

Amyloid-Related Imaging Abnormalities And Associated Factors In Lecanemab-Treated Patients With Alzheimer’s Disease: The JOY-ALZ Study

Monday-1178

Seong Hye Choi,¹ Sung Hoon Kang,² Jee Hyang Jeong,³ Jae-Sung Lim,⁴ Kee Hyung Park,⁵ Geon Ha Kim,⁶ Dong Won Yang,⁷ Seong-Ho Koh,⁸ Hojin Choi,⁸ Hyun Sook Kim,⁹ Yeonsil Moon,¹⁰ So Young Moon,¹¹ Eun-Joo Kim,¹² Jay C. Kwon,¹³ Young-gun Lee,¹⁴ Eun Ah Lee,¹⁵ Young Ho Park,¹⁶ Jung-Min Pyun,¹⁶ Yun Jeong Hong,¹⁷ Eun Ye Lim,¹⁸ Young Hee Jung,¹⁹ YongSoo Shim,²⁰ Seunghee Na,²¹ Hee-Jin Kim,²² Hanna Cho,²³ Hae Ri Na,²⁴ Si Eun Kim,²⁵ Heeyoung Kang,²⁶ Han-Kyeol Kim,²⁷ Yeshin Kim,² Chan-Nyoung Lee,²⁸ Byeong C. Kim,²⁹ Eun Joo Chung,³⁰ Jaeho Kim,³¹ Won-Jin Moon,³² Jae Seung Kim,³³ Danbee Kang,³⁴ Sujung Oh³⁴

¹Department of Neurology, Inha University College of Medicine, Incheon, Korea; ²Department of Neurology, Korea University Guro Hospital, Seoul, Korea; ³Department of Neurology, Ewha Womans University Seoul Hospital, Seoul, Korea; ⁴Department of Neurology, Asan Medical Center, Seoul, Korea; ⁵Department of Neurology, Gachon University Gil Medical Center, Gachon University College of Medicine, Incheon, Korea; ⁶Department of Neurology, Ewha Womans University Mokdong Hospital, Seoul, Korea; ⁷Department of Neurology, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; ⁸Department of Neurology, Hanyang University Guri Hospital, Guri, Korea; ⁹Department of Neurology, CHA Bundang Medical Center, Seongnam, Korea; ¹⁰Department of Neurology, Konkuk University Medical Center, Seoul, Korea; ¹¹Department of Neurology, Ajou University School of Medicine, Suwon, Korea; ¹²Department of Neurology, Pusan National University School of Medicine, Busan, Korea; ¹³Department of Neurology, Changwon Fatima Hospital, Changwon, Korea; ¹⁴Department of Neurology, Ilsan Paik Hospital, Goyang, Korea; ¹⁵Department of Neurology, Heavenly Hospital, Goyang, Korea; ¹⁶Department of Neurology, Seoul National University Bundang Hospital, Seongnam, Korea; ¹⁷Department of Neurology, UiJeongbu St. Mary’s Hospital, UiJeongbu, Korea; ¹⁸Department of Neurology, Eunpyeong St. Mary’s Hospital, Seoul, Korea; ¹⁹Department of Neurology, Hallym Sacred Heart Hospital, Anyang, Korea; ²⁰Department of Neurology, St. Vincent’s Hospital, Seoul, Korea; ²¹Department of Neurology, Incheon St. Mary’s Hospital, Incheon, Korea; ²²Department of Neurology, Hanyang University College of Medicine, Seoul, Korea; ²³Department of Neurology, Gangnam Severance Hospital, Seoul, Korea; ²⁴Department of Neurology, Bobath Memorial Hospital, Seongnam, Korea; ²⁵Department of Neurology, Haeundae Paik Hospital, Busan, Korea; ²⁶Department of Neurology, Gyeongsang National University College of Medicine, Jinju, Korea; ²⁷Department of Neurology, Wonju Severance Christian Hospital, Wonju, Republic of Korea; ²⁸Department of Neurology, Korea University Anam Hospital, Seoul, Korea; ²⁹Department of Neurology, Chonnam National University Medical School, Gwangju, Korea; ³⁰Department of Neurology, Busan Paik Hospital, Inje University College of Medicine, Busan, Korea; ³¹Department of Neurology, Dongtan Sacred Heart Hospital, Hwaseong, Korea; ³²Department of Radiology, Konkuk University Medical Center, Seoul, Korea; ³³Department of Nuclear Medicine, Asan Medical Center, Seoul, Korea; ³⁴Department of Clinical Research Design and Evaluation, SAIHST, Sungkyunkwan University, Seoul, Korea

- Incidences of symptomatic ARIA, ARIA-E, superficial siderosis, and intracerebral hemorrhage were lower than those reported in the CLARITY AD trial.
- ARIA-E was associated with APOE ε4 homozygosity, lower baseline cognitive function, and microhemorrhages and superficial siderosis on baseline MRI.
- ARIA-H was associated with older age, APOE ε4 homozygosity, and baseline microhemorrhages.

INTRODUCTION	METHODS	RESULTS	RESULTS	CONCLUSIONS																																																																																														
• In May 2024, lecanemab was approved by the Korean Ministry of Food and Drug Safety (MFDS) and was launched commercially in November 2024. • ARIA and IRRs occurred less frequently with lecanemab in the CLARITY AD Asian subgroup than in the overall study population. These findings suggest possible ethnoracial differences. • To evaluate longterm safety and effectiveness and precision medicine, Korean JOint registrY for ALzheimer's treatment and diagnostics (JOY-ALZ) has been underway since 2024. • We aimed to evaluate the real-world safety and clinical outcomes of lecanemab using follow-up data through April 2026 from participants enrolled in the JOY-ALZ by December 2025.	• JOY-ALZ is a prospective, multicenter, real-world observational registry conducted in memory clinics across Korea to collect real-world data (RWD) from individuals across the AD continuum. • Lecanemab was administered intravenously every 2 weeks at 32 hospital according to the MFDS label and the appropriate use recommendations of the Korean Dementia Association. • The clinical evaluation included the MMSE, MoCA, CDR, Functional Activities Questionnaire (FAQ), and Ascertain Dementia 8 (AD8). • Monitoring MRI was performed before the third, fifth, seventh, and fourteenth infusions using a standardized MRI protocol on the same MR scanner for each participant.	• From 657 patients at risk for ARIA, who received at least one dose of lecanemab and underwent at least one MRI evaluation, 106 developed at least one ARIA (16.1%): 27 (4.1%) had ARIA-E with or without ARIA-H and 79 (12 %) had isolated ARIA-H. • Superficial siderosis was observed in 12 (1.8%). No ICH larger than 1 cm or deaths were observed. Symptomatic ARIA occurred in four patients (0.6%), all of whom were associated with ARIA-E; concomitant ARIA-H was observed in two patients. • In the Cox proportional hazards regression analyses, any ARIA was associated with older age, APOE ε4 homozygosity, and baseline MRI microhemorrhages and superficial siderosis (Figure 1A). ARIA-E with or without ARIA-H was associated with higher CDR-SB scores, APOE ε4 homozygosity, and baseline MRI microhemorrhages and superficial siderosis (Figure 1B). Isolated ARIA-H was associated with older age, APOE ε4 homozygosity, and baseline microhemorrhages (Figure 1C).	Figure 1. risk factors of ARIA (A) <table><tr><td></td><td>HR (95%CI)</td></tr><tr><td>Age</td><td>1.03 (1.01-1.06)</td></tr><tr><td>CDR-SB</td><td>1.07 (0.995-1.16)</td></tr><tr><td>APOE ε4 status</td><td></td></tr><tr><td>Non-carrier</td><td>Reference</td></tr><tr><td>Heterozygote</td><td>0.95 (0.60-1.49)</td></tr><tr><td>Homozygote</td><td>3.17 (1.86-5.38)</td></tr><tr><td>Antiplatelet use</td><td></td></tr><tr><td>No</td><td>Reference</td></tr><tr><td>Yes</td><td>1.24 (0.79-1.94)</td></tr><tr><td>No. of microhemorrhages</td><td>1.48 (1.30-1.68)</td></tr><tr><td>Superficial siderosis</td><td></td></tr><tr><td>No</td><td>Reference</td></tr><tr><td>Yes</td><td>4.03 (1.42-11.43)</td></tr><tr><td>Fazekas score</td><td></td></tr><tr><td>0</td><td>Reference</td></tr><tr><td>1</td><td>0.69 (0.41-1.16)</td></tr><tr><td>2</td><td>1.00 (0.57-1.77)</td></tr><tr><td>3</td><td>0.91 (0.40-2.06)</td></tr></table> Increased risk of any ARIA Hazard Ratio (95% CI) (log scale) (B) <table><tr><td></td><td>HR (95%CI)</td></tr><tr><td>CDR-SB</td><td>1.17 (1.04-1.32)</td></tr><tr><td>APOE ε4 status</td><td></td></tr><tr><td>Non-carrier</td><td>Reference</td></tr><tr><td>Heterozygote</td><td>0.55 (0.22-1.40)</td></tr><tr><td>Homozygote</td><td>2.87 (1.08-7.62)</td></tr></table> Increased risk of ARIA-E with or without ARIA-H Hazard Ratio (95% CI) (log scale) No. of microhemorrhages Superficial siderosis <table><tr><td></td><td>HR (95%CI)</td></tr><tr><td>No</td><td>Reference</td></tr><tr><td>Yes</td><td>8.67 (1.76-42.84)</td></tr></table> (C) <table><tr><td></td><td>HR (95%CI)</td></tr><tr><td>Age</td><td>1.04 (1.01-1.08)</td></tr><tr><td>CDR-SB</td><td>1.03 (0.94-1.14)</td></tr><tr><td>APOE ε4 status</td><td></td></tr><tr><td>Non-carrier</td><td>Reference</td></tr><tr><td>Heterozygote</td><td>1.05 (0.62-1.78)</td></tr><tr><td>Homozygote</td><td>3.57 (1.91-6.67)</td></tr><tr><td>Antiplatelet use</td><td></td></tr><tr><td>No</td><td>Reference</td></tr><tr><td>Yes</td><td>1.38 (0.83-2.30)</td></tr><tr><td>No. of microhemorrhages</td><td>1.48 (1.27-1.72)</td></tr><tr><td>Superficial siderosis</td><td></td></tr><tr><td>No</td><td>Reference</td></tr><tr><td>Yes</td><td>2.99 (0.71-12.63)</td></tr><tr><td>Fazekas score</td><td></td></tr><tr><td>0</td><td>Reference</td></tr><tr><td>1</td><td>0.71 (0.40-1.27)</td></tr><tr><td>2</td><td>0.92 (0.47-1.76)</td></tr><tr><td>3</td><td>0.92 (0.36-2.32)</td></tr></table> Increased risk of isolated ARIA-H Hazard Ratio (95% CI) (log scale)		HR (95%CI)	Age	1.03 (1.01-1.06)	CDR-SB	1.07 (0.995-1.16)	APOE ε4 status		Non-carrier	Reference	Heterozygote	0.95 (0.60-1.49)	Homozygote	3.17 (1.86-5.38)	Antiplatelet use		No	Reference	Yes	1.24 (0.79-1.94)	No. of microhemorrhages	1.48 (1.30-1.68)	Superficial siderosis		No	Reference	Yes	4.03 (1.42-11.43)	Fazekas score		0	Reference	1	0.69 (0.41-1.16)	2	1.00 (0.57-1.77)	3	0.91 (0.40-2.06)		HR (95%CI)	CDR-SB	1.17 (1.04-1.32)	APOE ε4 status		Non-carrier	Reference	Heterozygote	0.55 (0.22-1.40)	Homozygote	2.87 (1.08-7.62)		HR (95%CI)	No	Reference	Yes	8.67 (1.76-42.84)		HR (95%CI)	Age	1.04 (1.01-1.08)	CDR-SB	1.03 (0.94-1.14)	APOE ε4 status		Non-carrier	Reference	Heterozygote	1.05 (0.62-1.78)	Homozygote	3.57 (1.91-6.67)	Antiplatelet use		No	Reference	Yes	1.38 (0.83-2.30)	No. of microhemorrhages	1.48 (1.27-1.72)	Superficial siderosis		No	Reference	Yes	2.99 (0.71-12.63)	Fazekas score		0	Reference	1	0.71 (0.40-1.27)	2	0.92 (0.47-1.76)	3	0.92 (0.36-2.32)	• The incidences of symptomatic ARIA, ARIA-E, superficial siderosis, and ICH associated with lecanemab were lower in this real-world cohort than in the CLARITY AD trial and comparable to those observed in the CLARITY AD Asian subgroup analysis. • ARIA-E is associated with lower baseline cognitive function, APOE ε4 homozygosity, and baseline microhemorrhages and superficial siderosis on MRI. • ARIA-H was associated with older age, APOE ε4 homozygosity, and baseline microhemorrhages.
	HR (95%CI)																																																																																																	
Age	1.03 (1.01-1.06)																																																																																																	
CDR-SB	1.07 (0.995-1.16)																																																																																																	
APOE ε4 status																																																																																																		
Non-carrier	Reference																																																																																																	
Heterozygote	0.95 (0.60-1.49)																																																																																																	
Homozygote	3.17 (1.86-5.38)																																																																																																	
Antiplatelet use																																																																																																		
No	Reference																																																																																																	
Yes	1.24 (0.79-1.94)																																																																																																	
No. of microhemorrhages	1.48 (1.30-1.68)																																																																																																	
Superficial siderosis																																																																																																		
No	Reference																																																																																																	
Yes	4.03 (1.42-11.43)																																																																																																	
Fazekas score																																																																																																		
0	Reference																																																																																																	
1	0.69 (0.41-1.16)																																																																																																	
2	1.00 (0.57-1.77)																																																																																																	
3	0.91 (0.40-2.06)																																																																																																	
	HR (95%CI)																																																																																																	
CDR-SB	1.17 (1.04-1.32)																																																																																																	
APOE ε4 status																																																																																																		
Non-carrier	Reference																																																																																																	
Heterozygote	0.55 (0.22-1.40)																																																																																																	
Homozygote	2.87 (1.08-7.62)																																																																																																	
	HR (95%CI)																																																																																																	
No	Reference																																																																																																	
Yes	8.67 (1.76-42.84)																																																																																																	
	HR (95%CI)																																																																																																	
Age	1.04 (1.01-1.08)																																																																																																	
CDR-SB	1.03 (0.94-1.14)																																																																																																	
APOE ε4 status																																																																																																		
Non-carrier	Reference																																																																																																	
Heterozygote	1.05 (0.62-1.78)																																																																																																	
Homozygote	3.57 (1.91-6.67)																																																																																																	
Antiplatelet use																																																																																																		
No	Reference																																																																																																	
Yes	1.38 (0.83-2.30)																																																																																																	
No. of microhemorrhages	1.48 (1.27-1.72)																																																																																																	
Superficial siderosis																																																																																																		
No	Reference																																																																																																	
Yes	2.99 (0.71-12.63)																																																																																																	
Fazekas score																																																																																																		
0	Reference																																																																																																	
1	0.71 (0.40-1.27)																																																																																																	
2	0.92 (0.47-1.76)																																																																																																	
3	0.92 (0.36-2.32)																																																																																																	
REFERENCES				• Park KH, et al. Lecanemab: Appropriate Use Recommendations by Korean Dementia Association. Dement Neurocogn Disord. 2024;23:165-187. • Kim GH, et al. A Protocol of Korean JOint Registry for ALzheimer's Treatment and Diagnostics (JOY-ALZ). Dement Neurocogn Disord. 2026;25:25-41.																																																																																														
CONTACT				Seong Hye Choi: seonghye@inha.ac.kr																																																																																														
ALZHEIMER'S ASSOCIATION AAIC 26																																																																																																		