

M184

SEX-BASED OUTCOMES OF LECANEMAB IN EARLY ALZHEIMER’S DISEASE: A COMPREHENSIVE MULTICENTER, REAL-WORLD, RETROSPECTIVE STUDY (LEADER)

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Introduction

- In the US, women account for nearly two-thirds of individuals living with AD dementia and have approximately twice the lifetime risk of developing AD dementia compared with men.¹
- Despite this disproportionate burden, sex-stratified treatment outcomes are infrequently reported. Evaluating real-world effectiveness and safety in women is important for understanding potential sex-related differences in therapeutic outcomes.^{2,3}
- Lecanemab is indicated for patients with AD at the MCI or mild dementia stage with confirmed amyloid pathology.⁴ **Lecanemab in Early Alzheimer’s Disease: A Comprehensive Multicenter, Real-World, Retrospective Study (LEADER)** evaluates real-world utilization and clinical outcomes of lecanemab in the US.
- This subgroup analysis from the LEADER study describes the real-world effectiveness and safety of lecanemab by sex.

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.
- This subgroup analysis evaluated baseline characteristics, treatment duration, treatment outcomes, and safety by sex.
- 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.
- 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**); 55.8% (n=241) were female and 44.2% (n=191) were male.
- Baseline characteristics including age, disease stage, APOE ε4 status, race, and ethnicity were not statistically different between sexes (P values ranging from 0.683–0.967; Mann-Whitney U and Chi-squared tests).

Table 1. Baseline Demographics (N=432)

	Females N=241	Males N=191
Age, mean (SD)	73.9 (6.8)	74.1 (7.3)
Disease stage, n (%)		
MCI due to AD	156 (64.7)	120 (62.8)
Mild AD dementia	85 (35.3)	71 (37.2)
APOE ε4 status		
APOE ε4 heterozygous	129 (53.5)	102 (53.4)
APOE ε4 homozygous	33 (13.7)	25 (13.1)
APOE ε4 noncarrier	74 (30.7)	58 (30.4)
Not reported	5 (2.1)	6 (3.1)
Race, n (%)		
Black	9 (3.7)	8 (4.2)
White	220 (91.3)	171 (89.5)
Other	12 (5.0) [†]	12 (6.3) [‡]
Ethnicity, n (%)		
Not of Hispanic or Latino origin	206 (85.5)	162 (84.8)
Hispanic or Latino origin	31 (12.9)	26 (13.6)
Not reported	4 (1.7)	3 (1.6)

*Age at baseline was not reported for n=1 female. [†]Other included Asian (n=3), Multiracial (n=3), Native American (n=1), and Other, not specified (n=5); [‡]Other included Asian (n=2), Multiracial (n=2), and Other, not specified (n=8).

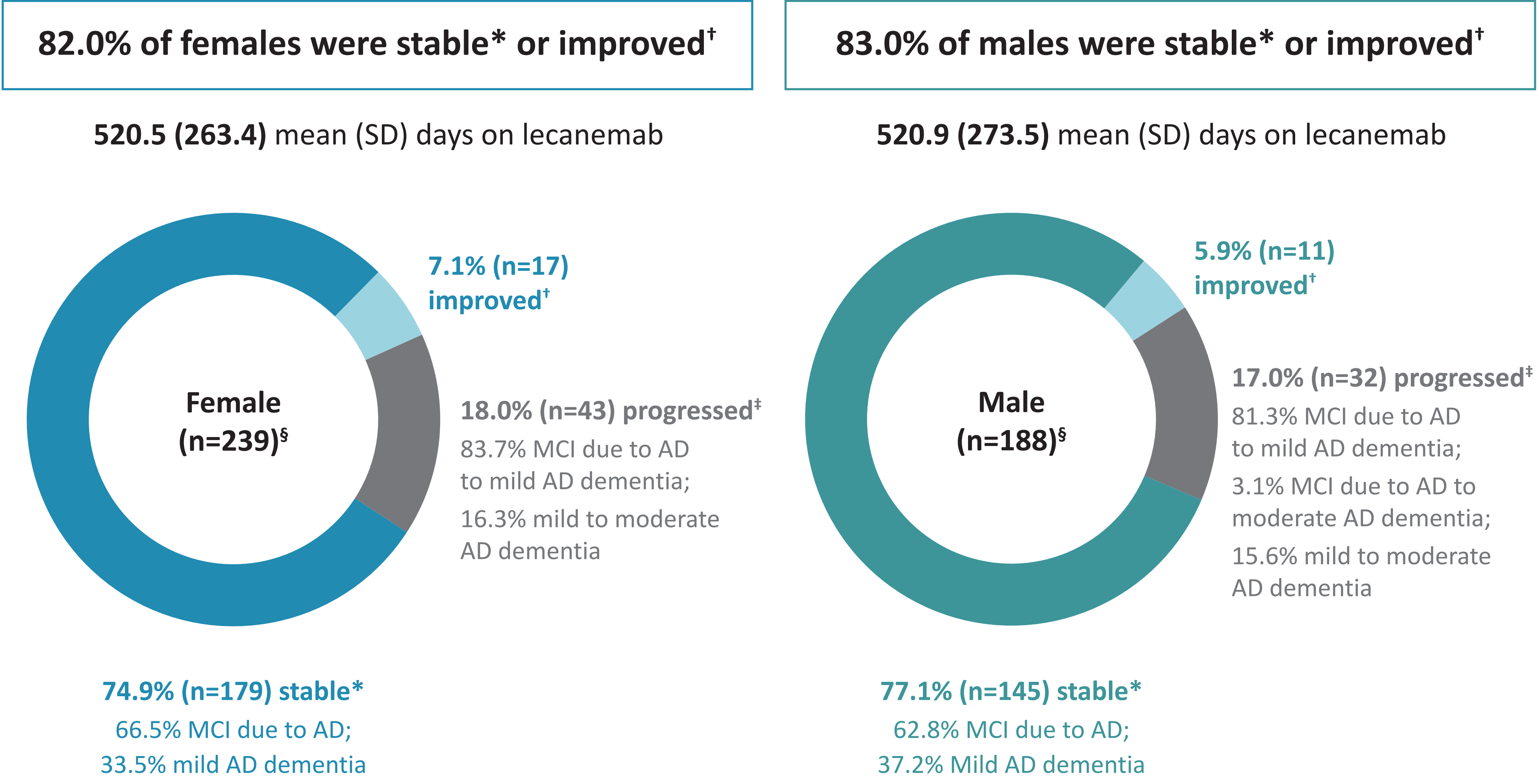
Effectiveness

- Disease stage remained stable or improved in 82.0% of females and 83.0% of males after a mean (SD) treatment duration of 520.5 (263.4) and 520.9 (273.5) days, respectively (**Figure**).
- Clinical outcomes were comparable between sexes, with no significant difference in clinician-assessed disease stage change (P=0.985; Wilcoxon rank-sum test).
- Paired changes in MMSE and MoCA scores were not significantly different between sexes (**Table 2**), (P=0.109 and P=0.926; Mann-Whitney U test).

Safety

- Treatment persistence was high in both women and men, with 84.7% of females and 89.0% of males remaining on lecanemab at chart extraction (**Table 3**).
- There was no significant difference in ARIA incidence between sexes (P=0.284; Chi-squared test). The distribution of ARIA-E, ARIA-H, and concurrent ARIA-E and ARIA-H events was comparable across groups (**Table 4**).
 - ARIA-E occurred in 6.2% of females and 6.3% of males.
 - ARIA-H occurred in 6.6% of females and 9.4% of males.
- Most ARIA events were asymptomatic and radiographically mild to moderate in severity (**Table 4**).
 - Moderate or severe ARIA-E events were observed more frequently in females than males.
- No macrohemorrhages, intracerebral hemorrhages, or treatment-related deaths were reported.

Figure. Change in Clinician-Evaluated Disease Stage During the Treatment Period by Sex (n=427)



*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. Disease stage was based on clinical judgment; [‡]Change in disease stage was not reported for n=2 female patients and n=3 male patients.

Table 2. Paired Change in MMSE and MoCA Scores by Sex

	Females	Males
MMSE, mean (SD)	N=84	N=77
Baseline score	24.6 (2.9)	24.7 (3.1)
Follow-up score	22.7 (4.2)	23.6 (4.2)
Change in score	−1.9 (3.6)	−1.1 (3.5)
Follow up duration (days)	714.0 (327.1)	673.6 (301.9)
MoCA, mean (SD)	N=71	N=54
Baseline score	21.8 (3.1)	22.2 (2.9)
Follow-up score	20.8 (4.3)	21.2 (4.1)
Change in score	−1.0 (2.8)	−0.9 (2.9)
Follow up duration (days)	567.0 (277.9)	572.9 (266.7)

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

Treatment status, n (%)	Females N=241	Males N=191
Continued treatment at time of chart extraction	204 (84.6)	170 (89.0)
Discontinued treatment	37 (15.4)	21 (11.0)
Reason for discontinuation*		
Other non-medical events (eg, personal, treatment stopped at 18 months [physician/ patient discretion])	22 (9.1)	11 (5.8)
Non-ARIA adverse events	12 (5.0)	8 (4.2)
ARIA-H	1 (0.4)	4 (2.1)
ARIA-E	4 (1.7)	0 (0)
Concurrent ARIA-E and ARIA-H	3 (1.2)	0 (0)
Time commitment	2 (0.8)	0 (0)
Cost of treatment	1 (0.4)	1 (0.5)

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

Table 4. Incidence of ARIA by Sex (N=432)

ARIA status, n (%)	Females N=241	Males N=191
Any ARIA*	26 (10.8)	27 (14.1)
ARIA-E*	15 (6.2)	12 (6.3)
Symptom status		
Asymptomatic	11 (4.6)	7 (3.7)
Symptomatic	2 (0.8)	3 (1.6)
Not reported	2 (0.8)	2 (1.0)
Radiographic severity		
Mild	11 (4.6)	11 (5.8)
Moderate	3 (1.2)	1 (0.5)
Severe	1 (0.4)	0 (0)
ARIA-H*	16 (6.6)	18 (9.4)
Symptom status		
Asymptomatic	15 (6.2)	14 (7.3)
Symptomatic	1 (0.4)	2 (1.0)
Not reported	0 (0)	2 (1.0)
Radiographic severity		
Mild	12 (5.0)	15 (7.9)
Moderate	3 (1.2)	3 (1.6)
Severe	1 (0.4)	0 (0)
Isolated ARIA-H	11 (4.6)	15 (7.9)
Radiographic severity		
Mild	10 (4.1)	13 (6.8)
Moderate	1 (0.4)	2 (1.0)
Severe	0 (0)	0 (0)
Concurrent ARIA-E and ARIA-H	5 (2.1)	3 (1.6)

*Includes counts for concurrent ARIA-E and ARIA-H.

Conclusions

- In this real-world cohort of patients receiving lecanemab maintenance therapy, clinical outcomes and safety profiles were similar between female and male patients.
- Disease-stage stability or improvement was observed in more than 80% of patients regardless of sex over a mean observation period of ~17 months.
 - There was no significant difference in clinician-assessed disease stage between females and males.
- Safety observations were generally similar between groups and were consistent with the FDA-approved label.⁴
- These findings provide important real-world evidence supporting consistent treatment outcomes across sexes and contribute to the growing understanding of lecanemab use in female patients.
- Ongoing collection of longer-term and more diverse real-world data will further clarify potential sex-specific treatment outcomes and inform equitable implementation of disease-modifying therapies in clinical practice.