Background: A previous report demonstrated better efficacy of 13.3 mg/24h versus 9.5 mg/24h patch on function and cognition in mild-to-moderate Alzheimer’s disease. Here we describe the efficacy and safety outcomes in declining patients treated with 13.3 mg/24h patch versus 9.5 mg/24h patch and memantine. Methods: In this retrospective analysis, patients declining and entering the double-blind phase, previously treated with 9.5 mg/24h patch during the initial open label phase, were matched 1:1 (memantine users versus non-memantine) by means of propensity scores. The change from baseline in ADCS-IADL scale and ADAS-cog subscale was assessed at Weeks 24 and 48 in patients treated with 13.3 mg/24h alone and those taking 9.5 mg/24h patch and memantine concomitantly (memantine was used at the investigator’s discretion). The use of memantine was not randomized. Data analysis was performed using ANCOVA including factors for treatment, country and baseline score of the respective efficacy parameter. Safety evaluations included incidence of adverse events (AEs) and serious AEs (SAEs). Results: 142 patients were included (71 per group). Gender, race, age, BMI and MMSE were comparable between the two groups. 61.3% patients were female and 87.3% were ≥65 years. Patients treated with 13.3 mg/24h patch showed statistically greater benefit in function (ADCS-IADL) at weeks 24 and 48 versus those receiving concomitantly 9.5 mg/24h patch and memantine (Figure-1A). ADAS-cog outcomes were comparable between the two groups (Figure-1B). The incidence rate of AEs, AEs leading to discontinuation and SAEs were 63.4 vs 54.9%, 2.8 vs 4.2% and 8.5 vs 8.5% in 13.3 mg/24h patch alone versus 9.5 mg/24h patch with concomitant memantine, respectively. Conclusions: Based on patients matched by propensity scores, this analysis found greater IADL benefit in patients up-titrated from 9.5 mg/24h to 13.3 mg/24h as compared to those receiving 9.5 mg/24h patch and concomitant memantine throughout. Although this analysis cannot replace a properly randomized trial, it suggests that a treatment regimen with up-titration from 9.5 mg/24h to 13.3 mg/24h may be more beneficial to AD patients compared to a regimen with combination of rivastigmine 9.5 mg/24h patch and memantine.1 Cummings J. et al. Dement Geriatr Cogn Disord.2012; 33(5):341-53.

Donepezil can improve daily activities and promote rehabilitation for severe Alzheimer’s patients in long-term care health facilities

Kenichi Meguro, Mari Kasai, Kyoko Akanuma, Mitsupe Meguro, Satoshi Yamaguchi, Tohoku University, Sendai, Japan. Contact e-mail: k-megu@umin.ac.jp

Background: Cholinesterase inhibitors have the effect of delaying the progression of Alzheimer’s disease (AD). We previously reported the retrospective analysis of donepezil’s positive effect on lifetime expectancy (AAIC 2013), probably due to stimulating daily activities. Since a therapeutic approach or rehabilitation for severe AD patients is controversial, we performed a prospective intervention for patients in Long-Term Care Health Facilities (LTCF).

Methods: Two LTCFs (N1, N2) were enrolled. N1 is a 150-bed facility with a 50-bed dementia special unit. A physician can prescribe donepezil there, and psychosocial intervention (reality orientation and reminiscence) is performed. N2 is a 126-bed facility without donepezil but psychosocial intervention is performed. Thirty two severe patients (MMSE<10) in N1 and N2 (16 vs 16) were compared for the effect of donepezil (10 mg/d for 3 months) with or without psychosocial intervention (n=8 vs 8 for each facility). The Vitality Index was used for assessing daily activities and the introduction of rehabilitation.

Results: The response ratio (MMSE 3+) of donepezil was 37.5% in N1. A combined donepezil with psychosocial intervention improved the Vitality Index total score, and Communication, Eating, and Rehabilitation subscores (Wilcoxon, p<0.05). Most of them were smoothly introduced for rehabilitation, and the ratio of fall accident decreased. Only psychosocial intervention in N2 improved the total score (Wilcoxon, p<0.05).

Conclusions: A combined therapeutic approach of donepezil and psychosocial intervention can have a positive effect even for severe patients through introduction of rehabilitation and decrease of fall accidents.

Revise the administration of the ADAS-Cog

Kimberly Schafer1, Paul Aisen2, Richard Mohs3, Amy E. Veroff4, Donald Connor5, David Salmon6, David S. Miller7, Mary Sano8, Peter Boehm9, Christopher Weber10, Nicholas Greco, IV11, Satoshi Yamaguchi, Kenichi Meguro, Mari Kasai, Kyoko Akanuma, Mitsue Meguro, Satoshi Yamaguchi, Tohoku University, Sendai, Japan. Contact e-mail: kschafer@ucsd.edu

Background: The ADAS-Cog (Rosen et al., 1984) is widely used as the primary or co-primary outcome measure in clinical trials. The administration manual for the ADAS-cog was first prepared in 1994 by Richard Mohs, revised in 1998, and has been broadly distributed by the Alzheimer’s Disease Cooperative Study (ADCS). The manual needed updating and revision to reduce inconsistent interpretations of administration instructions and scoring. The goal was to revise the US version which could then serve as a primary reference for use in other regions and languages.

Methods: The ADCS formed a working group of 21 people representing 10 academic and industry institutions. Members were selected based on experience administering the ADAS-cog, training raters and analyzing ADAS-cog data. The manual was revised collaboratively in an iterative manner via group emails. The guiding principle for this process was to maximize performance, minimize ambiguity, and facilitate its use by trained research staff. The workflow was from the ADCS out to the group, email dialogue among group members, with the ADCS managing version control. Revisions were sent for further group review, in a “bulls-eye” approach of larger circles of review and discussion leading to a centrally revised manual. Where the larger group did not reach consensus, final decisions were made by a smaller leadership group.

Results: The revised manual significantly improves and clarifies administration and scoring instructions. The most extensive revisions were in the Constructional Praxis section and language items. Examples of revisions will be provided.