

Eptastigmine

A Viewpoint by Massimo Franceschi

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The scientific effort called Decade of the Brain has led to significant progress in our understanding of the pathogenesis of Alzheimer's disease and has given us a number of insights into possible therapeutic and prophylactic approaches.

However, clinicians are still disappointed that the therapeutic tools are limited to cholinesterase (ChE) inhibitors, the use of which is based on evidence of a cholinergic deficit in cerebral cortex.

The ChE inhibitor eptastigmine has so far been studied in 14 phase I, 3 phase II and 3 phase III clinical trials for an overall exposure of 1402 patient-years.

In the first double-blind placebo-controlled clinical trial of eptastigmine, which involved 320 patients with Alzheimer's disease treated for 25

weeks (214 of whom received eptastigmine 10 or 15mg 3 times daily), the drug significantly decreased the rate of cognitive decline as measured by ADAS-Cog, CIBIC-Plus and ADL scores.

Cholinergic adverse effects are rare and mild. Slight neutropenia (neutrophil count 1000 to 1500/ μ l) has been observed in 4% of patients treated with eptastigmine compared with 1.6% of patients who received placebo. Significant neutropenia (<1000/ μ l) has been found only in 2 patients, 1 of whom was given eptastigmine at higher than recommended doses. These effects generally revert spontaneously or after dosage reduction.

The results of a further 2 phase III double-blind placebo-controlled clinical trials involving a total of 841 patients with Alzheimer's disease are expected to confirm the tolerability profile of eptastigmine, offering a slight but significant change in the dramatic natural history of Alzheimer's disease. ▲