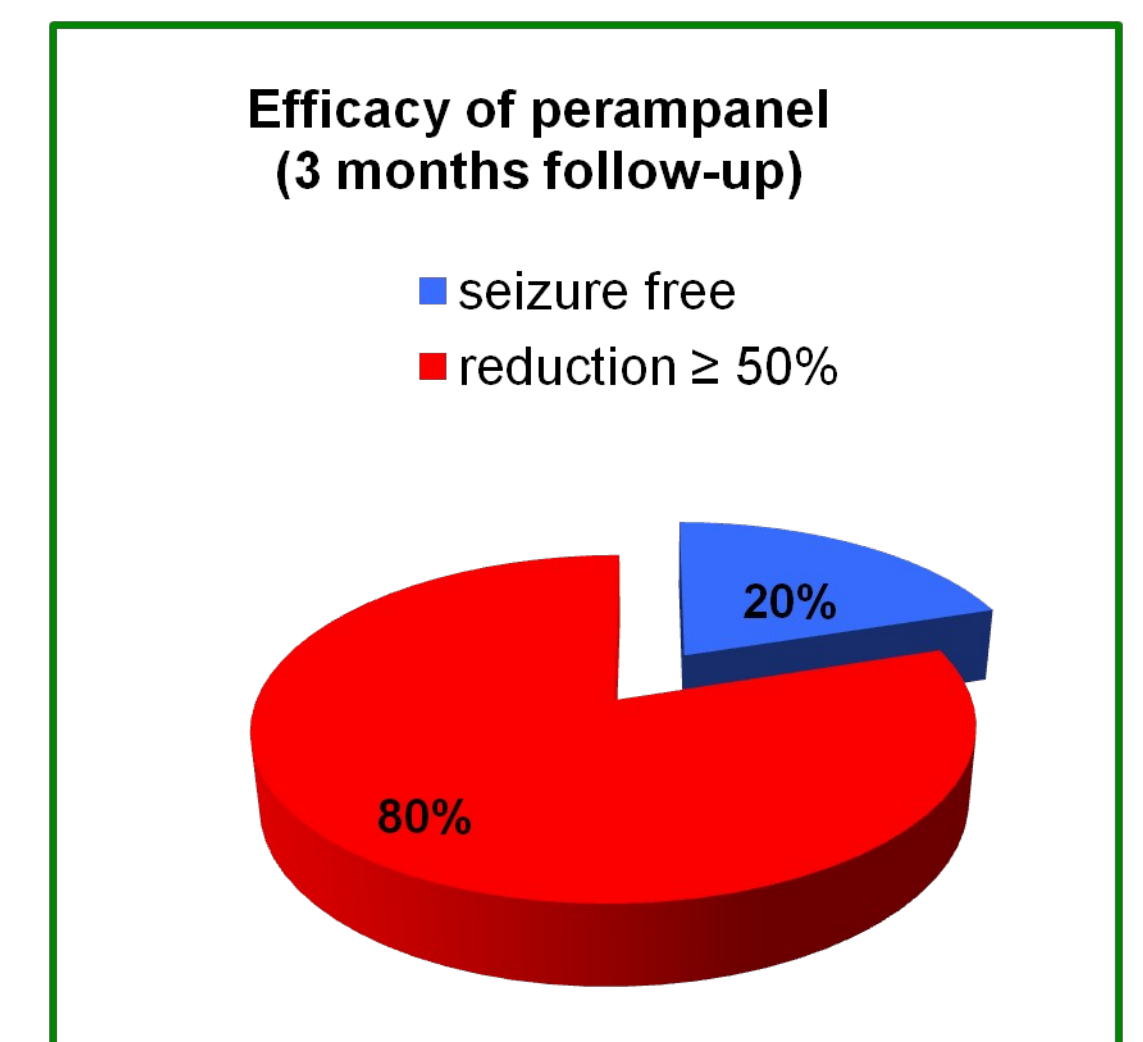
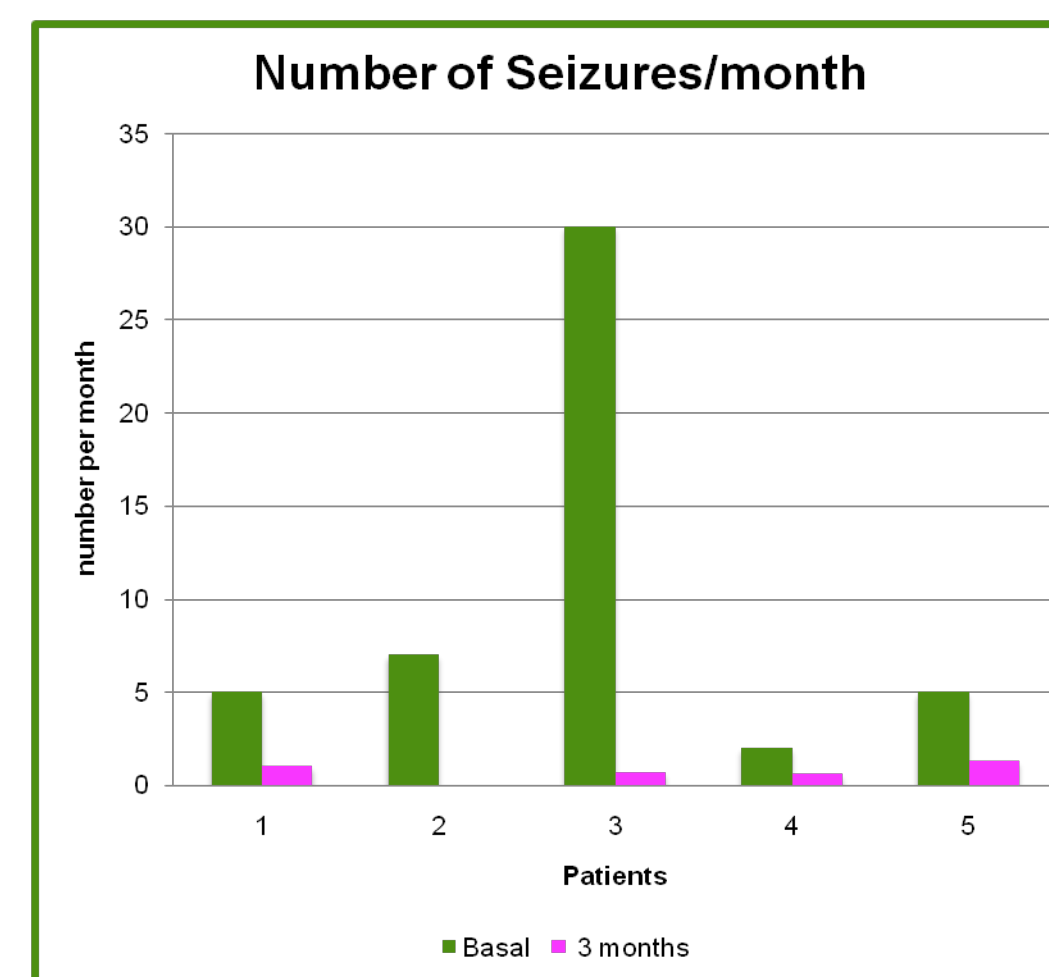
No side effects were observed

The evaluation of EEG background activity is ongoing

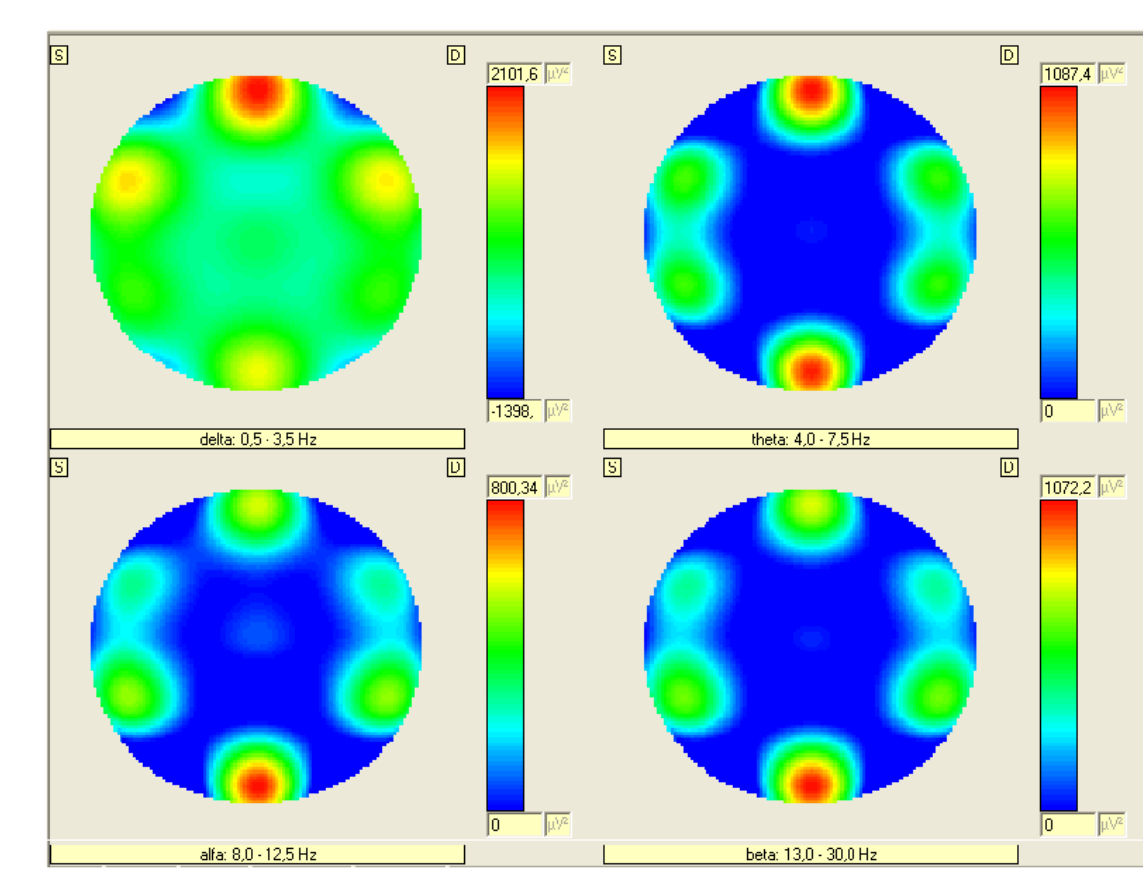
Age	Sex	Histology	Tumor site	Surgery	Disease Progression	CT (during follow-up)	RT (during follow-up)	Seizure Type	Other AEDs	Perampanel dosage (mg/day)	Seizure number in the last month (pre-perampanel)	Number Seizure/month at 3 months	Number Seizure/month at finally follow-up (6months)	Side Effects
75	M	GBM	F sn	GTR	YES	CCNU	NO	SP	LCM 300 LEV 3000	6	5	1	1	NO
48	M	GBM	F sn	GTR	YES	bevacizumab	NO	SP+S GTC	LCM 400 LEV 3000	6	7	NO	NO	NO
46	M	LGO	F-P sn	BIOPSY	NO	TMZ	NO	SP+S GTC	VPA 1500 LEV 3000 LTG 200	6	30	0.7	0.5	NO
40	F	LGA	F sn	GTR	NO	NO	NO	SP+S GTC	LTG 400	4	2	0.6	ongoing	NO
33	M	MET	multifocal	NO	NO	NO	NO	SP	LEV 3000 ESL 1200	4	5	1.3	ongoing	NO

Legend

-Histology: GBM: glioblastoma; LGO: oligodendroglioma low grade; LGA: astrocitoma low grade; MET: metastasis -Tumor site: F: frontal; F-P: fronto-parietal -Surgery: GTR: gross total resection -CT: CCNU: lomustine; TMZ: temozolomide -RT: radiotherapy -Seizure type: SP: simple partial; SP+S GTC: simple partial secondarily generalized -AEDs (antiepileptic drugs): LCM: lacosamide; LEV: levetiracetam; VPA: valproic acid; LTG: lamotrigine; ESL: eslicarbazepina acetato



Baseline



At 6 months

Conclusions:

We present the preliminary data of an ongoing study; despite this limitation, our findings indicate that, in our patients with BTRE, perampanel seems to have a good efficacy on seizure control, without observed side effects.

Use of new AED such as perampanel in add-on, could help clinicians in the management of BTRE patients, in seizure control and reducing side effects.

References:

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Rösche J, Piek J, Hildebrandt G, Grossmann A, Kirschstein T, Benecke. Perampanel in the treatment of a patient with glioblastoma multiforme without IDH1 mutation and without MGMT promotor methylation. *FortschrNeurolPsychiatr.* 2015 ,83(5):286-9.