EFFICACY OF MEMANTINE IN MODERATE TO SEVERE ALZHEIMER’S DISEASE: TIME-TO-EVENT ANALYSIS IN A POOLED POPULATION

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Introduction: Several randomized, placebo-controlled trials have demonstrated significant benefits of memantine vs. placebo in patients with moderate to severe Alzheimer's disease (AD). Data from those trials have not yet been analyzed in terms of time needed to reach a particular clinical event.

Aims: To compare memantine- and placebo-treated patients from pooled trials in moderate to severe AD using Kaplan-Meier (K-M) analyses.

Methods: Three randomized, double-blind, placebo-controlled trials of memantine (10 mg BID) in moderate to severe AD were pooled; efficacy outcomes included measures of cognition (SIB), function (ADCS-ADL₁₉), behavior (NPI), and global status (CIBIC-Plus). For each measure, a meaningful event was defined as the smallest baseline-to-endpoint decline experienced by at least 50% of placebo-treated patients; the K-M method was used to compare time estimates to reach this point in the two treatment groups and an unadjusted log-rank test was performed on the intent-to-treat population using observed cases.

Results: Meaningful events were determined by declines of 5 points on the SIB, 4 points on the ADCS-ADL₁₉, 3 points on the NPI, and a final score ≥5 for the CIBIC-Plus. Significant time-to-event differences in favor of memantine were observed for the SIB (placebo, median time-to-event: 166 days; memantine: >197 days; P< 0.001 overall), ADCS-ADL₁₉ (placebo: 171 days; memantine: >197 days; P=0.010), and NPI (placebo: 166 days; memantine: >197 days; P=0.004), but not for the CIBIC-Plus (P=0.537).

Conclusions: Time-to-event analyses support the view that memantine is efficacious in delaying cognitive, functional, and behavioral declines in patients with moderate to severe AD.