Early- versus Late-onset Alzheimer's Disease—3-year Outcomes of Cholinesterase Inhibitor Treatment in Routine Clinical Practice.

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2014

Document Version:
Publisher's PDF, also known as Version of record

Early- versus Late-onset Alzheimer's Disease —

3-year Outcomes of Cholinesterase Inhibitor Treatment in Routine Clinical Practice

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Conclusions

This Alzheimer's disease (AD) study, which was performed in a routine clinical setting, showed that more sensitive cognitive measures, such as ADAS-cog, are required to detect a potentially faster decline among patients with early-onset AD. Despite better functional performance and fewer concomitant medications at the start of ChEI treatment, patients with early-onset AD had a similar rate of deterioration in ADL and need for institutionalization compared with the late-onset group. This emphasizes the clinical importance of functional assessments, even among younger patients. The possibility that younger individuals live longer after a diagnosis of AD raises questions about the need to provide 24 h care adapted specifically to this group.

Background

Alzheimer's disease (AD) is an insidiously progressive neurodegenerative disorder that is characterized by multiple cognitive impairments and gradual loss of independence in carrying out activities of daily living (ADL). Currently, the predominant therapy for mild-to-moderate AD is the administration of cholinesterase inhibitors (ChEIs), which have been shown to have positive effects on symptoms compared with placebo in randomized clinical trials. There is an increased interest in dominantly inherited and early-onset AD, and in new treatments aimed at blocking the course of the disease. Therapies that are expected to modify disease progression should be assessed thoroughly over many years, and advances in the understanding of their expected long-term outcomes in individuals with different ages at AD onset require well-designed observational studies. This study aimed to identify potential differences in clinical characteristics, longitudinal outcomes, and end points in patients with early- vs late-onset AD in routine clinical practice.

Methods

The Swedish Alzheimer Treatment Study (SATS) is a prospective, open, nonrandomized, multicenter study for the assessment of ChEI treatment in a routine clinical setting. In total, 1,258 outpatients with a clinical diagnosis of probable or possible AD were included in the SATS. Of these, 1,021 participants were defined as having mild-to-moderate AD (Mini-Mental State Examination (MMSE) score, 10–26) at the start of ChEI therapy (baseline), and were enrolled in the present study. The age at AD onset was estimated by a clinician who specializes in dementia disorders. The age at onset was younger than 65 years in 143 individuals (14%), and 65 years or older in 874 participants (four missing data). Patients were assessed using cognitive tests (MMSE and Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog)) and functional-capacity scales (Instrumental Activities of Daily Living scale (IADL) and Physical Self-Maintenance Scale (PSMS)) at the baseline, after 2 months (MMSE only), and every 6 months for 3 years. Eventual dates of nursing home placement and death were recorded.

Table 1 lists the results of t tests that were performed to analyze two independent groups (early- and late-onset AD), and those of χ^2 tests that were used to analyze categorical variables. The mean annual cognitive and functional changes depicted in Table 2 and Figure 1 were calculated as the change in score from the baseline to the participant's last assessment, divided by the number of months between these assessments, and multiplied by 12. Kaplan–Meier graphs were used to illustrate the differences in time to nursing home placement and death (Figures 2 and 3). The distribution of time was compared using the log-rank test.

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Poster presented at the 7th Clinical Trials Conference on Alzheimer's Disease, Philadelphia, PA, USA; November 20-22, 2014

Results

Table 1. Baseline characteristics

	Early-onset AD	Late-onset AD	*P* value
Number of patients (*n*)	143	874	
Female gender	57%	65%	0.091
APOE genotype			**<0.001**
two ε4 alleles	29%	13%	
one ε4 allele	46%	54%	
Estimated age at onset, years[a]	58.6 ± 4.7	74.4 ± 4.9	**<0.001**
Age at the start of ChEI treatment, years[a]	62.7 ± 5.4	77.3 ± 4.7	**<0.001**
Duration of AD, years[a]	4.1 ± 3.4	2.9 ± 1.7	**<0.001**
Education, years[a]	10.1 ± 2.8	9.3 ± 2.5	**0.004**
MMSE score (range, 30–0)[a]	21.4 ± 3.8	21.4 ± 3.7	0.987
ADAS-cog score (range, 0–70)[a]	19.5 ± 9.6	21.0 ± 8.8	0.074
IADL score (range 8–31)[a]	13.9 ± 5.3	16.3 ± 5.4	**<0.001**
PSMS score (range 6–30)[a]	6.7 ± 1.2	7.6 ± 2.4	**<0.001**
Number of concomitant medications[a]	1.8 ± 1.7	3.1 ± 2.5	**<0.001**
ChEI dose[b]	66% ± 19%	63% ± 18%	0.052

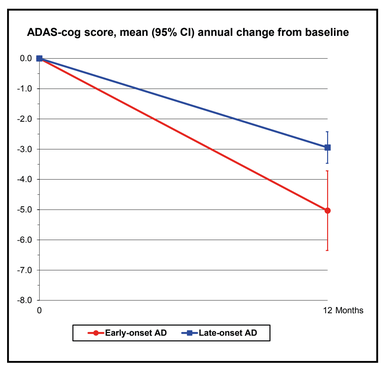
[a]Mean ± standard deviation (SD)
[b]Mean percentage of the maximum recommended dose, i.e., 10 mg for donepezil, 12 mg for rivastigmine, and 24 mg for galantamine.
AD, Alzheimer's disease; ADAS-cog, Alzheimer's Disease Assessment Scale-cognitive subscale; APOE, apolipoprotein E; ChEI, cholinesterase inhibitors; IADL, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; PSMS, Physical Self-Maintenance Scale

Table 2. Mean (95% CI) annual change from the baseline

	Early-onset AD	Late-onset AD	*P* value
MMSE score	–1.1 (–2.7, 0.4)	–1.4 (–1.8, –0.9)	0.691
IADL score	–2.6 (–3.1, –2.1)	–2.7 (–2.9, –2.4)	0.846
PSMS score	–1.2 (–1.5, –0.9)	–1.2 (–1.4, –1.1)	0.580

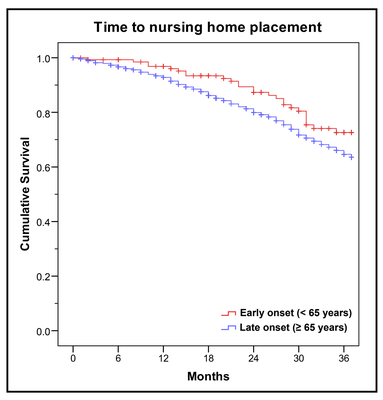
AD, Alzheimer's disease; CI, Confidence interval; IADL, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; PSMS, Physical Self-Maintenance Scale

Figure 1.



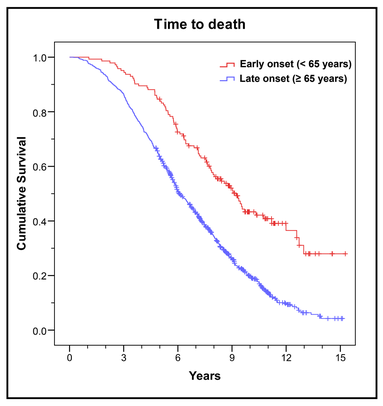
During the study, the mean annual deterioration in ADAS-cog score from the baseline for the early- and late-onset groups was 5.0 points (95% CI, 3.7–6.4 points) vs 2.9 points (95% CI, 2.4–3.5 points; $P = 0.003$).

Figure 2.



Kaplan–Meier graph of the distribution of time from the start of ChEI treatment (approximately the time of AD diagnosis) to nursing home placement for patients with early- and late-onset AD (log rank test, $P = 0.064$). The proportion of individuals who were admitted to nursing homes during the study was 18% of the early-onset and 23% of the late-onset patients ($P = 0.196$). The mean time from the baseline to nursing home placement was 22.3 months (95% CI, 18.7–25.8 months) and 19.3 months (95% CI, 18.0–20.7 months; $P = 0.156$) for the early- and late-onset groups, respectively.

Figure 3.



Kaplan–Meier graph of the distribution of time from the start of ChEI therapy to death for the individuals with early- and late-onset AD (log rank test, $P < 0.001$). After the 3-year study, 6% of the early- and 15% of the late-onset patients had died ($P = 0.002$), and after up to 15 years of follow-up, 57% and 81% ($P < 0.001$) had deceased, respectively. The mean survival time from the baseline was 6.5 years (95% CI, 6.0–7.1 years) and 5.6 years (95% CI, 5.4–5.8 years; $P = 0.005$) for the early- and late-onset groups, respectively.