



Rapid Reduction of Plasma Oligomeric Amyloid Beta as a Target Engagement Biomarker for Lecanemab Treatment

Pan-Woo KO¹,

1. Department of Neurology, Kyungpook National University, School of Medicine, Daegu, Korea

Background and Objective

Lecanemab, a monoclonal antibody targeting amyloid- β (A β) protofibrils, slows decline in early Alzheimer's disease (AD). While amyloid PET confirms pathology, accessible blood-based markers are urgently needed to monitor target engagement in routine clinical practice.

The Multimer Detection System–Oligomeric A β (MDS-OA β , PeopleBio Inc.) selectively measures the oligomerization tendency of plasma A β — a key pathogenic feature, as oligomeric A β is regarded as the most neurotoxic species.

We assessed the utility of MDS-OA β as a pharmacodynamic monitoring biomarker by tracking its change during the initial phase of lecanemab therapy.

Methods

Design. Prospective, single-arm, before–after study.

Patients. 10 patients with early AD (MCI or mild dementia), all amyloid-positive on [¹⁸F]florapronol (Alzavue) PET/CT.

Treatment. Lecanemab 10 mg/kg IV every 2 weeks.

Biomarker. Plasma MDS-OA β quantified at baseline and after the 5th dose (10 weeks).

Reference ranges (diagnostic): <0.78 low · 0.78–0.92 borderline · >0.92 high ng/mL.

Analysis. Paired t-test for the change in MDS-OA β . Safety monitored by brain MRI for amyloid-related imaging abnormalities (ARIA).

Table. Baseline Characteristics.

Characteristic	Value
No. of patients	10
Age, years	68.4 ± 8.4
Female sex	9 (90%)
BMI, kg/m ²	22.4 ± 3.0
APOE ϵ 4 carrier	6 (60%)
E3/E3 · E3/E4 · E4/E4	4 · 5 · 1
Hypertension	3 (30%)
Diabetes mellitus	2 (20%)
Dyslipidemia	3 (30%)
Chronic renal failure	1 (10%)
MMSE score	24.1 ± 3.0
CDR 0.5 · 1.0	6 (60%) · 4 (40%)
GDS score	3.4 ± 0.8
Lecanemab dose, mg	450 ± 53

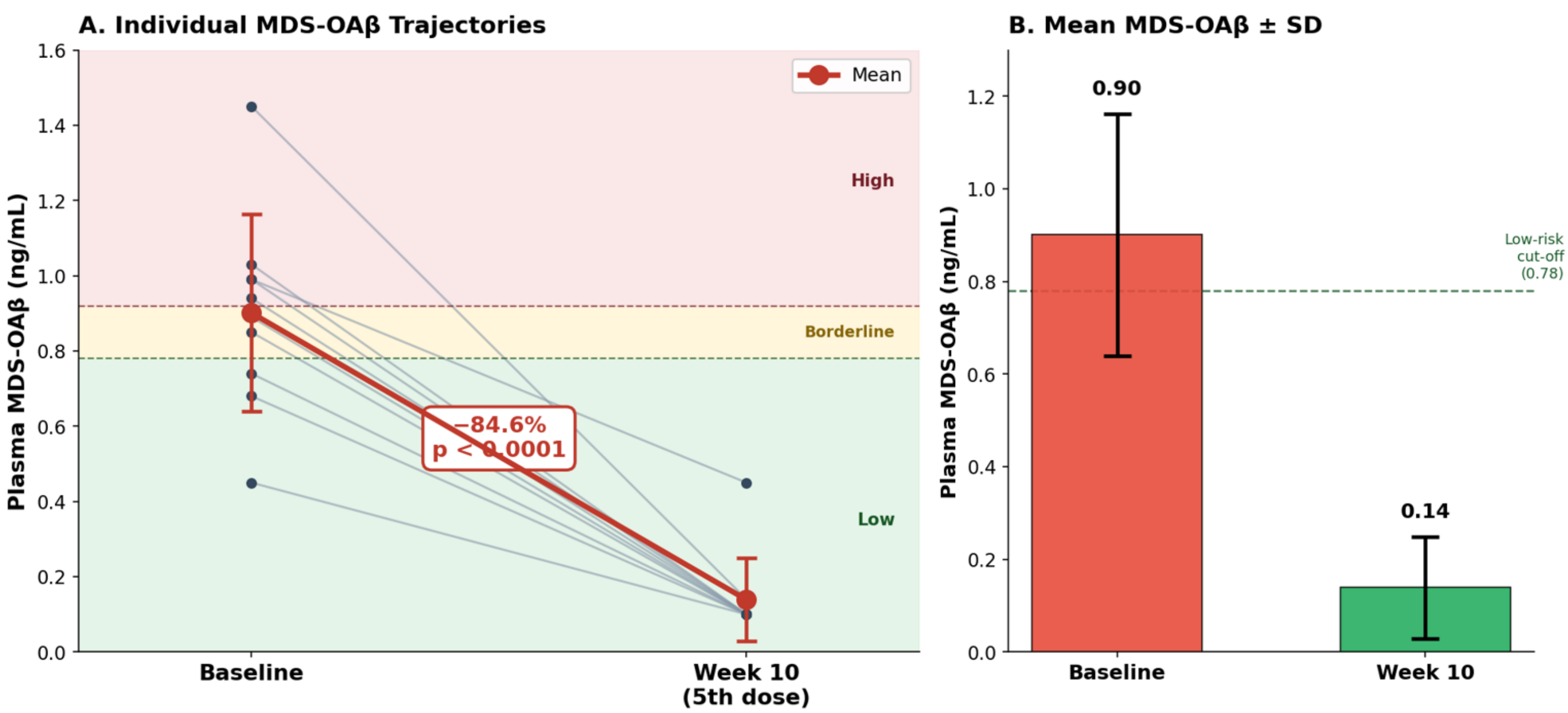


Figure. Baseline plasma MDS-OA β was 0.90 ± 0.26 ng/mL (high-risk profile). After 5 doses it fell to 0.14 ± 0.11 ng/mL (mean difference −0.76 ng/mL; p < 0.0001). Every patient showed a reduction, and all reached the low-risk range — consistent with effective clearance or neutralization of toxic oligomers.

Results and Conclusion

The mean age of participants was 68.4 ± 8.4 years (90% female), with 60% being APOE ϵ 4 carriers. Baseline clinical status indicated early-stage disease (mean MMSE 24.1 ± 3.0; CDR 0.5 in 60%). At baseline, the mean plasma MDS-OA β level was 0.90 ± 0.26 ng/ml, indicative of a high-risk profile. Following 10 weeks of treatment (5 doses), MDS-OA β levels significantly decreased to 0.14 ± 0.11 ng/ml (Mean Difference: -0.76 ng/ml; p < 0.0001). Notably, all patients (100%) exhibited a reduction in MDS-OA β levels to within the low-risk range (<0.78 ng/ml), suggesting effective clearance or neutralization of toxic oligomers. No symptomatic ARIA was observed.

Conclusions

Lecanemab treatment induced a rapid and significant reduction in plasma oligomeric A β levels measured by MDS-OA β within just 10 weeks. The normalization of oligomerization tendency in all patients provides robust evidence of target engagement. These findings suggest that MDS-OA β is a sensitive, non-invasive biomarker for monitoring early pharmacodynamic effects, potentially complementing amyloid PET in managing early AD patients.