Seizure (2004) **13S**, S71–S72

SEIZURE

www.elsevier.com/locate/yseiz

Commentary on Faught and Brodie

Jacqueline A. French*

University of Pennsylvania, The Neurology Institute, Hospital of the University, 3400 Spruce Street, Philadelphia, PA 19104, USA

Commentary on articles by Drs. Faught and Brodie

When a new antiepilepsy agent is being evaluated it is critical, but not always feasible, to have access to two different kinds of information. The first is efficacy data from rigorous, prospective, randomized double-blind trials. The second is information on the drug's ''effectiveness'' in a large population of patients, with a broad spectrum of seizure types, who are treated in a more ''real world'' situation. With zonisamide, we are fortunate to have an abundance of both kinds of information.

The data from the controlled clinical trials reported by Drs. Faught and Brodie complement those from pre- and postmarketing studies conducted in Japan. On the one hand, clinicians can be confident that zonisamide is safe and works well in refractory partial seizures, as demonstrated in US and European pivotal trials, and that its efficacy appears be similar to, if not better than, other new antiepilepsy drugs (AEDs), such as gabapentin, lamotrigine, tiagabine, and topiramate, which have been evaluated in the same way. Nevertheless clinicians may not be sure exactly where zonisamide fits into their clinical practice because it has been tested in the type of patients dissimilar to the patients they see every day. With access to data on the use of zonisamide over a 10-year-period in Japan, clinicians in the United States and Europe will have a head start on integrating this agent into their AED armamentarium.

It is important to note that the US and European trials studied the use of zonisamide as adjunctive therapy. Japanese experience suggests that this agent may, in fact, be better tolerated and more effective as monotherapy. Thus, the favorable safety and efficacy profile of zonisamide seen in the adjunctive, randomized trials may actually not reflect the maximum potential of this agent.

In the European trial, there were few patients with secondary generalization of seizures and in the US trials the results were not analyzed by seizure type. The Japanese experience indicates that zonisamide is effective for secondary generalization, thus, it would be instructive to have an analysis of the randomized data according to seizure type to confirm this finding.

The US data demonstrate, in a very elegant fashion, the significant reduction in adverse events when the dose of zonisamide is titrated slowly. For example, slower titration reduced the incidence of difficulty in concentrating from 15 to 3% and that of somnolence from 39 to 15%. Rarely do clinicians have the opportunity to see this kind of compelling data on dose titration, although with a number of drugs in clinical practice, it appears advisable to stick to the maxim of ''start low, go slow.'' These data confirm that zonisamide is no exception.

With the Japanese, US, and European data, we have a large database of safety information, which provides valuable insights into the incidence of

*Tel.: +1 215 349 5166; fax: +1 215 349 5733.
E-mail address: frenchj@mail.med.upenn.edu (J.A. French).

1059-1311/$30 – see front matter
doi:10.1016/j.seizure.2004.04.011

various adverse events not only in clinical trials, but also in real world practice. Nevertheless, clinicians must remain continually vigilant—a low incidence or absence of a particular adverse event in the context of a clinical trial or in the somewhat different Japanese population should not make us complacent.

In summary, although ideally, we still need to reconfirm through randomized trials the role of zonisamide in monotherapy and different seizure types, the pivotal trial results and Japanese experience provide an excellent foundation on which clinicians in the United States and Europe can build their knowledge of this drug.