



Six-Month Real-World Amyloid PET Outcomes After Lecanemab Treatment: Greater Amyloid Reduction in the MCI Stage of Alzheimer’s Disease

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BACKGROUNDS

- Lecanemab has demonstrated robust amyloid-lowering efficacy in randomized trials; however, real-world evidence regarding stage-dependent biological and short-term clinical responses remains limited.
- We evaluated six-month changes in amyloid burden using positron emission tomography (PET) and examined whether amyloid reduction and early cognitive outcomes differ by disease stage in routine clinical practice.

METHODS

- Among 89 patients who received lecanemab, 50 individuals with baseline amyloid positivity and follow-up amyloid PET were included in the primary amyloid PET efficacy analysis.
- Amyloid burden was quantified using the Centiloid scale. Longitudinal Centiloid trajectories were analyzed using linear mixed-effects models including disease stage, time from baseline amyloid PET, and the disease stage × time interaction, with adjustment for cumulative dose exposure, age, sex, and APOE ε4 carrier status. Cognitive and functional outcomes were assessed using mixed-effects models.

RESULTS

- Amyloid burden decreased substantially during follow-up. After adjustment for cumulative dose exposure, age, sex, and APOE ε4 carrier status, the disease stage × time interaction was significant ($\beta = +1.62$ Centiloid/month; 95% CI, 0.80 to 2.43; $p < 0.001$), indicating a faster rate of Centiloid reduction in patients with mild cognitive impairment (MCI) than in those with dementia (estimated -2.34 vs -0.72 Centiloid/month).
- Conversion to amyloid-negative status (full treatment-related amyloid clearance) occurred in 9 of 50 patients (18.0%) and was more frequent at the MCI stage ($p = 0.022$).
- Patients treated at the MCI stage also showed more favorable short-term cognitive and functional trajectories than those treated at the dementia stage.

Table 1.Treatment exposure, discontinuation, and safety outcomes

Outcome	Overall (n = 89)
Ongoing treatments, n (%)	75 (84.3%)
#of lecanemab infusions,mean ± SD	11.7 ± 7.5
Treatment discontinuation, n (%)	14 (15.7%)
Reasons for discontinuation, n (%)	
Adverse events	9 (64.2%)
Caregiver request	4 (28.6%)
Other reasons	1 (7.1%)
Infusion-related reaction, n (%)	10 (11.2%)
ARIA-E, asymptomatic, n (%)	0 (0%)
ARIA-E, symptomatic, n (%)	1 (1.1%)
ARIA-H, asymptomatic, n (%)	13 (14.6%)
ARIA-H, symptomatic, n (%)	0 (0%)

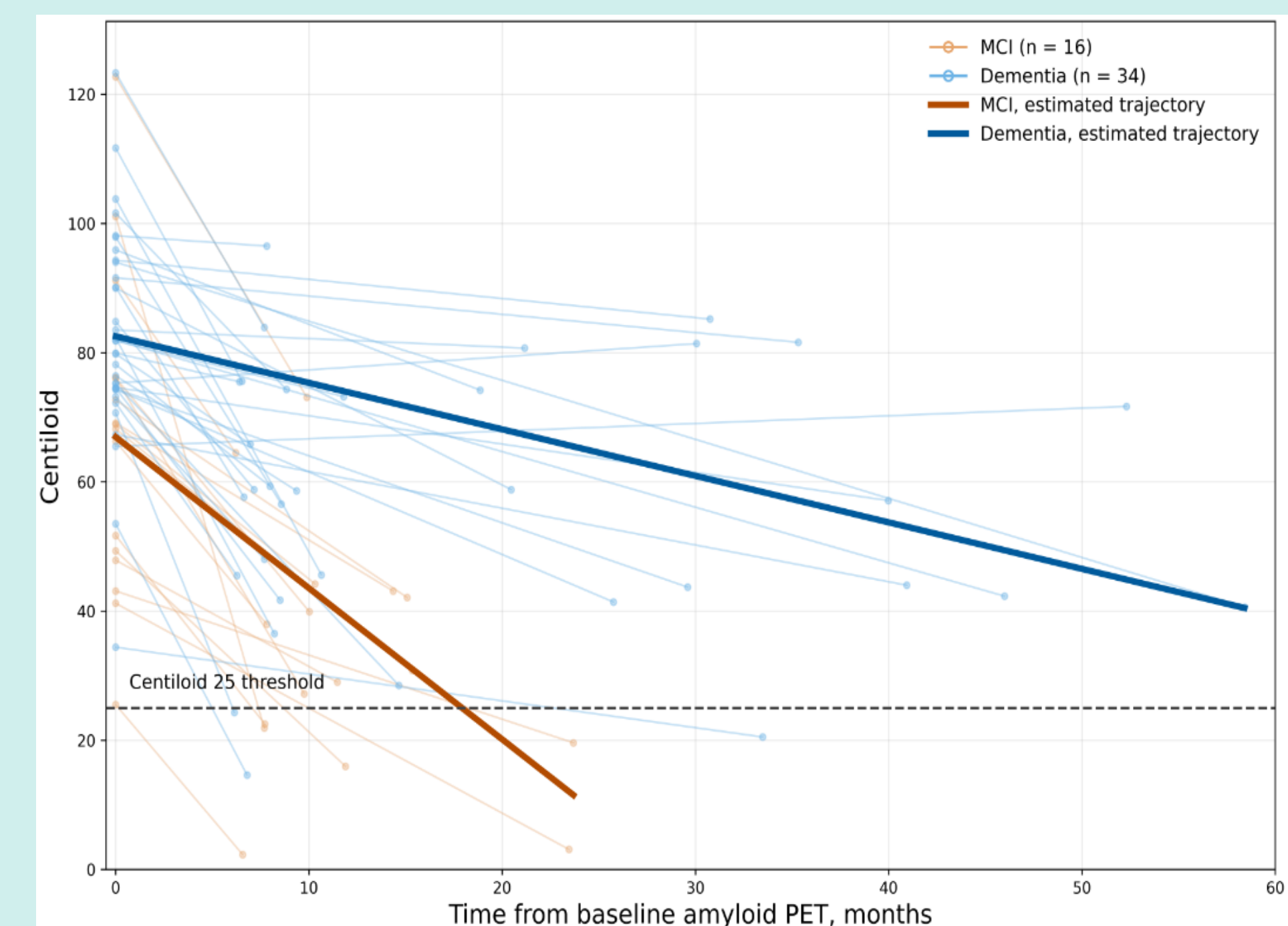
Table 2. Amyloid PET outcomes at baseline and 6 months by disease stage

Outcome	Overall (n = 51)	MCI (n = 16)	Dementia (n = 35)	p value
Baseline Centiloid	76.2 ± 22.4	66.9 ± 24.4	80.4 ± 20.5	0.046*
6-month Centiloid	48.4 ± 23.6	32.3 ± 19.3	55.7 ± 21.8	<0.001*
Interval between baseline amyloid PET and first lecanemab infusion (days)	329.8 ± 399.6	189.4 ± 160.1	393.9 ± 458.3	0.090
Interval between baseline and 6-month amyloid PET (days)	508.1 ± 399.5	363.9 ± 162.6	573.9 ± 456.9	0.081
ΔCentiloid	−27.8 ± 16.7	−34.6 ± 14.7	−24.7 ± 16.9	0.048*
Relative amyloid reduction (%)	−39.2 ± 22.9	−54.7 ± 19.4	−30.7 ± 20.5	<0.001*
Full TRAC, n (%)	10 (19.6%)	6 (37.5%)	4 (11.4%)	0.030*

Table 3. Six-month changes in cognitive and functional outcomes by disease stage

Outcome	Overall (n=51)	p value (within)	MCI (n=16)	Dementia (n=35)	Adjusted β (SE)	p value (adjusted)
ΔMMSE	−0.92 ± 2.09	0.003*	-0.06 ± 0.77	-1.31 ± 2.37	−1.34 (0.50)	0.011*
ΔMMSE−EV	−2.04 ± 5.91	0.021*	+1.33 ± 3.99	-3.58 ± 6.05	−5.06 (1.56)	0.002*
ΔCDR	+0.10 ± 0.26	0.011*	+0.03 ± 0.13	+0.13 ± 0.31	+0.09 (0.06)	0.134
ΔCDR-SOB	+0.50 ± 1.05	0.001*	+0.09 ± 0.42	+0.69 ± 1.20	+0.62 (0.25)	0.015*
ΔGeriatric Depression Scale	-1.86 ± 5.05	0.013*	-2.63 ± 6.08	-1.48 ± 4.54	+0.95 (1.80)	0.599
ΔInstrumental ADL	+0.12 ± 0.22	<0.001*	+0.03 ± 0.09	+0.17 ± 0.24	+0.15 (0.05)	0.006*
ΔADCS−ADL	−1.79 ± 9.16	0.301	+1.00 ± 5.20	-3.05 ± 10.34	−4.08 (3.50)	0.256
ΔZarit Burden Interview	+1.35 ± 12.91	0.545	+6.22 ± 9.61	-0.40 ± 13.65	−6.95 (4.49)	0.133

Figure 1. Longitudinal Centiloid trajectories following lecanemab treatment according to disease stage



- Individual Centiloid trajectories are plotted against exact time from baseline amyloid PET for participants with MCI and dementia. Model-estimated trajectories from the linear mixed-effects model are overlaid for each disease stage. The dashed horizontal line indicates the Centiloid 25 threshold for amyloid negativity.

CONCLUSIONS

- In real-world clinical practice, lecanemab treatment was associated with substantial amyloid reduction, with faster amyloid clearance observed at the MCI stage.
- These findings support the potential value of earlier intervention with anti-amyloid therapy, although longer follow-up and controlled comparisons are needed to determine whether early biomarker changes translate into sustained clinical benefit.