

Letter to the Editor



Baseline Clinical and Neuropsychological Characteristics of Amyloid PET-Confirmed Alzheimer's Disease Treated With Lecanemab: Early Experience at a Tertiary Hospital in Korea

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Dear Editor,

Amyloid- β plaques are a pathological hallmark of Alzheimer's disease (AD). Following its approval as a disease modifying therapy for AD, lecanemab targeting amyloid- β has recently been introduced into clinical practice in Korea.¹⁻³ As one of the earliest centers to initiate treatment with lecanemab, we describe the baseline characteristics of amyloid- β positive AD patients treated during the first 6 months of clinical use. We further explored whether clinical characteristics differed according to age group and apolipoprotein E (APOE) carrier status.

At the time of lecanemab initiation, patients completed a computerized cognitive test (Seoul Cognitive Status Test, SCST) assessing five cognitive domains (attention, language, visuospatial function, memory, and executive function), along with self-report questionnaires on depression (Geriatric Depression Scale, 30 items), anxiety (Geriatric Anxiety Inventory, 20 items), and personality traits (International Personality Item Pool-50 items based on five factor model: neuroticism, extraversion, openness, agreeableness, conscientiousness). During the initial six months (March to September 2025), 113 patients (37 men and 76 women with mean age of 71.4 [51-90] years) were included in the analysis after completing cognitive assessments and questionnaires.

Patients included individuals with amyloid positron emission tomography-confirmed AD clinical syndrome who visited the clinic, consisting of 32 (28.3%) patients with dementia and 81 (71.7%) with mild cognitive impairment (MCI). Among total 113 patients, 93 patients were rated 0.5 (82.3%) and 20 rated 1 (17.7%) on the Global score of Clinical Dementia Rating (CDR-G), and the mean score on Korean version of Mini-Mental State Examination~2 (K-MMSE~2) was 24.4. The distribution of APOE genotypes was as follows: $\epsilon 2/\epsilon 3$ (n=3), $\epsilon 3/\epsilon 3$ (n=45), $\epsilon 3/\epsilon 4$ (n=49) or $\epsilon 4/\epsilon 4$ (n=15), and $\epsilon 2/\epsilon 4$ (n=1). The mean SCST total z-score was -1.9, with memory the lowest (mean z=-2.6) and attention the highest (mean z=-0.6). In partial correlation analyses adjusted for age, sex, education, and APOE genotype, Clinical Dementia Rating-Sum of Boxes (CDR-SB) score, used as an index of clinical severity, was correlated with scores of K-MMSE~2, Korean version of Instrumental Activity of Daily Living (K-IADL),

Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Kim H, Lee J, Lee BH; Data curation: Kim H, Lee J, Park HK, Lee KB, Kim JP; Formal analysis: Lee BH; Methodology: Lee J, Lee BH; Project administration and supervision: Park HK, Lee KB, Kim JP, Lee BH; Writing - original draft: Kim H, Park HK, Lee BH; Writing - review & editing: Lee J, Park HK, Kim JP, Lee BH.

and SCST cognitive domain z-scores but not with depression or anxiety. Among personality traits, extraversion showed a weak negative correlation with CDR-SB ($r=-0.204, p=0.047$).

Age-stratified 2 groups (<70 and ≥70 years groups) did not differ in CDR-G (<70 years group: 31 [79.5%] for CDR 0.5 and 8 [20.5%] for CDR 1 vs. ≥70 years group: 62 [83.8%] for CDR 0.5 and 12 [16.2%] for CDR 1), CDR-SB, K-MMSE~2, and K-IADL scores (**Table 1**). However, the <70 years group had lower z-scores on SCST (z-scores of total score, attention, visuospatial, and executive function), greater depression and anxiety scores, and higher neuroticism compared with ≥70 years group. The <70 and ≥70 years groups commonly showed correlations between CDR-SB and K-MMSE~2, SCST z-scores, and K-IADL, with no correlations observed for depression or anxiety. Only in the <70 years group, extraversion was negatively correlated with CDR-SB ($r=-0.358, p=0.048$).

APOE ε4 carriers and noncarriers (n=112, excluding one patient with the ε2/ε4 genotype) did not differ in demographics, CDR-SB, K-MMSE~2, K-IADL, depression, anxiety, or personality traits, while carriers scored significantly higher in four cognitive domains (attention, language, visuospatial, and executive function) except memory on SCST.

In conclusion, the majority of patients treated with lecanemab during the initial implementation at our hospital had MCI or early stage of AD and showed a high prevalence of APOE ε4 carrier status. The <70 years group exhibited worse cognitive performance, and higher depression, anxiety, and neuroticism than the ≥70 years group. Regarding the finding of higher psychological distress in the <70 years group, this may be attributed to the challenges of disease acceptance while remaining more socially and functionally active

Table 1. Baseline characteristics according to age group

Baseline characteristics	All (n=113)	<70 yr (n=39)	≥70 yr (n=74)	Statistics
Demographics and clinical measures in total group				
Age	71.40±8.35 (51-90)	62.28±5.89	76.20±4.59	
Education	13.76±4.22 (2-22)	15.54±3.32	12.82±4.36	
Sex (male:female)	37:76	13:26	24:50	
APOE ε4 (noncarrier:carrier)*	48:64	18:20	30:44	
K-MMSE~2	24.36±3.01 (14-30)	24.90±3.58	24.08±2.65	
CDR-SB	2.89±1.46 (0.5-7.0)	2.83±1.43	2.92±1.49	
K-IADL	0.42±0.31 (0.0-1.5)	0.35±0.26	0.46±0.32	
Cognitive tests and psychological features by age group				
Cognitive tests (n=112)				
Total SCST z-score		-2.46±1.57	-1.62±1.01	$t=-2.994, p=0.004$
Attention		-1.25±1.57	-0.29±1.08	$t=-3.400, p=0.001$
Language		-1.25±1.07	-0.93±1.13	NS
Visuospatial function		-1.50±1.31	-0.79±1.02	$t=-2.942, p=0.005$
Memory		-2.68±1.26	-2.63±1.06	NS
Executive function		-1.55±1.51	-0.80±0.90	$t=-2.884, p=0.006$
Psychological factors				
Depression		10.28±7.21	7.67±5.84	$t=2.083, p=0.040$
Anxiety (n=107)		6.97±6.24	3.30±4.41	$t=3.208, p=0.002$
Personality traits (n=104)				
Neuroticism		29.24±8.01	25.48±6.93	$t=2.630, p=0.010$
Extraversion		30.32±7.46	29.46±4.74	NS
Openness		29.76±6.37	28.39±5.53	NS
Agreeableness		33.70±5.53	33.10±4.63	NS
Conscientiousness		35.57±6.65	37.22±6.67	NS

APOE: apolipoprotein E, K-MMSE~2: Korean version of Mini-Mental State Examination~2, CDR-SB: Clinical Dementia Rating-Sum of Boxes, K-IADL: Korean version of Instrumental Activity of Daily Living, SCST: Seoul Cognitive Status Test, NS: not significant.

*After excluding one patient with the ε2/ε4 genotype, 112 patients were included in the APOE ε4 carrier versus noncarrier analysis.

compared to older group. Alternatively, it may imply that psychological symptoms are more likely to be included among the early clinical manifestations of AD within the younger age group than in the older group. APOE ϵ 4 carriers showed higher scores than noncarriers across all cognitive domains except memory in the MCI or early AD stage. These results may reflect the exclusive inclusion of early stage of AD and can be consistent with the antagonistic pleiotropy hypothesis of APOE gene, where the variant selectively impairs memory while preserving other cognitive domains. Further studies are needed to further elucidate these mechanisms.

A more detailed understanding of the baseline characteristics of patients treated with lecanemab may help delineate factors associated with variability in treatment response to anti-amyloid therapy. This study, however, has limitations as a preliminary investigation focused on describing the baseline characteristics of early AD patients who received lecanemab during its early clinical introduction. Future research should include a larger sample size and a comprehensive analysis of the complex relationships among these clinical and psychological factors.

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