



ABSTRACT 13660: LONG-TERM EFFICACY AND SAFETY OF LECANEMAB IN CHINESE PATIENTS WITH ALZHEIMER’S DISEASE: A MULTICENTER REAL-WORLD STUDY



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Background

The long-term real-world effectiveness of Lecanemab and clinical indicators predictive of its therapeutic efficacy remain unclear.

Methods

This multicenter, prospective real-world cohort study enrolled patients with Alzheimer's disease (AD) from nine centers across Southwest China. Participants received intravenous Lecanemab (10 mg/kg) every 2 weeks for up to 18 months, with assessments at baseline and 2.5, 7, 13, and 18 months. Cognitive outcomes included ADAS-cog14, CDR-SB, MoCA, MMSE, and FAB. Aβ-PET/CT was repeated at 13 months to evaluate amyloid clearance. Propensity score-matched control cohorts, including patients receiving conventional oral symptomatic treatment and an ADNI natural history cohort, were established for comparison. Linear mixed-effects models were used to assess longitudinal cognitive trajectories, and correlation and multivariable logistic regression analyses were performed to identify predictors of treatment response. Patient-reported treatment efficacy and tolerability were assessed using an online Global Clinical Impression (GCI) survey.

Results

Table 1. Baseline characteristics (n = 122)

Variables	Value
Age (years)	68.48 ± 10.25
Sex, female (%)	(81, 66.39%)
BMI (kg/m ²)	21.57 ± 3.28
Duration (years)	2.00 (2.00-3.00)
CDR, n (%)	
0.5	(47, 38.52%)
1	(50, 40.98%)
2	(25, 20.50%)
Education (years)	12.00 (9.00-15.00)
Family history, n (%)	(19, 15.57%)
Comorbidities, n (%)	
Diabetes	18 (14.75%)
Hypertension	22 (18.03%)
History of malignant tumor surgery	2 (1.64%)
Coronary artery disease, n (%)	3 (2.46%)
ACCI	3.00 (2.00-3.00)
APOE ε4 status, n (%)	
Non-carriers	55 (45.08%)
Carriers	
Heterozygotes	53 (43.44%)
Homozygotes	14 (11.48%)
Smoking, n (%)	13 (10.66%)
Drinking, n (%)	10 (8.20%)
Current use of medication, n (%)	
Acetylcholinesterase inhibitor monotherapy	67 (54.91%)
Combination therapy	44 (36.07%)
No anti-dementia medication	11 (9.02%)
Fazekas, n (%)	
0	13 (10.66%)
1	74 (60.66%)
2	31 (25.41%)
3	4 (3.27%)
Baseline ARIA-H, n (%)	12 (9.84%)

- Sustained Cognitive Benefits Over 13 Months(Adjusted Analysis)** Linear mixed-effects models adjusting for sex, age, education, APOE genotype, and disease duration demonstrated robust and sustained cognitive improvements following Lecanemab initiation (Figure 1A-E):
 - ADAS-cog14** scores decreased significantly at month 2.5 ($\beta = -2.58$, $P < 0.001$), month 7 ($\beta = -2.20$, $P < 0.001$) and month 13 ($\beta = -2.03$, $P = 0.005$).
 - CDR-SB** scores reduced significantly at month 2.5 ($\beta = -0.31$, $P = 0.001$) and month 13 ($\beta = -0.26$ $P = 0.020$).
 - MoCA** scores improved significantly at month 2.5 ($\beta = 1.00$, $P = 0.005$) and month 7 ($\beta = 1.43$, $P < 0.001$).
 - MMSE** scores showed significant improvement at month 7 ($\beta = 0.80$, $P = 0.024$).

13-Month Clinical Staging & Amyloid Clearance

After 13 months of treatment, 84.00% (42/50) of patients maintained stable CDR staging, and 66.67% (32/48) achieved complete amyloid-β clearance (defined as Centiloids < 12, Figure 1F-H).

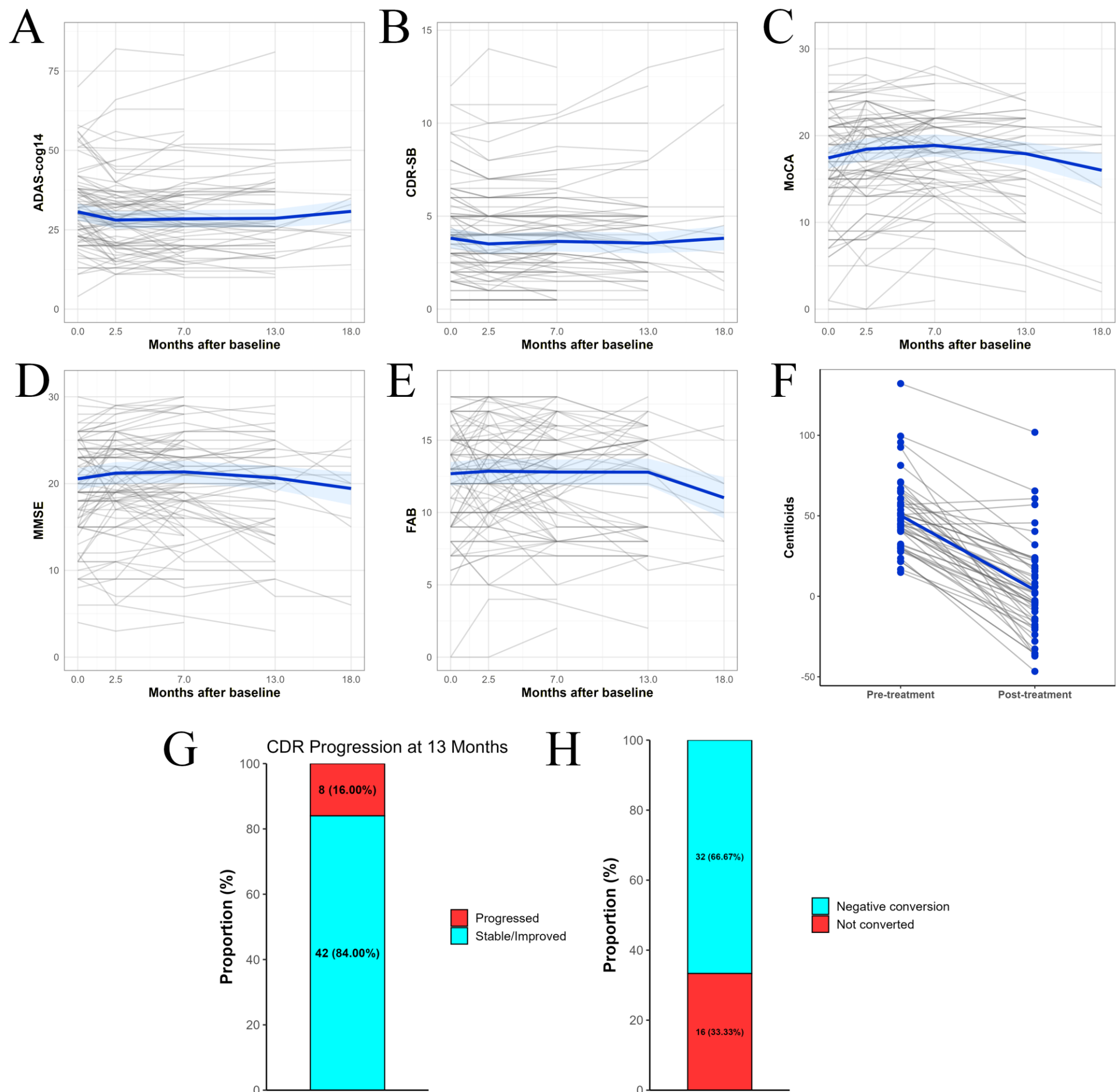


Figure 1 Cognitive trajectories and biomarker outcomes during Lecanemab treatment

Cognitive Outcomes Compared with Untreated Patients

Compared with the demographically matched ADNI cohort, after adjustment for baseline CDR stage, the Lecanemab-treated group showed a more favorable cognitive trajectory during follow-up (Figure 2A). MoCA scores declined numerically in the ADNI group but increased in the Lecanemab-treated group, with a significant between-group difference in change (2.091 ± 1.025 ; P for interaction=0.043). MMSE scores declined significantly in the ADNI group but remained stable in the Lecanemab-treated group, with a marginal between-group difference in change (1.659 ± 0.893 ; P for interaction=0.065). Similar findings were observed after matching for baseline CDR stage (Figure 2B).

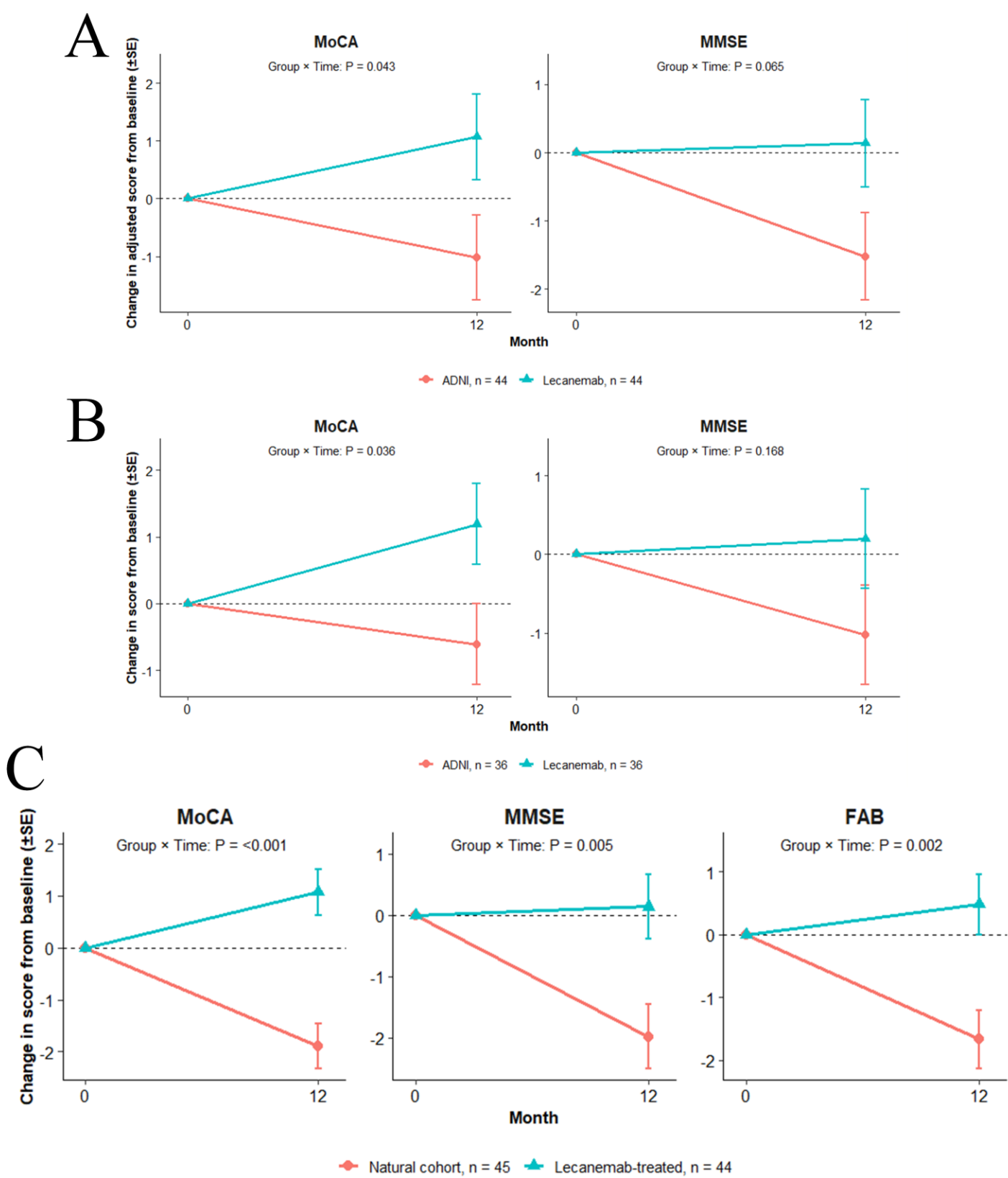


Figure 2. Comparison of cognitive trajectories between Lecanemab-treated group and control cohorts

Compared with the matched untreated natural history cohort from our center, the Lecanemab-treated group also showed more favorable longitudinal changes across MoCA, MMSE, and FAB scores (Figure 2C). Significant between-group differences in change were observed for MoCA (2.957 ± 0.615 ; P for interaction<0.001), MMSE (2.114 ± 0.737 ; P for interaction=0.005), and FAB (2.144 ± 0.659 ; P for interaction=0.002).

Prediction of MCID Responders

To identify baseline clinical predictors of treatment response, we performed univariate and multivariate logistic regression analyses, defining response as a ≥ 4 -point reduction in ADAS-cog14 score. Among 78 patients with available 7-month data, 30 (38.46%) were classified as significant responders. However, no baseline clinical variables were significantly associated with treatment response at either 7 or 13 months (all $P > 0.05$).

GCI Questionnaire Results

Of the 97 patients who completed at least one follow-up visit, 86 provided questionnaire data, corresponding to a response rate of 88.66% (86/97, Figure 3A-D). Most respondents had mild disease severity (59.77%). Overall, 50.58% showed at least slight global improvement, and 65.12% were rated as having at least slight treatment effectiveness. Adverse reactions were uncommon and generally mild, with 76.74% reporting no adverse reactions and no severe adverse reactions observed.

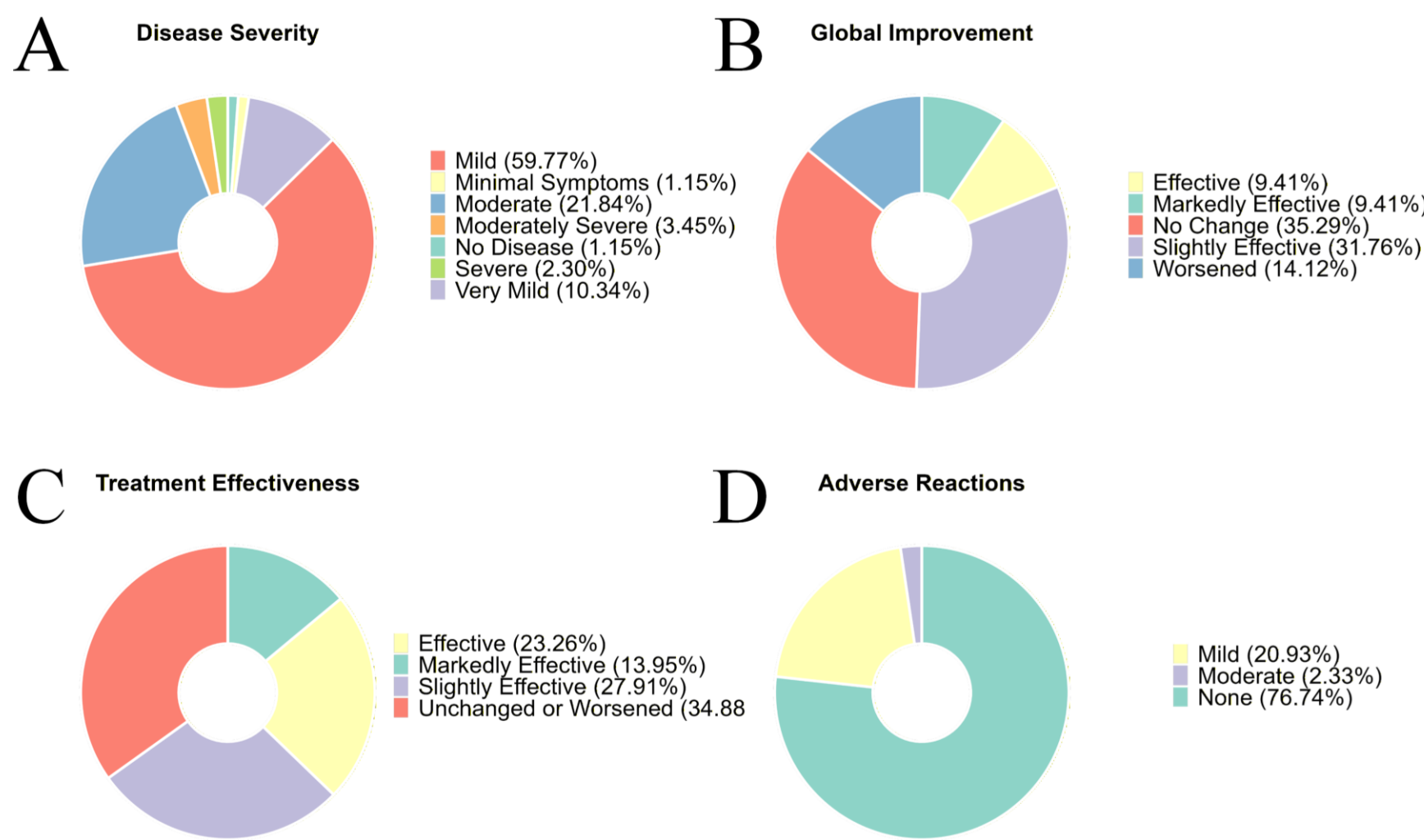


Figure 3. Global Clinical Impression (GCI) questionnaire results (n=86)

Safety and Treatment Discontinuation

ARIA-A/H occurred in 10.73% of patients (13/121), and infusion-related reactions were observed in 5.79% (7/121). Overall, 14 patients discontinued treatment, corresponding to a discontinuation rate of 11.57% (14/121). The main reasons for discontinuation were inconvenience related to frequent hospital visits for infusions (5/14, 35.71%), perceived lack of efficacy (4/14, 28.57%), financial limitations (3/14, 21.43%), and ARIA-related adverse events (2/14, 14.29%).

Conclusion

In this multicenter real-world cohort of Chinese AD patients, long-term lecanemab therapy demonstrated favorable safety, and improved cognition and slowed progression compared with both ADNI natural history cohort and Chinese AD patients. High cerebral amyloid clearance was achieved at 13 months, but no significant correlation with cognitive benefit, and no baseline characteristics were identified as predictors of clinical response.