



Dynamic Changes In Biomarkers And Cognition With Lecanemab In Alzheimer's Disease: A Case Series Study

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Background

- Lecanemab, a monoclonal antibody targeting amyloid-beta, has shown efficacy in global trials for early Alzheimer's disease (AD). However, real-world data on its effects on blood-based biomarkers and clinical outcomes in Chinese patients are limited.

Methods

- This study is a prospective, single-arm, open-label, small case series designed to observe and evaluate the efficacy and safety of Lecanemab in Chinese patients with early-stage Alzheimer's disease (AD). All enrolled patients underwent clinical assessments and blood biomarker tests at baseline (month 0), and Lecanemab treatment at months 3, 6, and 12 to monitor changes in neuropsychological assessment indicators, fluctuations in blood biomarkers, and the occurrence of adverse events.

Results

- After 6 months of treatment, no significant improvement was observed in cognitive scale scores (MMSE, MoCA, CDR-SB) (Table 1).
- Plasma p-tau181, GFAP, and NfL demonstrated a declining trend. This positive change in biomarkers was accompanied by relative stability in the neuropsychological test scores (MMSE, MoCA, CDR-SB). Analysis of blood biomarkers revealed a decrease in p-tau181 levels at 3 months ($p=0.025$) (Table 2).

Table 1. Dynamic Changes of Neuropsychological Scale Scores in 11 Patients with Early -Stage Alzheimer's Disease (Mean $\pm$ Standard Deviation), [Median (Interquartile Range)]

	MoCA	MMSE	CDR	CDR-SB	NPI	iADL
Baseline	19.45 $\pm$ 4.16	16.64 $\pm$ 3.56	0.50 (0.5,0.5)	1.86 $\pm$ 1.47	0.00 (0,2.00)	15.52 $\pm$ 2.40
3months	19.73 $\pm$ 4.27	17.45 $\pm$ 3.33	0.50 (0.5,0.5)	2.27 $\pm$ 1.42	3.00 (0,1.00)	16.00 $\pm$ 2.46
6months	22.25 $\pm$ 5.18	18.88 $\pm$ 4.16	0.50 (0, 0.38)	2.88 $\pm$ 2.71	6.00 (0,2.50)	16.50 $\pm$ 2.84
12months	19.50 $\pm$ 4.27	19.50 $\pm$ 2.08	0.75(0.5,1.00)	2.13 $\pm$ 1.38	3.50 (0,7.00)	18.00 $\pm$ 4.08

Note: MoCA: Montreal Cognitive Assessment; MMSE: Mini - Mental State Examination; CDR: Clinical Dementia Rating; CDR - SB: Clinical Dementia Rating Sum of Boxes; NPI: Neuropsychiatric Inventory; iADL: Instrumental Activities of Daily Living.

Table 2. Dynamic Changes of Blood Biomarkers in 11 Patients with Early – Stage Alzheimer's Disease (Mean $\pm$ Standard Deviation, pg/ml)

	A β 1-40	A β 1-42	A β 1-42/40	p-Tau 181	p-Tau217	GFAP	NfL
Baseline	127.65 $\pm$ 66.03	5.89 $\pm$ 2.66	0.05 $\pm$ 0.017	6.80 $\pm$ 1.89	6.00 $\pm$ 2.66	198.27 $\pm$ 86.91	81.26 $\pm$ 27.01
3months	140.56 $\pm$ 50.63	6.31 $\pm$ 1.67	0.05 $\pm$ 0.006	5.43 $\pm$ 1.35	5.65 $\pm$ 1.44	174.79 $\pm$ 73.82	80.03 $\pm$ 26.22
6months	142.62 $\pm$ 35.76	6.27 $\pm$ 1.82	0.05 $\pm$ 0.004	5.32 $\pm$ 1.50	5.61 $\pm$ 2.90	150.38 $\pm$ 75.16	81.59 $\pm$ 28.70
12months	127.52 $\pm$ 28.19	6.17 $\pm$ 1.49	0.05 $\pm$ 0.005	3.70 $\pm$ 1.26	4.02 $\pm$ 1.76	258.96 $\pm$ 124.37	69.77 $\pm$ 46.15

Note: A β : Amyloid - beta; p - Tau: Phosphorylated Tau; GFAP: Glial Fibrillary Acidic Protein; NfL: Neurofilament Light Chain.

- Moreover, baseline p-tau181 levels showed a negative correlation with MMSE ($r=-0.673$, $P=0.023$) and MoCA ($r=-0.683$, $P=0.020$) scores, suggesting a strong association between Tau pathology burden and the degree of cognitive impairment (Table 3).

Table 3. Correlation between Blood Biomarkers and Neuropsychological Scale Scores in 11Patients with Early - Stage Alzheimer's Disease (r/P Value)

	MMSE (r/P)	MoCA (r/P)	CDR (r/P)	CDR-SB (r/P)	NPI (r/P)	iADL (r/P)
A β 1-40	-0.13/0.69	-0.21/0.54	-0.12/0.73	0.47/0.15	-0.04/0.91	-0.01/0.98
A β 1-42	-0.22/0.51	-0.32/0.33	-0.27/0.43	0.47/0.15	-0.20/0.55	0.16/0.63
A β 1-42/1-40	0.25/0.45	0.23/0.49	-0.05/0.88	-0.29/0.38	-0.07/0.84	0.03/0.94
p-tau181	-0.67/0.02*	-0.68/0.02*	0.17/0.62	0.24/0.49	-0.16/0.64	0.34/0.31
p-tau217	-0.53/0.09	-0.33/0.33	-0.05/0.89	0.10/0.76	-0.28/0.41	0.09/0.79
GFAP	-0.31/0.35	-0.45/0.17	-0.33/0.33	0.48/0.14	-0.55/0.08	0.31/0.35
NfL	0.47/0.89	-0.41/0.22	-0.06/0.99	0.59/0.06	0.25/0.94	0.09/0.79

Note: r:Spearman correlation coefficient; P:P-value;MMSE:Mini-Mental State Examination;MoCA:Montreal Cognitive Assessment;CDR:Clinical Dementia Rating;CDR - SB:Clinical Dementia Rating Sum of Boxes; NPI:Neuropsychiatric Inventory; iADL:Instrumental Activities of Daily Living; *Indicates $P<0.05$.

- Regarding safety, one case of amyloid-related imaging abnormalities (ARIA) was reported, one case had its treatment terminated due to the continuous exacerbation of cognitive symptom, while no infusion-related reactions occurred.

Conclusion

- This case series demonstrates that six months of Lecanemab treatment can reduce plasma p-tau181 levels in patients with early Alzheimer's disease. Although no significant improvement in cognitive function was observed, the positive changes in biomarkers were associated with stabilized cognitive performance. The dynamic changes in p-tau181 correlated with the degree of baseline cognitive impairment, supporting its potential as a biomarker for treatment response. These findings show that lecanemab reduces plasma p-tau181 levels, providing important evidence for optimizing the management strategy of disease-modifying therapies in AD.