

Utility of Cerebrospinal Fluid and Positron Emission Tomography Biomarkers in Patients Receiving β -Amyloid Immunotherapy

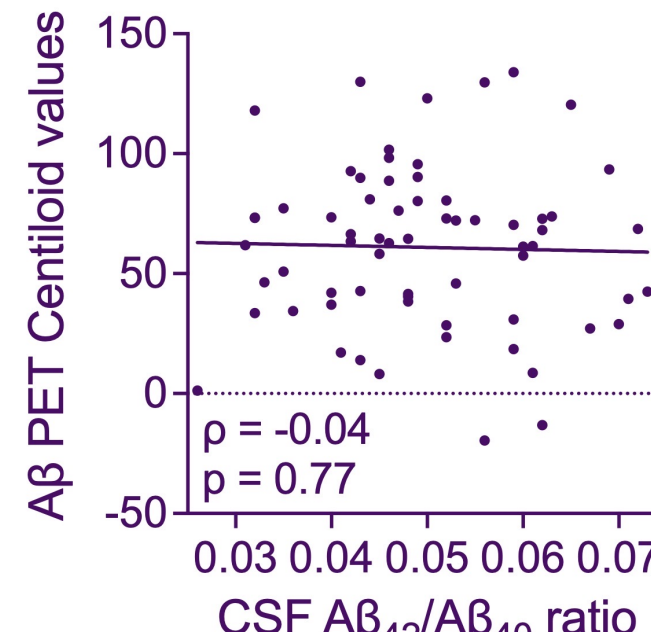
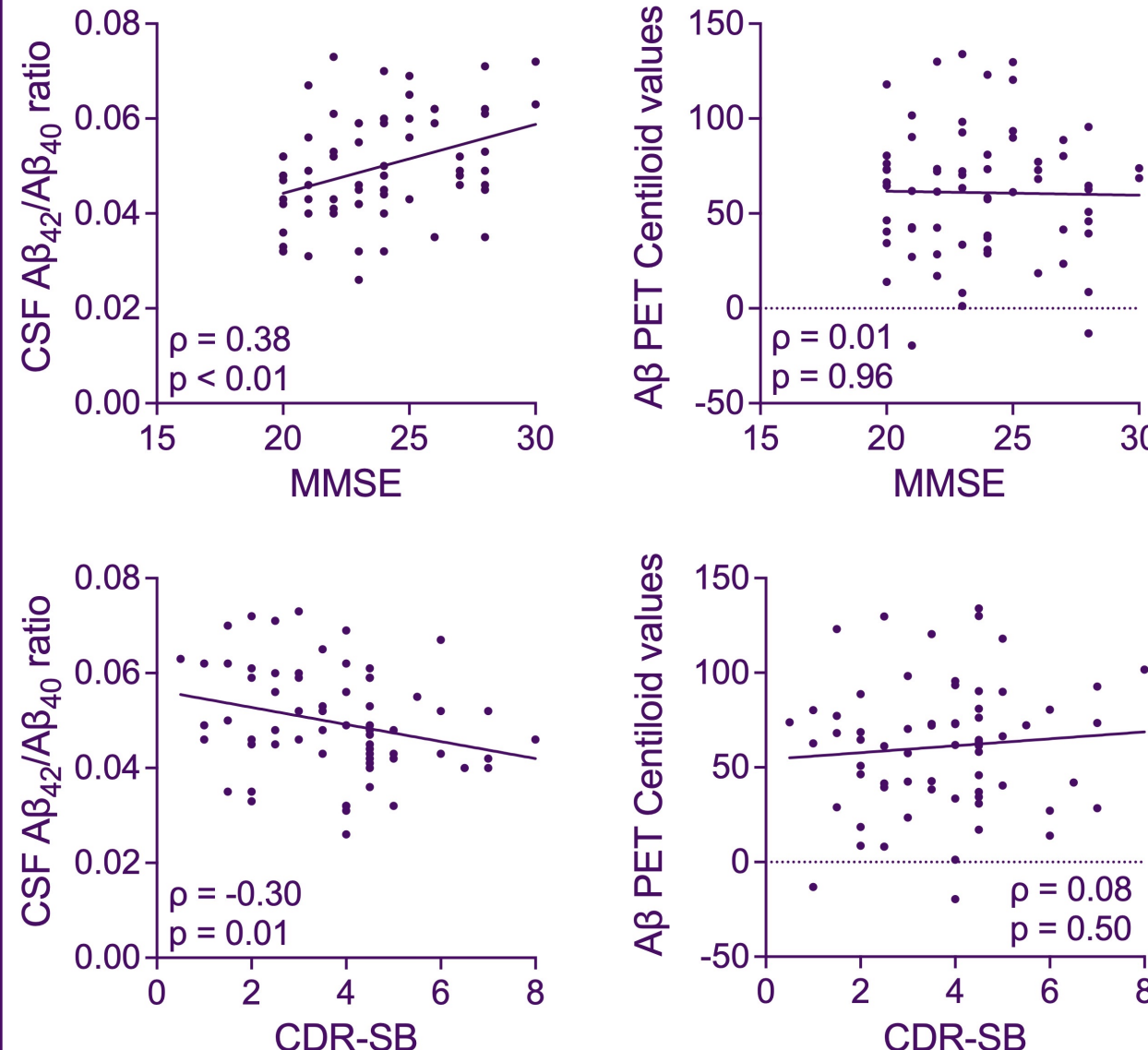
P2-06

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- The CSF $A\beta_{42}/A\beta_{40}$ ratio was more strongly associated with clinical severity than amyloid PET Centiloid values.
- CSF biomarkers could provide complementary clinical information when evaluating patients for β -amyloid immunotherapy.
- Soluble $A\beta$ pathology may play a prominent role in clinical disease severity in patients receiving β -amyloid immunotherapy.

INTRODUCTION	METHODS	RESULTS	DISCUSSION CONCLUSIONS																					
Amyloid-targeting therapy (ATT), including lecanemab and donanemab, is now used for Alzheimer’s disease (AD). In Japan, both amyloid PET and CSF Aβ analysis are used to determine eligibility for ATT. Iwata. <i>J Prev Alzheimers Dis.</i> 2026 Amyloid PET reflects fibrillar amyloid plaque burden, whereas the CSF Aβ₄₂/Aβ₄₀ ratio may reflect soluble Aβ pathology. This study aimed to evaluate how the CSF Aβ₄₂/Aβ₄₀ ratio and amyloid PET Centiloid values relate to cognitive and clinical severity in patients initiating ATT.	Single-center, hospital-based, cross-sectional study. We analyzed pretreatment data from patients with mild cognitive impairment or mild dementia due to AD before the initiation of lecanemab or donanemab. CSF Aβ concentrations were measured using Lumipulse Aβ assays. Associations of neuropsychological test scores with the CSF Aβ₄₂/Aβ₄₀ ratio and amyloid PET Centiloid values were assessed using Spearman correlation and linear regression analyses.	Patient characteristics (n = 66) n (%) or median (IQR) <table><tr><td>Age, y</td><td>78.5 (76–83)</td></tr><tr><td>Male</td><td>20 (30.3)</td></tr><tr><td>MMSE</td><td>23 (21–26)</td></tr><tr><td>CDR global score</td><td>0.5 (0.5–1)</td></tr><tr><td>CDR SB</td><td>4 (2.5–4.5)</td></tr><tr><td>APOE genotype</td><td></td></tr><tr><td> ε4 heterozygote</td><td>28 (42.4)</td></tr><tr><td> ε4 homozygote</td><td>5 (7.6)</td></tr><tr><td>CSF Aβ₄₂/Aβ₄₀ ratio</td><td>0.048 (0.042–0.059)</td></tr><tr><td>Amyloid PET Centiloid value</td><td>64.0 (38.7–79.5)</td></tr></table> Associations between CSF and PET biomarkers 	Age, y	78.5 (76–83)	Male	20 (30.3)	MMSE	23 (21–26)	CDR global score	0.5 (0.5–1)	CDR SB	4 (2.5–4.5)	APOE genotype		ε4 heterozygote	28 (42.4)	ε4 homozygote	5 (7.6)	CSF Aβ ₄₂ /Aβ ₄₀ ratio	0.048 (0.042–0.059)	Amyloid PET Centiloid value	64.0 (38.7–79.5)	Associations with cognitive tests  In linear regression analyses, the CSF Aβ₄₂/Aβ₄₀ ratio, but not amyloid PET Centiloid values, was significantly associated with MMSE scores (p < 0.01) and CDR-SB (p < 0.05) after adjusting for age, sex, and APOE genotype.	The CSF Aβ₄₂/Aβ₄₀ ratio reflects brain levels of soluble Aβ rather than insoluble Aβ burden. Andersson. <i>Nat Aging.</i> 2025 Cognitive impairment in patients receiving ATT may therefore be more strongly influenced by soluble Aβ pathology than by amyloid plaque burden. CONTACT Satoshi SAITO, MD, PhD saitou.satoshi.43m@kyoto-u.jp  Department of Neurology, National Cerebral and Cardiovascular Center COI: Lecture fees from Eli Lilly, Eisai, Kowa, Otsuka, Daiichi Sankyo, and PDR Pharma. ALZHEIMER’S ASSOCIATION AAIC 26
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