LONG-TERM TACRINE TREATMENT: EFFECT ON NURSING HOME PLACEMENT AND MORTALITY

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INTRODUCTION

The most important question arising from controlled studies of tacrine was whether the acute, symptomatic effects of tacrine treatment observed over 30 weeks (Knapp et al., 1994) translated into effects on long-term outcomes of the natural history of Alzheimer's disease (AD) such as nursing home placement and mortality. Figure 1 shows a schematic representation of the natural history of AD. MMSE score is used as a surrogate of disease severity, and disease milestones are indicated.

Almost 75% of patients in the United States will eventually enter a nursing home with an average stay of more than 3 years (Welch et al., 1992). Although nursing home placement may be a somewhat imprecise endpoint, it is a major decision point for the family. Duration of illness, declining cognitive function, lost activities of daily living, and severity of behavioral symptoms are important risk factors for nursing home placement and are good indicators for the severity of illness and, therefore, caregiver burden.
Patients who completed the 30-week double-blind study and those who terminated early were eligible to receive long-term, open-label tacrine treatment at the discretion of the study physician in consultation with the family.

Approximately 2 years after the last patient completed the double-blind phase, the protocol was amended to allow collection of follow-up information on nursing home placement and mortality. Attempts were made, through the study centers, to contact the families of all 663 patients who originally entered the study. Data were collected to determine whether patients continued to take tacrine; at what daily dose; and whether they were living at home, in a nursing home, or had died (Knopman et al., 1996).

RESULTS

Follow-up data on nursing home placement were available for 595 (90%) of the 663 patients randomized to treatment in the 30-week study. Mortality data were available for all 663 patients who entered the study, 81 of whom had died.

Data were analyzed by logistic regression. Nursing home placement and mortality were analyzed first at the end of double-blind treatment (Week 30). Follow-up data were then analyzed based on patients' treatment status: all patients by last tacrine dose taken regardless of time off drug prior to follow-up ("all patients"); and patients who were on tacrine at follow-up or who had been off drug for 60 days or less prior to an event, by last dose taken ("on tacrine").