EPILEPSY

A new add-on therapy for epilepsy

An ongoing need exists for new antiepileptic therapies to be brought to the clinic, especially as approximately one-third of individuals are insensitive to currently available medications, leaving their epilepsy uncontrolled. In a phase III clinical trial, eslicarbazepine acetate (ESL) was assessed as an adjunctive therapy in the presence of between one and two other antiepileptic agents. ESL reduced the frequency of refractory partial-onset seizures in adults, with an efficacy comparable to other antiepileptic drugs and favorable tolerability, according to lead investigator Patrício Soares-da-Silva, from the University of Porto, Portugal.

The trial was conducted in two parts. To confirm that there were no differences in seizure frequency under the patients' various existing antiepileptic therapy regimens, all participants in the trial received placebo for an initial 8-week period. Subsequently, the 402 patients were randomly allocated to groups receiving ESL (at doses of 400 mg, 800 mg or 1,200 mg) or placebo, once a day. Participants receiving 800 mg or 1,200 mg ESL had a reduced standardized seizure frequency (least squares mean values 5.66 and 5.35, respectively) compared with those receiving placebo (least squares mean value 7.64) over the 12-week maintenance period. In that time frame, the proportion of responders (i.e. those exhibiting a 50% or greater reduction in the standardized seizure frequency) in the intention-to-treat population increased following treatment with ESL at doses of 800 mg (34% increase in responders) and 1,200 mg (43%), compared with placebo (20%). The frequency of adverse events also rose with increasing doses of ESL, although such events were mild to moderate in nature; dizziness, headache, diplopia, somnolence and vertigo were the most commonly reported adverse effects.

ESL is extensively metabolized to esilcarbazepine and belongs to the same family of compounds as the antiepileptic agent carbamazepine. Collectively, these drugs are believed to mediate their effects through the blockade of voltage-gated sodium channels. "The proven efficacy [of ESL] in patients refractory to carbamazepine, justifies further investigation into the mechanism of action of both drugs," observes Soares-da-Silva.

The combined results from this and other phase III clinical trials led the European Medicines Agency to deliver a 'positive opinion' on ESL in February 2009. "It means that commercialization of ESL in Europe will start soon," explains Soares-da-Silva.

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Original article Elger, C. *et al.* Efficacy and safety of eslicarbazepine acetate as adjunctive treatment in adults with refractory partial-onset seizures: a randomized, double-blind, placebo-controlled, parallel-group phase III study. *Epilepsia* **50**, 454–463 (2009).

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