

ZONISAMIDE IN PATIENTS WITH BRAIN TUMOR-RELATED EPILEPSY: EVALUATION OF SEIZURE CONTROL, QUALITY OF LIFE AND COGNITIVE PERFORMANCES

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Objective:

Epilepsy heavily affects the quality of life (QoL) of patients with brain tumor because in addition to taking treatments for the oncological illness, patients are required to live with the long-term taking of antiepileptic drugs (AEDs).

AED side effects are common in these patients and can negatively influence their perceptions of their QoL.

We conducted an observational pilot study in patients with brain tumor-related epilepsy (BTRE) to verify efficacy, tolerability, and impact on QoL and global neurocognitive performances of Zonisamide (ZNS) in add-on.

Methods:

Patients with BTRE, with uncontrolled seizure activity, receiving standard AED therapy were included in this study.

ZNS was added as first or second add-on.

Patients will be followed for 6 months, and at baseline and at finally follow-up underwent neurological examination, evaluation of adverse events, and cognitive and QoL tests.

Seizure diary was given.

Results:

Patient Profiles

We recruited a total of 13 patients (8 male and 5 female, mean age 49.6) with BTRE presenting uncontrolled seizures.

•Four patients dropped out for scarce compliance (see Table 1).

•Nine patients reached the 6 months follow-up, of which four were with stable neurooncological disease and five with disease progression.

Efficacy

In the 9 patients who reached 6 month follow up, the mean weekly seizure number before ZNS had been 3.2 ± 5.0 and was reduced to 0.18 ± 0.41 at final follow-up ($p=0.05$) (see Fig.1)

Responder rate

Seven patients of the total patient population ($n=13$) achieved a $\geq 50\%$ of seizure reduction at final follow-up compared with the baseline.

The responder rate was 53.8%

QoL and neuropsychological Tests evaluation

Of the 13 enrolled patients, 9 patients underwent neuropsychological tests at baseline (4 declined neuropsychological testing and soon after dropped out); 8 repeated the tests at 6 months (1 was aphasic).

•Functional status remained stable over time (see Table 2).

•Cognitive tests showed stability in all domains except for fluency test that significantly worsened (see Table 2).

•In all patients EORTC QLQ-C30 score remained stable (see Table 2).

•**QOLIE 31P-V2 showed a significant improvement in distress scores related to cognitive ($p=0.04$) and social functions ($p=0.02$)** (see Table 2).

•**No side effects were observed.**

•AEP test showed stable scores over time (see Table 2)

Table 1

	Age	Sex	Level of education (years)	Histology	Tumor site	Surgery	Disease Progression	CT (during follow-up)	RT (during follow-up)	Seizure type	Other AEDs	ZNS dosage (mg/d ay)	Seizure number in the last month	Seizure number (final follow-up)	Side effects	Drop-out reason
1*	32	M	13	OA II WHO	F-P left	PR	No	TMZ	No	SP	LEV 3000	300	4	-	No	Scarce compliance
2	40	M	8	GBM	T left	PR	Yes	TMZ	Yes	SP	VPA 1500	300	60	1	No	
3	61	M	13	GBM	T right	PR	Yes	TMZ	Yes	CP	VPA 300	300	2	0	No	
4*	52	F	8	MEN	P-O left	GTR	No	No	No	CP+SGTC	LEV 3000 LCM 350 CLB 2	300	2	-	-	Scarce compliance
5	46	M	13	GBM	F-T right	PR	No	FTMU	No	CP	LEV 2000	300	3	0	No	
6	59	F	13	MEN	P-O left	GTR	No	No	No	CP+SGTC	LEV 1000	400	12	4	No	
7	37	M	13	OA II WHO	F left	PR	No	TMZ	No	CP	LEV 1000	300	30	30	No	
8*	39	M	13	GBM	F right	PR	No	TMZ	No	SP	LEV 3000	300	60	-	-	Scarce compliance
9	58	F	13	MEN	F-P right	GTR	No	No	No	CP	LEV 2000	300	2	1	No	
10	50	F	13	MET	multiple	PR	Yes	No	No	CP+SGTC	PB 100	200	2	0	No	
11 §	61	F	5	GBM	T left	PR	Yes	TMZ	No	SP	OXC 900 PB 50	300	2	0	No	
12	57	M	13	GBM	F right	PR	Yes	TMZ	Yes	SP+SGTC	PB 100	300	2	4	No	
13*	53	M	18	OD II WHO	T right	PR	No	No	No	SP	LEV 3000	-	4	-	No	Scarce compliance

Legend

-Histology: OA: oligoastrocitoma; OD: oligodendroglioma; GBM: glioblastoma; MEN: meningioma; MET: metastasis

-Tumor site: F: frontal; F-P: fronto-parietal; T: temporal; P-O: parieto-occipital; F-T: fronto-temporal

-Surgery: PR: partial resection; GTR: gross total resection

-RT: radiotherapy

-CT: TMZ: temozolomide; FTMU: fotemustine

-Seizure type: SP: simple partial; PC: complex partial; CP+SGTC: complex partial secondarily generalized; SP+SGTC: simple partial secondarily generalized

-AEDs (antiepileptic drugs): LEV: levetiracetam; VPA: valproic acid; LCM: lacosamide; CLB: clobazam; PB: fenobarbital; OXC: oxcarbazepine

*drop-out

§Deceased

Fig. 1

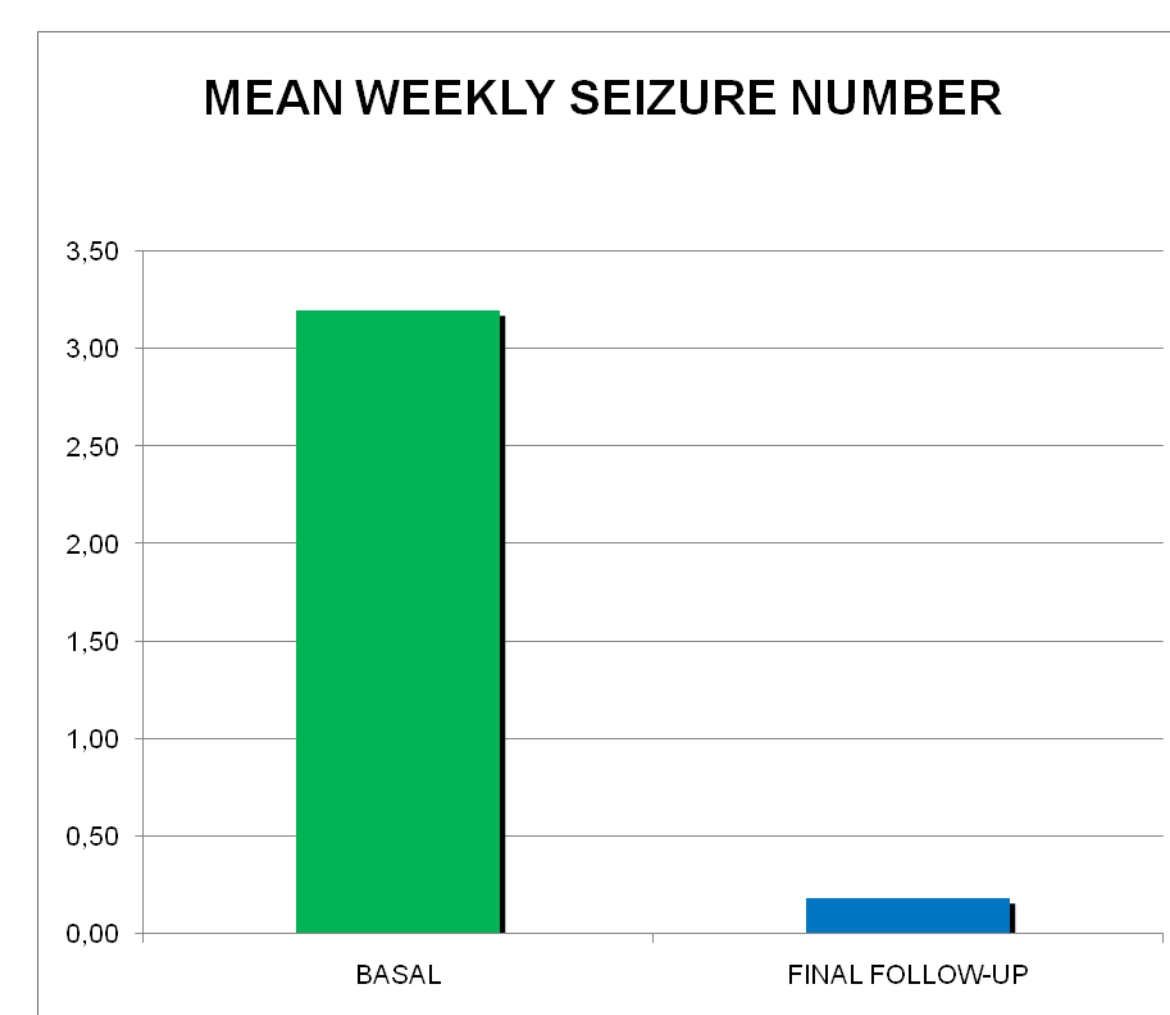


Table 2: Comparison between neuropsychological tests before and after 6 months of treatment with Zonisamide

TEST	Baseline (means±SD)	6 months (means±SD)	P
KPS	100 ± 0	91 ± 11.3	0.06
BI	100 ± 0	91 ± 11.3	0.06
MMSE	29.5 ± 0.9	28.1 ± 2.7	0.20
RAVLT Immediate recall	36.4 ± 12.6	35.6 ± 13.3	0.78
RAVLT Delayed recall	1.5 ± 2.2	2.9 ± 2.6	0.27
TMT - A	40.3 ± 12.4	48.0 ± 20.4	0.42
TMT - B	74.2 ± 27.2	105.4 ± 58.3	0.13
Fluency test	31.0 ± 6.3	22.6 ± 11.7	0.04
QOLIE 31P(V2)			
Energy/fatigue	58.1 ± 14.8	64.4 ± 12.9	0.22
Emotional well being	54.6 ± 20.6	63.1 ± 19.9	0.29
Social function	57.9 ± 26.8	70.7 ± 23.8	0.14
Cognitive function	58.8 ± 23.8	62.0 ± 31.3	0.53
Medication effects	70.6 ± 23.6	64.5 ± 28.6	0.18
Seizure worry	47.9 ± 40.2	69.5 ± 40.8	0.07
Overall QoL	59.1 ± 16.9	61.6 ± 17.4	0.50
<i>Distress related to:</i>			
Energy/fatigue	2.5 ± 0.7	2.2 ± 0.7	0.52
Emotional well being	2.5 ± 0.7	2.1 ± 0.6	0.20
Social function	2.9 ± 0.3	2.0 ± 0.9	0.02
Cognitive function	2.9 ± 0.6	2.0 ± 1.1	0.04
Medication effects	2.8 ± 0.9	2.1 ± 0.6	0.14
Seizure worry	2.6 ± 1.5	2.9 ± 1.2	0.52
Overall QoL	2.8 ± 0.5	2.4 ± 0.5	0.08
Health thermometer	53.8 ± 9.2	65.0 ± 12	0.06
EORTC QLQ-C30			
Functional Scale	77.4 ± 15.4	81.6 ± 14.8	0.32
Symptoms Scale	12.4 ± 7.7	11.9 ± 6	0.64
QoL	62.5 ± 7.7	63.6 ± 15.4	0.86
AEP	40.3 ± 14.3	43.0 ± 16.2	0.38

Legend
KPS = Karnofsky Performance Status; BI = Barthel Index; MMSE = Mini Mental State Examination;
RAVLT = Rey Auditory verbal Learning test; TMT-A = Trail Making Test part A; TMT-B = Trail Making Test part B; AEP = Adverse Event Profile

Discussion:

✓ZNS as add-on in our patients appears to be efficacious in controlling seizures and well tolerated.

✓In our study, all tests scores were stable, suggesting that adding ZNS did not alter patients' perceptions of their QoL.

Furthermore the decrease of distress' level indicating that our patients were less worried about their cognitive and social difficulties related epilepsy.

✓Our results confirm that when choosing an AED, in addition to efficacy, the drug's impact on patient QoL also needs to be considered, especially for patients facing many psychosocial challenges, such as those with BTRE.

✓Use of ZNS in add-on in patients BTRE may represent a valid alternative as add-on in this particular patient population. However larger samples are necessary in order to draw definitive conclusions.

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