EFFICACY AND TOLERABILITY OF ESLICARBAZEPINE AS ADJUNCTIVE THERAPY IN PATIENTS WITH DRUG-RESISTANT PARTIAL EPILEPSY: PRELIMINARY DATA

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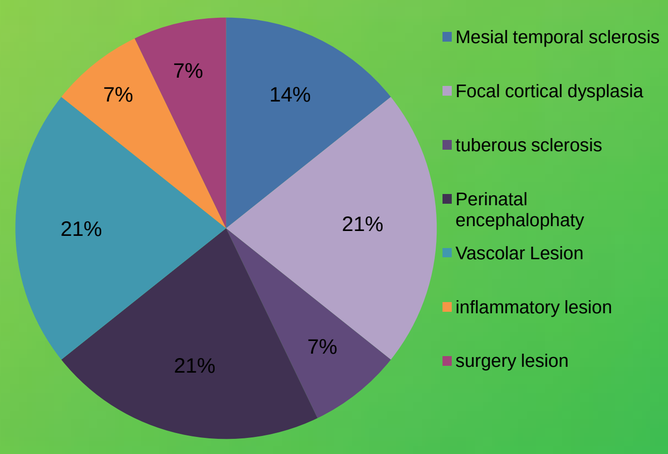
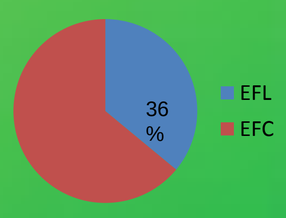
Purpose: to assess efficacy and tolerability of ESL as add-on treatment in patients with refractory partial epilepsy.

Method: a prospective, open label, longitudinal study conducted in 39 patients with refractory partial epilepsy. The study included three periods: baseline (3 months), drug titration (2 weeks), observation, during which ESL could be increased until the maximum tolerated dose. Inclusion criteria were: age over 16 years, diagnosis of focal epilepsy, resistance to at least 2 previous antiepileptic drugs (AED), stable concomitant antiepileptic therapy within 3 months. Exclusion criteria were: progressive neurological disease, poor compliance, history of pseudo-seizures, pregnancy. Efficacy has been evaluated by comparing the mean monthly seizure frequency of the last quarter observation period with baseline seizure frequency using t-test for dependent samples.

Results: 39 patients were enrolled. Clinic and demographic features (age, sex, age of onset and duration of the disease, aetiology, type of seizures, neuropsychological profile, RMN abnormalities, number of previous and concomitant AED) have been evaluated. Thirty-two patients (82%) were receiving polytherapy. The mean number of antiepileptic drugs tried before ESL was 6±3,39 (2-15). ESL was administrated at a daily mean dose of 1042,42±373,45 mg (400-2000). The mean duration of observation was 6±2.3 months (3-10): 5 patients didn't reach three months and were excluded from efficacy analysis. A statistically significant reduction of the mean monthly seizure rate was observed (10,22±14,67 vs 17,44±22,3, p = 0.03). Seven patients withdrew ESL: 1 for seizure worsening, 1 for inefficacy, 1 for urticaria, 1 for pseudo-seizures, 3 for somnolence and dizziness. In 4 cases, side effects were mild and didn't lead to discontinuation.

Variables	
Age	mean 39,4 ± 11,8 (18-64)
Sex	21 M, 18 F
Diagnosis	14 EFL (36%), 25 EFC (64%)
MRI lesions	14 pazienti
No. of previous AED	mean 6 ± 3,39 (2-15); median 6
No. of associated AED	mean 1,85±0,70; 1 AED (18%); 2 AED (49%); 3 AED (33%)
Type of seizures	PE/PC 22 pz; PSG 17 pz

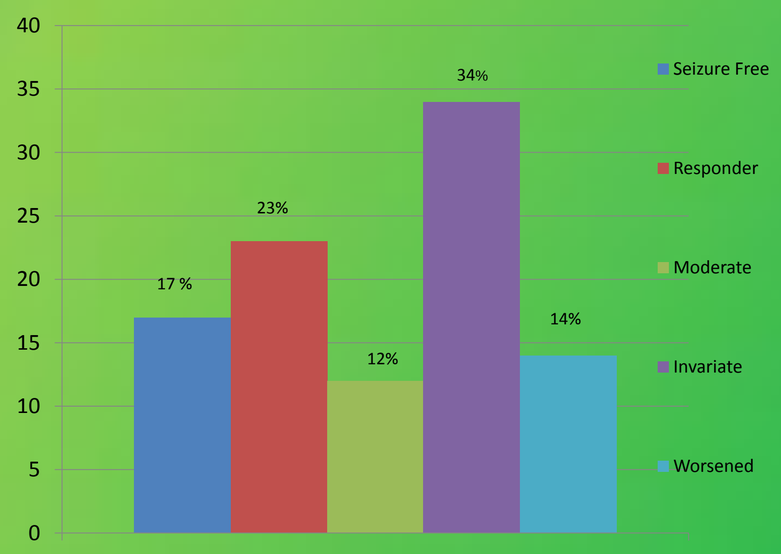




GROUP A (16 pts): seizure free + responders (40%)

GROUP B (19 pts): mild responders + not responders (60%)

	Group A	Group B
Etiology	EFC 9 pts (60%) EFL 6 pts (40%)	EFC 13 pts (68%) EFL 6 pts (32%)
Seizures per month– basal (mean)	21,5±23,9	14,25±21,08
Previous AED	4,6±3,14	6,9±3,48
Associated AED	1.5±0.6	2±0.74
ESL dose (mean)	960±294,71	1073±443,27



AED	1 AED (13 pz)	2 AED (19 pz)	3 AED (7 pz)	
LTG	2	5	2	9
CBZ	1			1
PHT		2		2
LCM	2	4	1	7
PB	2	4	1	7
LEV	3	6	3	12
VPA	1	8	1	10
TPM		1	3	10
CLB		4	6	10
ZNS	2	2	2	6
PRM	1			1
NTZ			1	1
FBM		1		1

Adverse effect	Daily dose	No. Of cases	Therapeutic decision
somnolence	1200-1600 mg	2 cases	Posologic reduction
diplopia	400 mg	2 cases	Posologic reduction LCM
dizziness	400 mg	2 cases	discontinuation
hyponatremia	1600 mg	1 case	observation
urticaria	400 mg	1 case	discontinuation
pseudo-seizures	400 mg	1 case	discontinuation
ESL MEAN DOSE: 755,5 mg			
diplopia, dizziness (4 cases): always in association with other Na-blocker AEDs (2 cases LTG, 2 cases LCM)			

Discussion: Eslicarbazepine acetate (ESL) is a new generation voltage-gated sodium channel blocker, approved for adjunctive treatment in adult subjects with partial-onset seizures. ESL shares with carbamazepine and oxcarbazepine the dibenzazepine nucleus, but it is structurally different at the 10,11-position. This chemical structure results in differences in ESL mechanism of action, and in different pharmacokinetic features with low drug interaction potential and a favourable safety profile.

Conclusions: our preliminary data suggest good efficacy and tolerability of ESL, administrated until a daily dose 2000 mg, as add-on therapy in drug-resistant partial epilepsy.

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