A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD
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Study Type: POE
Purpose: To evaluate the safety and efficacy of donepezil in patients with mild to moderate AD over 1 year.
Study Duration: 1 year trial
Trial Design: randomized, double-blinded, placebo-controlled, intention-to-treat, multicenter (28 sites), in 5 countries (Denmark, Finland, Norway, Sweden, Netherlands) placebo vs 5 mg for 28 days, then 10 mg donepezil (at physician’s judgement)
Patients: 286 patients, mean age ~73, ~70:30 female: male, 100% white, MMSE = ~19, baseline scores (GBS = 29.5; GBS-I = 18.2; PDS = 52.7; GDS = 4.15; NPI = ~13 - see below)
Inclusion: uncomplicated AD consistent with DSM-IV, MMSE score of 10-26, age 40 to 90, patients had to be otherwise health, able to walk, see and hear, reliable caregiver
Exclusion: insulin dependent DM, any endocrine disorder, asthma, COPD, clinical GI disease, hepatic or CV disease, other psychiatric dz, cancer, anemia of any type, No tricyclics, other anticholinergics
SSRI’s, neuroleptics, short-acting benzos were allowed in stable doses
Outcome Scores:
Primary Scale - GBS scale (GBS-I - orientation, memory, concentration); GBS-ADL (self-care, ADL’s); GBS-E (emotional); GBS-S (behavior)
Secondary Scale - MMSE; PDS (Progressive Deterioration Scale); NPI (Neuropsychiatric Inventory); GDS (Global Deterioration Scale)

1. Are the results valid?
* randomized? yes
* double-blinded? yes
* were groups similar? yes
* all patients accounted for? yes

2. What were the results: n = 142 (Donepezil grp); n = 144 (Placebo grp)
Primary Scale
GBS - the decline in the donepezil group was approximately 50% of the placebo group, p < .05
GBS-I seemed to be the scale with the best effect (p < .05)
GBS-ADL, GBS-E, GBS-S - no statistical difference

Secondary Scale
* MMSE - less deterioration in the donepezil grp (p < .05), by 2.2 points (2 to 4 point decline in non-treated patients)
* Less deterioration in the ADL as measured by the PDS in the donepezil grp for the following domains - memory, telephone, self-care (p < .05)
* GDS - twice as many in the donepezil group improved from baseline (p < .05)
* NPI - numbers reflect a relatively unimpaired patient with respect to behavioral abnormalities (p = NS)

Adverse Event | Donepezil | Placebo | ARI | NNH | p
---------------|-----------|---------|-----|-----|---
vertigo       | 7.7%      | 2.1%    | 5.6%| 18  | ?
asthenia (weakness) | 7.7%    | 3.5%    | 4.2%| 24  | ?
syncope       | 6.3%      | 2.8%    | 3.5%| 29  | ?
serious adverse effect| 24.6%  | 13.9%   | 10.7%| 9   | ?

3. Will the results help me?
* ~92% of patients tolerated the 10 mg dose, ~10% had to decrease back to 5 mg
* ~95% compliance in both groups
* 33.1% withdrew in the donepezil group, 32.6% in the placebo group
* difficult to assess clinical significance