Efficacy and safety of Eslicarbazepine acetate in pharmaco-resistant focal epilepsy: a real-life experience

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Objectives: Eslicarbazepine acetate (ESL) is a third generation member of the dibenzazepine family of antiepileptic drugs (AEDs), which also includes carbamazepine and oxcarbazepine. The efficacy and safety of ESL was demonstrated by RCTs and retrospective studies in clinical practice setting.(1,2) In Italy ESL was approved by about two years as add-on therapy in adults with refractory partial-onset epileptic seizures. The aim of this prospective real-life study is to evaluate the clinical and electroencephalographic effects of ESL in a group of consecutive adult patients with refractory focal epilepsy referred to our Center for Epilepsy.

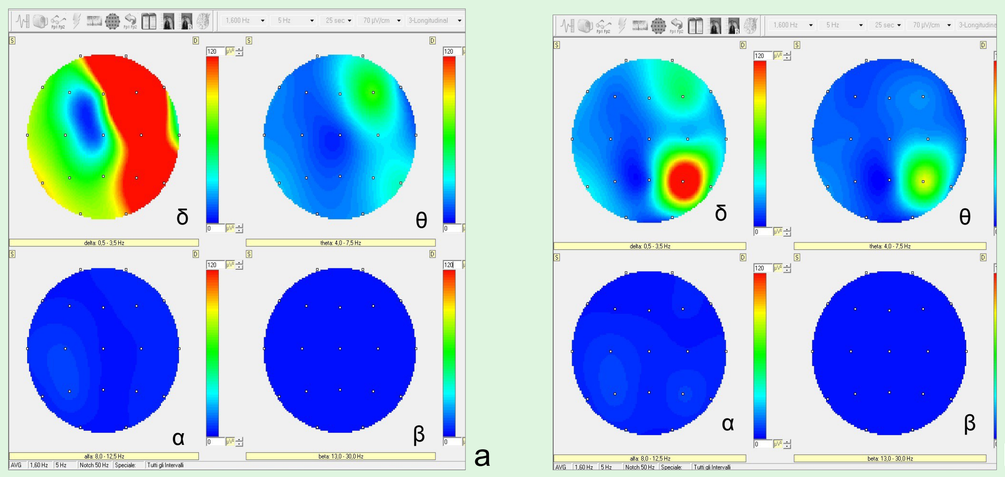

Fig. 1 Spectral analysis of various EEG bands pre- (a) and post- ESL (b)

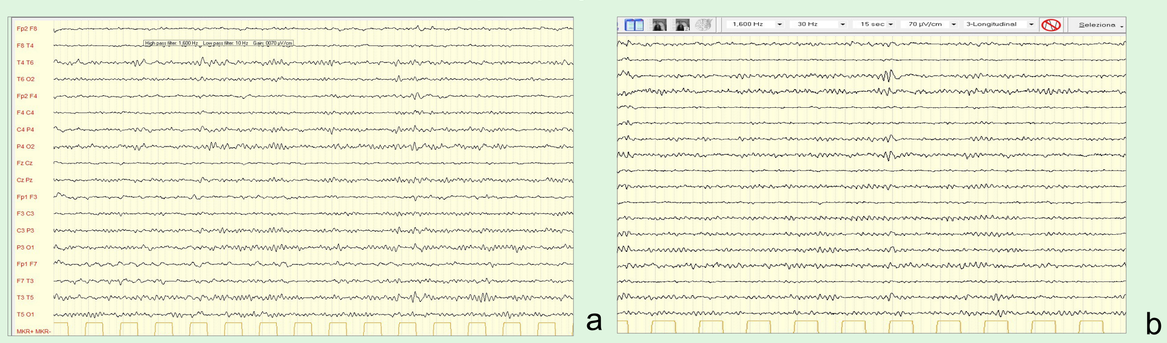

Fig .2 Example of EEG background activity pre- (a) and post-ESL (b)

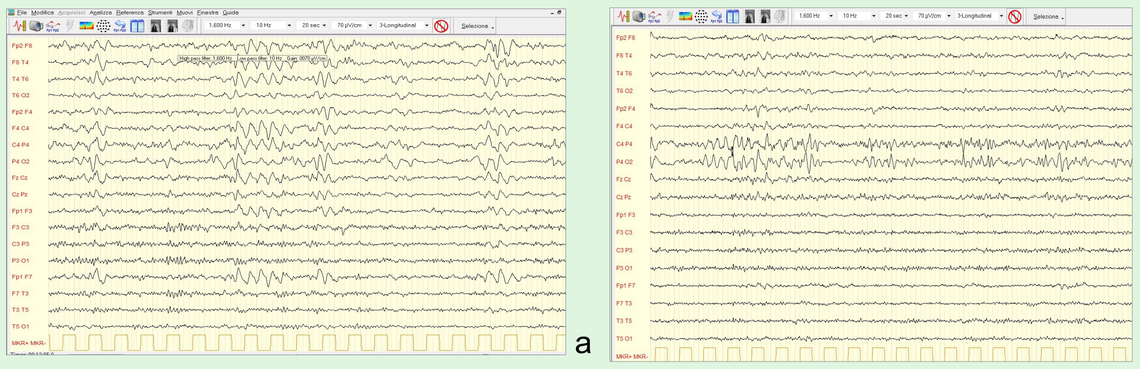

Fig. 3 Example of EEG slow and epileptiform activity pre- (a) and post- ESL (b)

Materials and Methods:
We observed 46 outpatients suffering from drug-resistant focal seizures with or without secondary generalization (21 M, 25 F, mean age 44 ys, mean duration of epilepsy 18,6 ys). Patients underwent neurological consultation, neuropsicological evaluation (QoLi-31, BDI-II, Stanford sleepiness scale) and EEG at baseline, 3, 6 and 12 months after starting ESL. Inspective and quantitative EEG evaluations were conducted. At each control blood count, liver and kidney function, electrolytes and fat profile were assessed, as well as variation in seizure frequency and occurrence of adverse effects. ESL was introduced at the initial dose of 400 mg/day with gradual increment to 800-1200 mg/day according to clinical response. In 11 patients a switch from OXC or CBZ was made.

Results:
4 patients dropped out after 2 weeks due to occurrence of dizziness (2), skin rash (1) and hyponatremia (1). 10 more patients dropped out, 5 at 3 months and 5 at 6 months (6 dizziness, 1 hyponatremia, 2 sleepiness, 1 constipation). 10 pt were still ongoing follow-up and 2 underwent surgery. In summary, at 12 months, we evaluated 20 patients with complete follow-up. Of them, 13/46 (28%) were seizure-free, 5 (11%) showed a reduction of seizure frequency >50%, 2 (4%) were unchanged. Overall, 14 patients (30%) discontinued treatment due to side effects. Improvement in cognitive performances, mood and alertness was observed. Inspective and quantitative EEG analysis pointed out an increment of alpha and a reduction of delta activity. The epileptic interictal abnormalities remained, but in some cases they were decreased and more localized.

	sesso	età	diagnosi	tipo crisi	AE	ESL T0	ESL T3	ESL T6	ESLT12	crisi mese T0	crisi/mese T3	crisi/mese T6	crisi/mese T12
1	M	45	Epi Temp Sint	PC	LEV-ZNS-DPH	800 mg	800 mg	1200 mg	1200 mg	6	1	1	0
2	M	53	Epi Temp Sint	PC	PB	800 mg	800 mg	1200 mg	1200 mg	16	8	2	1
3	F	38	Epi Temp Cript	PC	LTG-PB	800 mg	800 mg	800 mg	800 mg	2	1	0	0
4	F	20	Epi Temp Sint	PS+SG	LCM-CLB-TPM-PB-	800 mg	800 mg	800 mg	800 mg	16	4	4	2
5	M	25	Epi Temp Cript	PS+SG	VPA-CLB	800 mg	800 mg	800 mg	800 mg	3	0	0	0
6	F	40	Epi Temp Sint	PS	LTG-LCM	800 mg	800 mg	1200 mg	1200 mg	12	8	4	2
7	M	32	Epi Temp Sint	PS+SG	LTG-PB	800 mg	800 mg	800 mg	800 mg	8	4	4	2
8	M	40	Epi Temp Sint	PS	LTG-PB	800 mg	1200 mg	1200 mg	1200 mg	3	3	3	3
9	F	69	Epi Temp Sint	PC	PB-LTG-TPM	800 mg	800 mg	800 mg	800 mg	5	0	0	0
10	M	23	Epi Temp Sint	PS+SG	VPA	800 mg	800 mg	800 mg	800 mg	5	1	0	0
11	M	35	Epi Temp Cript	PC	VPA-CLB	800 mg	800 mg	800 mg	800 mg	3	3	3	3
12	F	69	Epi Temp Cript	PC	PB-LEV	800 mg	800 mg	800 mg	800 mg	12	0	0	0
13	F	39	Epi Temp Sint	PC+SG	PB	800 mg	800 mg	1200 mg	1200 mg	10	5	3	1
14	M	46	Epi Temp Sint	PC	PB-LEV-CBZ	800 mg	800 mg	1200 mg	1200 mg	5	2	1	0
15	F	20	Epi Occipit Cript	PC	TPM-LTG	800 mg	800 mg	800 mg	800 mg	3	0	0	0
16	F	50	Epi Temp Cript	PC+SG	CBZ-BDZ	800 mg	800 mg	800 mg	800 mg	1	0	0	0
17	M	41	Epi Temp Sint	PC+SG	LEV	800 mg	800 mg	800 mg	800 mg	1	0	0	0
18	M	38	Epi Temp Sint	PC+SG	LEV	800 mg	800 mg	800 mg	800 mg	2	2	1	0
19	F	78	Epi Temp Sint	PC	LTG-PB	400 mg	400 mg	400 mg	800 mg	3	0	0	0
20	M	31	Epi Temp Sint	PC	LCM-VPA	800 mg	800 mg	1200 mg	800 mg	2	1	1	0
21	M	65	Epi Temp Cript	PC	TPM	800 mg	800 mg	800 mg	800 mg	4	0	0	
22	M	71	Epi Temp Sint	PC	LEV	800 mg	800 mg	800 mg	800 mg	2	1	1	
23	M	30	Epi Temp Sint	PC+SG	LCM-OXC-DPH-CNZ	800 mg	800 mg	800 mg	800 mg	3	3	1	
24	F	20	Epi Temp Cript	PC+SG	VPA	800 mg	800 mg	800 mg	800 mg	1	0	0	
25	M	22	Epi Temp Cript	PC+SG	LEV-VPA	800 mg	800 mg	1200 mg	1200 mg	3	0	0	
26	M	53	Epi Pariet Sint	PS	PB-OXC	800 mg	800 mg	800 mg	800 mg	3	3	1	
27	F	42	Epi Temp Sint	PC+SG	LTG	800 mg	800 mg	1200 mg	1200 mg	8	4	2	
35	F	47	Epi Temp Cript	PC	LTG-VPA	800 mg	800 mg	800 mg	800 mg	3	0	0	
28	F	45	Epi Temp Sint	PC+SG	LEV	800 mg	800 mg	800 mg	800 mg	4	2	1	
29	F	40	Epi Temp Cript	PC	VPA	800 mg	800 mg	800 mg	800 mg	3	0	0	
30	M	35	Epi Temp Cript	PC	LTG	800 mg	800 mg	1200 mg	1200 mg	6	3	1	
31	M	45	Epi Temp Cript	PC	VPA	800 mg	800 mg	800 mg	800 mg	3	1	1	
32	F	41	Epi Occipit Cript	PC+SG	LTG-PB-VPA	800 mg	800 mg	800 mg	800 mg	4	4	2	
34	F	37	Epi Front Cript	PS+SG	LTG	800 mg	800 mg	800 mg	800 mg	2	2	2	
33	F	25	Epi Temp Sint	PC	ZNS-LCM-PB	800 mg	800 mg	800 mg	800 mg	6	3	1	
41	M	39	Epi Temp Sint	PC+SG	CBZ-LTG-PER	800 mg				4	4	4	
42	F	43	Epi Temp Cript	PC+SG	VPA-LEV-OXC	800 mg				5	0	0	
36	M	29	Epi Temp Sint	PC	CBZ-PB	800 mg	800 mg			4	3		
37	M	44	Epi Temp Sint	PC+SG	LTG-CBZ	1200 mg	1200 mg			3	3		
38	F	62	Epi Temp Sint	PC	LTG-ZNS	800 mg	800 mg			4	4		
39	M	45	Epi Temp Sint	PC+SG	TPM-VPA-CBZ	800 mg	800 mg			3	3		
40	M	23	Epi Temp Cript	PC+SG	LEV	800 mg	1200 mg			5	5		
43	M	69	Epi Temp Sint	PC	LTG-CBZ	800 mg				4			
44	F	75	Epi Temp Sint	PC+SG	LEV-OXC	800 mg				4			
45	F	73	Epi Temp Cript	PC	PB-LEV	400 mg				7			
46	M	70	Epi Temp Sint	PS	VPA-PB	800 mg				2			

Pts with follow up at T12
Pts with follow up at T6
Drop out at T6
Pts undergone to Neurosurgery
Drop out at T3
Drop out at 2 weeks

Discussion and conclusions: At 12 months 28% of the patients was seizure free and 11% was responders. The cognitive performances, alertness and mood were improved. Retention rate was 70%. Conclusion: These data, taking into account the limited sample of patients still included in the study,
confirm the efficacy and tollerability of ESL as add-on therapy in drug-resistant focal epilepsy . The preliminary EEG results are in correlation with the low profile of ESL neurotoxicity.

References

(1)Villanueva V et al. Long-term safety and efficacy of eslicarbazepine acetate in patients with focal seizures: results of the 1-year ESLIBASE retrospective study. Epil Res, 2014.
(2) Rocamora R. A review of the efficacy and safety of eslicarbazepine acetate in the management of partial-onset seizures. Ther Adv Neurol Disord, 2015.

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