Brand-to-Generic Levetiracetam Switching: a four-years prospective observational real-life study

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Purpose. The purpose of this study was to determine whether the switching from branded levetiracetam (LEV; ®Keppra) to a LEV generic equivalent product (®Matever) in an epilepsy cohort could result adequate in terms of seizures control and tolerability

Methods. To be eligible for the study, patients were taking ®Keppra as monotherapy or polytherapy for at least six months. Since March 2013 to April 2017, patients were proposed to switch to ®Matever as part of their follow-up. We evaluated number of seizures per month, drug-related adverse events, and electroencephalogram (EEG) before the switching (T0–baseline) and after six months from switching (T1). Furthermore, we reported the long-term follow-up of patients kept using ®Matever after the end of the study, considering the more recent visit for each patient (T2).

Results. 180 patients were recruited but 55 refused the switch. Among the remaining 125 patients, 59 (47%) were treated using ®Keppra as monotherapy and 66 (53%) were on ®Keppra as polytherapy. All 125 patients were subjected to switching from ®Keppra to ®Matever. Comparing patients before (T0) and after (T1) switching, we found no statistically significant differences in terms of seizures frequency (seizures/month, mean±SD, T0: 2.4±9.1; T1: 2.3±9.3) and occurrence of adverse effects. Patients treated with ®Matever in monotherapy compared to patients who refused the switch and kept using ®Keppra as monotherapy for a long-term follow-up to 48 months didn't show significant differences in term of number of seizures per month and drug-related adverse events. EEG findings were also unchanged.

Table 1. Clinical characteristics and EEG data of 125 epilepsy patients pre- (T0) and post- (T1) ®Keppra to ®Matever switching

	All patients (125 pts)		LEV in monotherapy (59 pts)		LEV in polytherapy (66 pts)	
	T0	T1	T0	T1	T0	T1
Seizures/m (n), mean±SD (P-value T0 to T1)	2.4±9.1 (0.599)	2.3±9.3	0.7±10.6 (0.317)	0.7±10.8	3.9±9.9 (0.655)	3.8±10
Seizures/m (n), median [range]	0 [0-90]	0 [0-90]	0 [0-16]	0 [0-16]	0 [0-90]	0 [0-90]
Seizure-free patients, n (%)	80 (64%)	80 (64%)	51 (41%)	51 (41%)	29 (23%)	29 (23%)
Adverse effects, n (%)	n/a	n/a	15 (25)	14 (24)	n/a	n/a
Interictal EEG findings						
Normal, n (%)	12 (10)	12 (10)	5 (8)	5 (8)	7 (10)	7 (10)
Unilateral left, n (%)	26 (20)	26 (20)	9 (15)	10 (17)	17 (25)	16 (24)
Unilateral right, n (%)	22 (18)	22 (18)	11 (18)	9 (15)	11 (16)	13 (19)
Bilateral, n (%)	65 (52)	65 (52)	34 (57)	35 (59)	31 (49)	30 (45)

m, month; **n**, number; **n/a**, not applicable; **pts**, patients**; SD**, standard deviation.

Table 2. Clinical characteristics of patients treated with ®Keppra in monotherapy who refused brand-to-generic switching compared to patients switched to ®Matever in monotherapy up to 48 months follow-up.

	®Keppra monotherapy (40 patients)	®Matever monotherapy (59 patients)
Sex, M/F	16/24	25/34
Age (y), mean ± SD	42.1±16.1	40.2±18.1
Age at onset (y), mean ± SD	21.2±17.9	22.2±17.9
Duration (y), mean ± SD	17.8±19.1	17.8±19.1
Family history of FC/epilepsy, n	19	28
Seizure type (F/G)	25/15	37/22
LEV dosage (mg), mean ± SD	1523.7±603.6	1576.3±798.5
Seizures/month (n), mean ± SD	0.7±7.9	0.7±8.8
Adverse effect LEV related, n (%)	2 (5)	4 (6)
Follow-up (m), mean ± SD	24.2±13.5	25.1±12.9

P-value > 0.05 for all means compared. **F**, focal; **FC**, febrile convulsion; **G**, generalised; **M**, months; **MG**, milligrams; **N**, number; **Pts**, patients; **SD**; standard deviation; **Y**, years.

Conclusion. In our sample, brand-to-generic LEV switching was effective and safe in both mono- and polytherapy regardless epilepsy syndromes.

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