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A THREE-YEAR UPDATE OF LECANEMAB IN EARLY ALZHEIMER’S DISEASE: A COMPREHENSIVE MULTICENTER, REAL-WORLD, RETROSPECTIVE STUDY (LEADER)

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Introduction

- Lecanemab is indicated for patients with AD at the MCI or mild dementia stage with confirmed amyloid pathology.¹
- Real-world evidence complements clinical trial data by capturing outcomes in broader patient populations.² Previously published real-world data on lecanemab have explored early utilization patterns and short-term treatment experience.³
- This analysis presents effectiveness and safety data from **Lecanemab in Early Alzheimer’s Disease: A Comprehensive Multicenter, Real-World, Retrospective Study (LEADER)** three years post-approval, broadening prior evidence by incorporating two additional sites, a larger patient cohort, and follow-up beyond 18 months. It represents one of the first real-world datasets to characterize maintenance phase lecanemab utilization across both IV and at-home SC regimens.

Methods

- LEADER is a multicenter, retrospective, real-world cohort study conducted across 12 geographically diverse US neurology clinics.
- A deidentified retrospective sample of lecanemab chart/EMR cases per site was collected for patients treated with ≥7 biweekly IV lecanemab infusions. Maintenance cases were defined as patients receiving ≥3 months of maintenance therapy including monthly IV or weekly SC dosing, following initiation with 18 months of biweekly IV lecanemab.
- Treatment outcomes included change in disease stage from baseline to last follow-up visit, based on clinician judgment and informed by routine clinical assessment.
- “Improved” was defined as an improvement in disease stage from mild AD dementia to MCI due to AD, “stable” as no change from baseline disease stage (mild AD dementia or MCI due to AD), and “progressed” as progression from MCI due to AD to mild AD dementia, or from mild to moderate AD dementia.
- Patient characteristics and treatment outcomes with lecanemab were analyzed descriptively.
- Safety outcomes included incidence and severity of ARIA and adverse events leading to treatment discontinuation.
- This descriptive statistical analysis includes data from 12 sites collected through May 8, 2026.

Results

Patient Demographics

- A total of 432 patients from 12 US study sites were included in the analysis (**Table 1**), of which 155 were treated with monthly IV and 14 with weekly SC maintenance treatment.
- Demographics were representative of the early AD population by age and sex, and of the general AD population by *APOE* ε4 status.^{4–8}
- At baseline, 63.9% of patients had MCI due to AD and 36.1% had mild AD dementia.
- Mean (SD) treatment duration was 520.7 (267.6) days.

Table 1. Baseline Demographics (N=432)

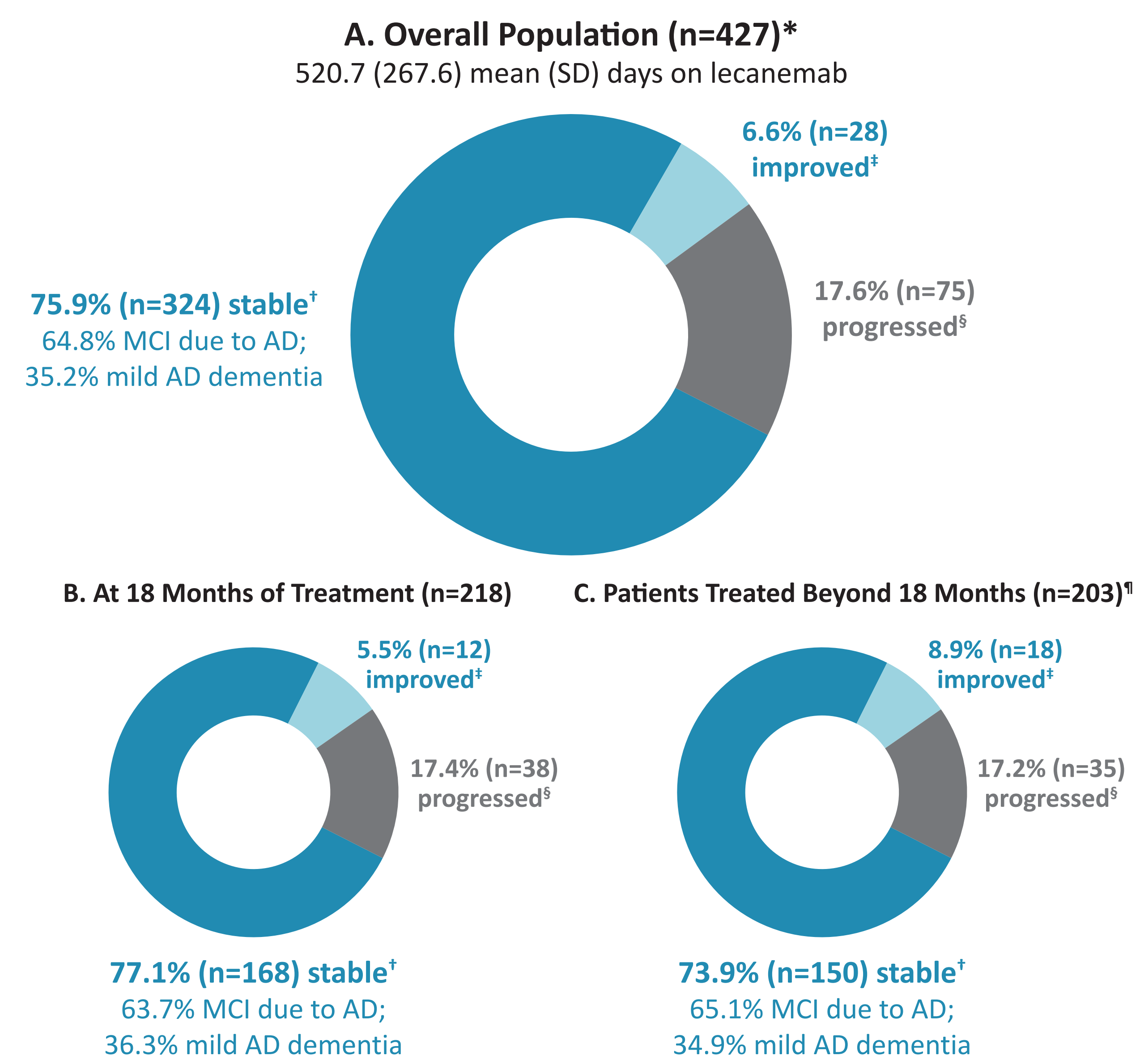
Demographics	N=432
Age,* mean (SD)	74.0 (7.0)
Sex, n (%)	
Female	241 (55.8)
Male	191 (44.2)
Disease stage, n (%)	
MCI due to AD	276 (63.9)
Mild AD dementia	156 (36.1)
APOE ε4 status, n (%)	
APOE ε4 heterozygous	231 (53.5)
APOE ε4 homozygous	58 (13.4)
APOE ε4 noncarrier	132 (30.6)
Not reported	11 (2.5)
Race, n (%)	
Black	17 (3.9)
White	391 (90.5)
Other†	24 (5.6)
Ethnicity, n (%)	
Not of Hispanic or Latino origin	368 (85.2)
Hispanic or Latino origin	57 (13.2)
Not reported	7 (1.6)

*Age at baseline was not reported for n=1 patient. †Other included Other, not specified (n=15), Asian (n=5), Multiracial (n=3), and Native American (n=1).

Effectiveness

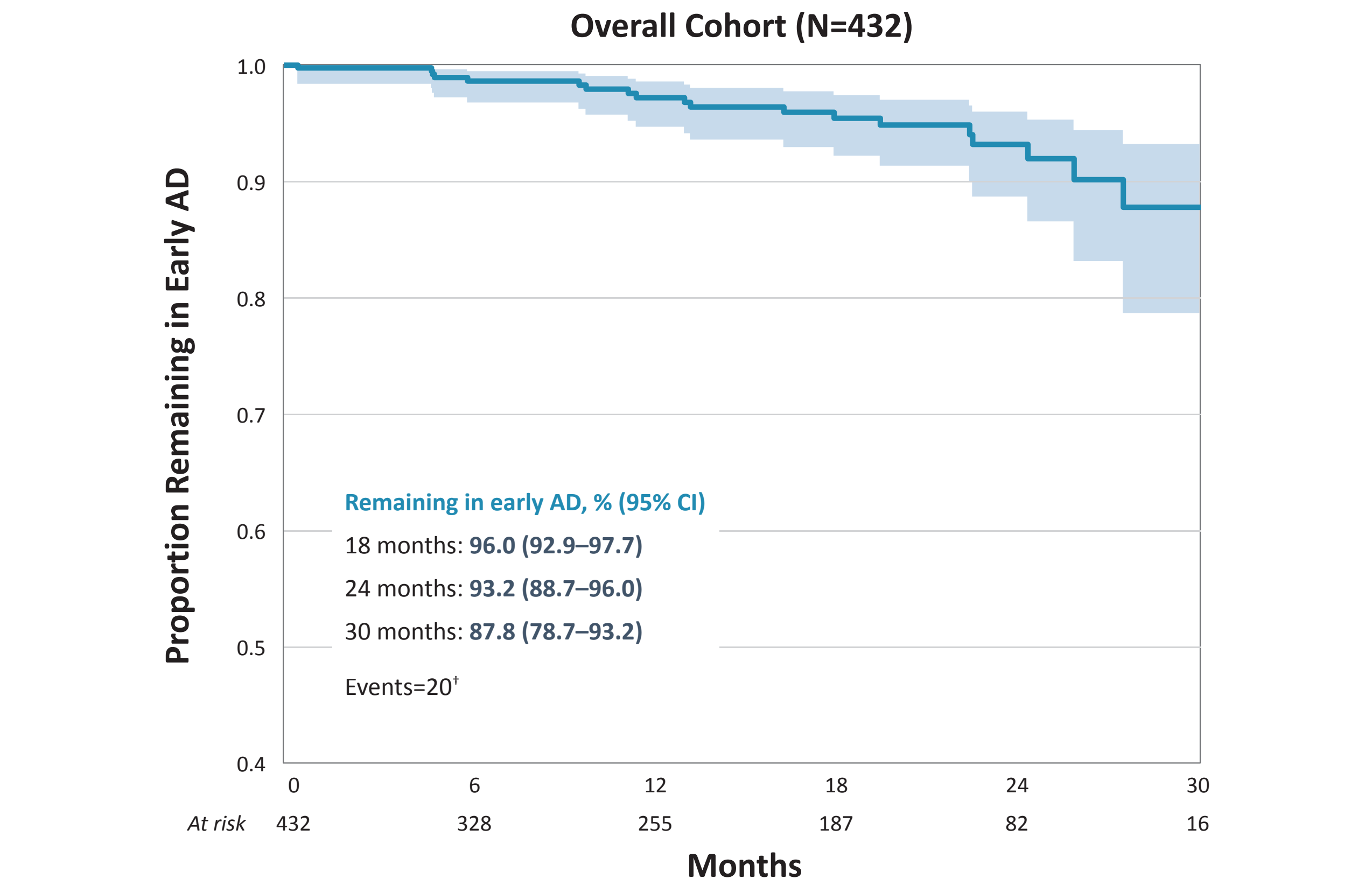
- Clinician-assessed disease stage remained stable or improved in 82.5% of patients with a mean (SD) treatment duration of 520.7 (267.6) days (**Figure 1A**).
- Disease stage stability or improvement was observed in 82.6% of patients at 18 months and 82.8% of patients treated beyond 18 months, with mean (SD) treatment durations of 537.3 (41.9) and 716.1 (137.7) days, respectively (**Figure 1B, C**).
- A total of 87.8% of patients in the LEADER study were estimated to remain in the early stages of AD after 30 months of treatment (**Figure 2**).

Figure 1. Change in Clinician-Evaluated Disease Stage



*Change in disease stage was unknown for n=5 patients; †Stable was defined as a patient staying in the same disease stage (MCI due to AD or mild AD dementia) from baseline throughout the course of lecanemab treatment; ‡Improvement was defined as a patient going from mild AD dementia at baseline to MCI due to AD over the course of lecanemab treatment; §Progression was defined as the patient going from MCI at baseline to mild/moderate AD dementia or mild AD dementia at baseline to moderate AD dementia throughout the course of lecanemab treatment; *Change in disease stage was unknown for n=1 patient.

Figure 2. Estimated Proportion of Patients Remaining in Early AD from First Lecanemab Dose*



Patient clinical status was based on clinician judgment. Shaded band=95% CI (Greenwood/log-log).
*Proportion of patients remaining in early AD (MCI due to AD or mild AD dementia) over time;
†Event was classified as progression to moderate or severe dementia.

Safety

- ARIA-E occurred in 6.3%, and ARIA-H occurred in 7.9% of patients (**Table 2**).
- In *APOE* ε4 homozygotes, ARIA-E occurred in 10.3% and ARIA-H in 12.1% of patients.
- Instances of ARIA were predominantly asymptomatic and mild to moderate in radiographic severity, with no macrohemorrhages, intracerebral hemorrhages, or treatment-related deaths reported.
- Treatment retention was high, with 86.6% of patients remaining on lecanemab treatment at chart extraction (**Table 3**).

Table 2. ARIA and Infusion-Related Reactions (N=432)

	N=432 n (%)
Any ARIA*	53 (12.3)
ARIA-E*	27 (6.3)
Asymptomatic	18 (4.2)
Symptomatic	5 (1.2)
Not reported	4 (0.9)
Mild	22 (5.1)
Moderate	4 (0.9)
Severe	1 (0.2)
ARIA-H*	34 (7.9)
Asymptomatic	29 (6.7)
Symptomatic	3 (0.7)
Not reported	2 (0.5)
Mild	27 (6.3)
Moderate	6 (1.4)
Severe	1 (0.2)
Isolated ARIA-H	26 (6.0)
Concurrent ARIA-E and ARIA-H	8 (1.9)
Intracerebral hemorrhage/macrohemorrhage >1 cm	0 (0)
Infusion-related reactions leading to discontinuation or dose modification	5 (1.2)

*Includes counts for concurrent ARIA-E and ARIA-H, n=8.

Table 3. Adverse Events Leading to Treatment Discontinuation (N=432)

Reason for discontinuation	N=432 n (%)
Discontinued treatment	58 (13.4)
ARIA-H	5 (1.2)
ARIA-E	4 (0.9)
ARIA-E and ARIA-H	3 (0.7)
Infusion-related reaction	1 (0.2)
Patient decision/logistics	14 (3.2)
Other/unspecified	7 (1.6)
Lack of efficacy	5 (1.2)
Other non-ARIA adverse events	20 (4.6)

Reason-for-discontinuation categories are not mutually exclusive (patients may be counted in >1).

Conclusions

- The study cohort was representative of the early AD population by age and sex and of the broader AD population by *APOE* ε4 status, with baseline comorbidities reflecting a typical older, multimorbid real-world population.^{4–8}
- In routine clinical practice, most patients receiving lecanemab remained clinically stable or improved over a mean treatment duration of 520 days (~17 months).
 - 87.8% of LEADER patients are estimated to remain in the early stages of AD at 30 months of ongoing treatment.
 - Results should be interpreted noting that the absence of a randomized control group precludes causal inference regarding treatment effectiveness.
- Safety outcomes, including ARIA, were consistent with the FDA-approved label.¹
- These findings suggest that the long-term, real-world effectiveness and safety profile of lecanemab is consistent with clinical trial experience, including IV and SC maintenance dosing regimens.^{1,9}
- Continued follow-up will further characterize long-term outcomes and safety of lecanemab in routine practice.

References: 1. LEQEMBI (lecanemab-irrm) prescribing information. Eisai Inc. <https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf> (Accessed July 2026). 2. Costa V, et al. Front Public Health. 2025;13:1512429. 3. Paczynski M, et al. JAMA Neurol. 2025;82:655–665. 4. Mendez MF. Continuum (Minneapolis, MN). 2019;25:34–51. 5. Zhu XC, et al. Ann Transl Med. 2015;3:38. 6. Reitz C, et al. Neurol Genet. 2020;6:e512. 7. Ward A, et al. Neuroepidemiology 2012;38:1–17. 8. Fortea J, et al. Nat Med. 2024;30:1284–1291. 9. van Dyck CH, et al. N Engl J Med. 2023;388:9–21. **Acknowledgments:** The study was conducted by Panacea85, funded by Eisai Inc. and Biogen. Medical writing support was provided by Panacea85, funded by Eisai Inc. and Biogen. **Disclosures:** MSab has received consulting/speaker fees from AbbVie, Alzinova, Anavex, Cognito, Eisai Inc., Eli Lilly, GSK, NeuroTherapia, Otsuka, Recall, and Signant; research/grant support from Alnylam, Biogen, BMS, Eisai Inc., Eli Lilly, GSK, Janssen, Ono, Neurim, and Novo Nordisk; has stock/options in Alzheon and Lighthouse Pharmaceuticals; and is a board member for CervoMed. BB has received consulting/speaker fees from Eisai Inc. and Eli Lilly and royalties/licenses from Cognitive Neuroscience Space. CC has received consulting/speaker fees from Eisai Inc. and Eli Lilly. TC has received consulting/speaker fees from ALZ-NET and Eisai Inc. and research/grant support from Karuna Therapeutics. GC has received research/grant support from Eisai Inc., Eli Lilly, Novartis, and Davos Alzheimer’s Collaborative. SG has received consulting/speaker fees from Eisai Inc. and Eli Lilly. CL has received consulting/speaker fees from Biogen, C2N Diagnostics, Eisai Inc., Eli Lilly, and Neurogen Biomarking and research/grant support from C2N Diagnostics, Davos Alzheimer’s Collaborative, Eisai Inc., Eli Lilly, and Neurogen Biomarking. MR has received consulting/speaker fees from Eisai Inc. and Eli Lilly. MSad has received consulting/speaker fees from Axsome, Alzheon, Biogen, Cognition, Eisai Inc., Eli Lilly, GSK, Oligomerix, Owkin, and Novartis; has stock/options in Pfizer; and a relationship with Fisher Center for Alzheimer’s Research Foundation. CS has received consulting/speaker fees from C2N Diagnostics, Eisai Inc., Eli Lilly, and Pfizer and research/grant support from Eisai Inc., Eli Lilly, Genentech, Novartis, and Roche. PS has received consulting/speaker fees from Acadia, Eisai Inc., and Eli Lilly; research/grant support from NIH; and is a board member for Alzheimer’s Association Houston and FTLDA San Antonio. JS has received consulting/speaker fees from Arrowhead, Biogen, Eisai Inc., Eli Lilly, Genentech, Global Learning Collaborative, and Merck and research/grant support from Alzheimer’s Association, Annovis Bio, Arbibio, Biogen, Eisai Inc., Eli Lilly, Karuna/BMS, NIH-NIA, and Novartis. BT has received consulting/speaker fees from Biogen, Eisai Inc., Lundbeck, Novo Nordisk, and Sunbird Bio and research/grant support from Acadia, Biogen, Cognition Therapeutics, EIP, Eisai Inc., NIH-NIA, and Novo Nordisk. DW has received consulting/speaker fees from American Stroke Association, Biogen, Eisai Inc., Lantheus, and Novartis and research/grant support from Acadia, Acumen, Alnylam, Alzheimer’s Association, Cerevel, Cognition, Eisai Inc., Eli Lilly, Novartis, Sage, Sanofi, Serono, and Roche. FF, CA, and DRJ are employees of Eisai Inc. NF reports no conflicts. **Abbreviations:** AD, Alzheimer’s disease; APOE, apolipoprotein E; ARIA, amyloid-related imaging abnormalities; ARIA-E, ARIA – edema/effusion; ARIA-H, ARIA – hemosiderin/microhemorrhage; CI, confidence interval; IV, intravenous; LEADER, Lecanemab in Early Alzheimer’s Disease: a Comprehensive Multicenter, Real-World, Retrospective Study; MCI, mild cognitive impairment; SC, subcutaneous; SD, standard deviation; US, United States.