Antiepileptic Shows Efficacy in Refractory Disease

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**PHILADELPHIA** — Carbamazepine, a new antiepileptic drug, showed greater efficacy than placebo, was notable because the study involved very refractory patients.

Based in part on these results, carba-

mazepine will be assessed in a phase III study for preventing seizures in patients with epilepsy. The study is also under way to assess the additional phase III studies in patients with diabetic peripheral neuropathy, essential tremor, and postherpetic neuralgia.

The phase II seizure study enrolled pa-

tients aged 8-70 years who had been diag-

osed with epilepsy for at least 1 year, had an established pattern of at least three par-

tial onset seizures per month, and had failed treatment with at least three antiepileptic drugs.

The patients who actually entered the study had a history of epilepsy for an average of 19-25 years and experienced an average of 9-11 seizures per month. About 15% were treated with antiepileptic monotherapy, about 50% were on two drugs, and about 35% were on three drugs. Nearly half had been treated with seven or more different antiepileptics during their lifetime.

About 100 patients were randomized to receive each of four carbanazepine regimens or placebo, with a total enrollment of 337 patients. Treatment intensities were 200, 300, 400, and 800 mg/day.

Following a baseline observation phase of 4 weeks, patients underwent a dose-es-

calation phase of 4 weeks until they reached their target dosage. They re-

mained on a stable dosage for 12 weeks, af-

ter which their response rate was assessed.

The three highest carbanazepine dosages all led to significant reductions in seizure frequency, compared with placebo. The re-

ductions in these groups were 21-29%, compared with a 6% drop in seizure fre-

quency in the placebo group. "The data, I believe, are compelling," said Dr. Faught, director of the epilepsy center at the University of Alabama, Birmingham.

Patients in the 100- and 200-mg/day groups had a 14-15% cut in their seizure fre-

quency, but this was not significantly differ-

ent from the placebo group.

The percentage of responding patients (those with at least a 90% decrease in their seizure rate) was 24% in the 300-

mg/day and 25% in the 1600-

mg/day groups. Both rates of lessening seizure frequency were significantly high-

er than the 12% rate seen in the placebo pa-

tients. The prevalence of responders was 12% in the 100- and 150-mg/day groups and 19% in the 800-mg/day group; neither of these rates was significantly higher than that of placebo.

The incidence of adverse events was similar to placebo in the three lowest carbas-

amate dosage groups. Patients on the 1000- and 1600-mg/day doses had more adverse events, compared with placebo patients. The most frequent adverse events were headache, somnolence, nasopharyngitis, and nausea.

Based on the safety and efficacy results a 300-mgdose of carbanazepine ap-

pears to be optimal, concluded the inves-

tigators. The study was sponsored by Johnson & Johnson, which is developing the drug. Dr. Faught has received research support and honoraria from Johnson & Johnson for consulting and speaking.

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**Patients With Epilepsy Who Had At Least a 50% Reduction In Seizure Rate**

![Carbamazepine dosage](https://example.com/carbazepine-dosage.png)

**Note:** Based on a 20-week randomized study of 537 to 70-year-olds.

**Source:** Dr. Faught

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**300 mg/day**

**800 mg/day**

**1600 mg/day**

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**Carbamazepine dosage**