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Lamotrigine therapy in patients requiring a change in antiepileptic drug regimen☆

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Quality of life

Summary

Introduction: The tolerability of lamotrigine as adjunctive and monotherapy in patients requiring a change in antiepileptic drug (AED) therapy was assessed in this multicenter, open-label study. Open-label studies conducted in the clinic setting may provide additional drug tolerability and effectiveness information that may not be evident in pre-approval clinical trials.
Methods: Adult patients with partial seizures received adjunctive lamotrigine for 16 weeks. Patients taking a single enzyme-inducing AED could convert to lamotrigine monotherapy for an additional 12 weeks. Patients were assessed at baseline, end of adjunctive therapy, and end of monotherapy using the Liverpool Adverse Experience Profile (AEP), Quality of Life in Epilepsy-31, a patient satisfaction rating, and a subjective investigator global assessment.
Results: Of the 547 patients enrolled (mean age 42.7 years, 58% female), 421 (77%) completed adjunctive therapy. Upon completion of the adjunctive phase, mean improvement from baseline was 4.3 points on the AEP, and investigators rated 71% of patients as improved in global status. Overall score on the QOLIE 31 improved by 10 points from baseline. One hundred and seventy-eight patients entered and 143 (80%) patients completed the monotherapy phase. In patients completing lamotrigine monotherapy, mean improvement from baseline was 5.9 points on the AEP, and investigators rated 92% as improved in global status. Overall score on the QOLIE 31 score improved by 15 points from baseline.

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Conclusion: Lamotrigine as adjunctive treatment and monotherapy may improve side effect burden and quality of life in patients requiring a change in AED therapy.

Introduction

This study was a large, multicenter, open-label investigation of adults with partial seizures who required a change in their current AED regimen because of inadequate seizure control, unacceptable side effects, or both. Open-label studies conducted in the clinic setting may provide additional drug tolerability and effectiveness information that may not be evident in pre-approval clinical trials. Because of restrictive inclusion and exclusion criteria, treatment groups in clinical trials for regulatory approval may not be representative of the population treated once a drug comes into general use. These trials, for various reasons, often do not accurately reflect the effectiveness of AEDs when used in the clinic setting. Despite their shortcomings, the value of large, open-label clinical studies includes an opportunity to document aspects of clinical response, including quality of life and safety issues that may be evident in the more routine use of the AED yet not apparent in more rigorous registration-based trials. Results from similarly designed studies with gabapentin and levetiracetam have been recently published.[1,2]

Lamotrigine [Lamictal®; 6-(2,3—dichlorophenyl)—1,2,4 triazine—3,5 diamine] is chemically unrelated to other currently marketed AEDs. The anticonvulsant effects of lamotrigine may result from its ability to block presynaptic voltage sensitive sodium channels, thereby stabilizing neuronal membranes and inhibiting the release of excitatory amino acid neurotransmitters (e.g. glutamate and aspartate) that play a role in the generation and spread of epileptic seizures.[3] An additional recently described mechanism involves regulation of the inward hyperpolarization current (Ih).[4,5] Eleven double-blind, placebo-controlled studies have demonstrated that lamotrigine is effective and well-tolerated when added to current antiepileptic therapy.[6] Lamotrigine has been shown to be safe and effective in double-blind trials for conversion to monotherapy[7] and for initial monotherapy.[8,9] However, the benefits of converting to lamotrigine monotherapy in terms of side effect reduction and quality of life improvement in a general clinical practice setting have not been reported.

Methods

Investigator selection

Investigators were predominantly community neurologists with active epilepsy practices in the United States.

Patient selection

Patients aged 16 years and above were considered for entry into the study if they had a confident diagnosis of epilepsy with partial seizures (simple or complex, with or without secondary generalization) and were taking one or two AEDs of any type. These patients required a change in therapy because of inadequate seizure control, unacceptable side effects, or both. Patients were required to be capable of completing seizure diaries and self-rated questionnaires.

Patients were not eligible to participate in the study if they had received lamotrigine within 30 days prior to enrollment; had a history of known or suspected hypersensitivity to lamotrigine or a history of nonepileptic seizures; were currently undergoing vagal nerve stimulation or planning surgery to control seizures during the study; were currently participating in another clinical trial or planning to enroll in another trial while participating in this trial; were pregnant or lactating; had a presence of severe hepatic or renal insufficiency, severe hematologic disease, or a clinically significant comorbidity of an unstable or progressive nature that could interfere with the objectives of this study. The study was approved by an Institutional Review Board at each investigational site, and written, informed consent was obtained from each patient.

Study objectives and endpoint measures

The primary objective of the study was to evaluate the tolerability of lamotrigine when added to current AED regimen and as conversion to monotherapy. Tolerability was assessed by the change in frequency and severity of adverse events measured by the Liverpool Adverse Experience Profile (AEP).[10] Patients rated each of the 19 items on a 4-point scale: 1 (never a problem), 2 (rarely a problem), 3