EFFICACY AND SAFETY OF ACETYLCHOLINESTERASE INHIBITORS (ACHIS) AND MEMANTINE: RESULTS OF A RECENT SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Many placebo-controlled trials have been completed, pre- and post-licensing, to investigate the use of three ACHIs (donepezil, rivastigmine and galantamine) and memantine in AD patients.

Aims: A systematic review was conducted to establish the up-to-date evidence base, and meta-analysis conducted to identify the efficacy and safety of these drugs compared to placebo treatment.

Methods: Literature databases and conference proceedings were screened to identify all randomised controlled trials including these drugs which reported efficacy and/or safety outcomes. Only trials within the European licensing limits with regard to dose and AD severity were included. Quality was assessed using CONSORT. Available data was combined in meta-analysis.

Results: 45 studies were identified which compared ACHIs with placebo, while 4 compared memantine. All ACHIs showed significant advantage over placebo in cognitive outcomes (combining ADAS-cog, MMSE and SIB scores) at 3 and 6 month timepoints (p< 0.05); the pooled results of two studies did not show significant advantage for memantine. Advantage for galantamine in behaviour (NPI scale) was observed (pooling 2 studies, p< 0.001): single studies for other interventions did not reach significance. A small increase in frequency of any adverse event is observed for ACHIs (relative risk around 1.1) but not for memantine. Weight loss, gastrointestinal events and treatment discontinuation due to adverse events were significantly more frequent for oral ACHIs.

Conclusions: The benefits of ACHIs on cognition in mild/moderate patients are well-established in RCTs for ACHEI. Memantine did not show cognitive improvement based on results of pooled studies.