

# Alzheimer's Trial Dims Outlook for Dimebon

BY JEFF EVANS

The investigational drug dimebon failed to show any benefit over placebo for patients with mild to moderate Alzheimer's disease on any of the efficacy end points in a 6-month, phase III trial, drug manufacturers Medivation Inc. and Pfizer Inc. announced.

Although the tolerability of the drug was confirmed in the efficacy study, called CONNECTION, and in a separate phase III safety and tolerability study, the results put the future of the drug in doubt.

Dr. Marwan N. Sabbagh said that he and other Alzheimer's disease (AD) investigators "were extremely disappointed with the results, and frankly, surprised."

The disappointing efficacy results in the CONNECTION trial came as a surprise because dimebon showed strong signs of efficacy in an earlier phase II trial



**Alzheimer's researchers 'were extremely disappointed with the results, and frankly, surprised.'**

DR. SABBAGH

of 183 patients in Russia (Lancet 2008; 372:207-15).

Four other phase III trials of dimebon (proposed generic name latrepirdine) are currently enrolling patients. In a 12-month trial called CONCERT, the drug is being tested in combination with donepezil (Aricept) in patients with mild to moderate AD.

Two other trials – CONTACT and CONSTELLATION – are testing dimebon in combination with donepezil or memantine (Namenda), respectively, for moderate to severe AD.

The fourth study, the HORIZON trial, is enrolling patients with Huntington's disease after dimebon was well tolerated and showed some signs of improving cognition in a phase II trial.

The remaining trials in AD patients will help to determine whether dimebon has a synergistic effect with donepezil or memantine, Dr. Sabbagh said. "If it doesn't show any shred of evidence in those two studies, I think the future of dimebon is seriously in doubt, unless it shows a benefit for Huntington's."

Dr. Sabbagh is the medical and scientific director of the Cleo Roberts Center of Clinical Research at the Banner Sun Health Research Institute, Sun City, Ariz. His center was involved in a phase I study of dimebon and is participating in the CONCERT trial. He said that he has no other relevant disclosures.

Investigators believed that dimebon blocked the induction of the mitochondrial membrane permeability transition pore, which when open may lead to a loss of energy production and intake of small molecules that contribute to cell death (Ann. N.Y. Acad. Sci. 2003;993:334-44).

Other studies have shown it increases neurite outgrowth and can raise amyloid-beta levels in interstitial brain fluid of transgenic mouse models of AD ("Dimebon's Effect May Challenge Amyloid Theory," September/October 2009, p. 11).

The rise and apparent fall of dimebon in the clinical drug development process mirrors the recent history of tramiprosate and tarenflurbil for AD, both of which had positive results in phase II trials that

were not replicated in phase III trials.

It could be near the end of 2011 before another drug for AD comes through the Food and Drug Administration's review process for potential approval. The candidates that will probably be reviewed first are semagacestat, a gamma-secretase inhibitor, and bapineuzumab, a monoclonal antibody against amyloid-beta, Dr. Sabbagh said.

The CONNECTION study enrolled

598 patients with mild to moderate AD at 63 sites in North America, Europe, and South America. Patients were randomized to dimebon 20 mg, dimebon 5 mg, or placebo three times daily for 6 months. ■

Jessica Merrill of "The Pink Sheet" contributed to this report. CLINICAL PSYCHIATRY NEWS and "The Pink Sheet" are published by Elsevier.

**PSYCHIATRISTS,  
YOUR PROFESSIONAL LIABILITY INSURER  
MAY NO LONGER BE SAFE OR SOUND.**

**MAKE SURE YOUR PROFESSIONAL  
LIABILITY INSURANCE  
IS PROVIDED BY A COMPANY  
WITH AN "EXCELLENT" RATING.  
AND DON'T SETTLE FOR  
ANYTHING LESS.**

**YOUR FUTURE COULD  
DEPEND ON IT!**

## Darwin National Assurance Company



Darwin is rated "Excellent" by A.M. Best Co. and anticipates a further upgrade in its rating very soon not a downgrade.

## Discounts

- 50% for Part-time
- 10% Claims free
- 50% as a New Graduate
- 5% Risk Management and a discounted course available on our website

(Please call 1-800-421-6694 for complete details on these discounts.)

Endorsed By:

**AMERICAN ACADEMY OF  
CHILD & ADOLESCENT  
PSYCHIATRY**



POLICY ADMINISTRATOR

95 Broadway, Amityville, NY 11701

**1-800-421-6694**

**www.americanprofessional.com**