EFFECTS OF MEMANTINE IN PATIENTS WITH MODERATE TO SEVERE ALZHEIMER’S DISEASE RECEIVING STABLE DOSES OF DONEPEZIL: A META-ANALYSIS

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Introduction: Memantine, an uncompetitive NMDA antagonist, is approved in the US and Europe for the treatment of moderate to severe Alzheimer’s disease (AD). This post hoc meta-analysis assessed the efficacy of memantine + donepezil combination therapy using data from two previously published 24-week, double-blind, placebo-controlled trials: Tariot et al., 2004 (MEM-MD-02), and Porsteinsson et al., 2008 (MEM-MD-12).

Aims: To compare the efficacy of memantine (20 mg/day) vs placebo across multiple domains in patients with moderate to severe AD receiving stable doses of donepezil.

Methods: A meta-analysis was performed on the population of patients with MMSE < 20 that were receiving treatment with donepezil. Efficacy was assessed using measures of cognition (Severe Impairment Battery; SIB, or AD Assessment Scale Cognitive subscale; ADAS-Cog), behaviour (Neuropsychiatric Inventory; NPI), function (AD Cooperative Study - Activities of Daily Living 19- or 23-item scale; ADCS-ADL 19/23), and global status (Clinician’s Interview-Based Impression of Change Plus Caregiver Input; CIBIC-Plus). For each measure, treatment groups were compared in terms of standardised mean difference (SMD) from baseline at Week 24 (LOCF).

Results: At Week 24, patients receiving memantine significantly outperformed those receiving placebo on all measures (SIB/ADAS-Cog: SMD=0.35 [95% CI: 0.19, 0.51; p< 0.0001], NPI: SMD=-0.20 [95% CI: -0.37, -0.04; p=0.02], ADCS-ADL 19/23: SMD=0.21 [95% CI: 0.05, 0.37; p=0.010], CIBIC-Plus: SMD=-0.23 [95% CI: -0.39, -0.06; p=0.006]).

Conclusions: Combination treatment of memantine (20 mg/day) and donepezil in patients with moderate to severe AD was associated with significant benefits in cognitive, behavioural, functional and global measures, in comparison to treatment with donepezil alone.