

Diagnostic Utility of Plasma p-tau217 for Detecting Cerebral Amyloid A Real-World Multicenter Japanese Memory-Clinic Cohort Study

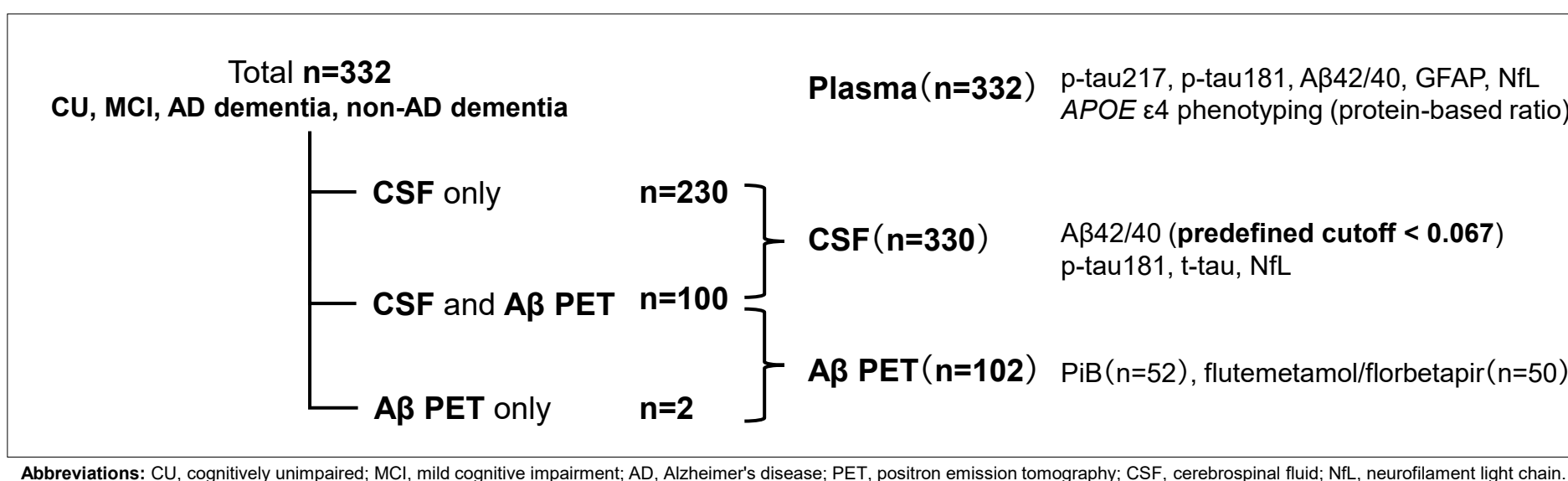
Takanobu Ishiguro¹ Masanori Kurihara² Yoichiro Nishida³ Emiko Kikkawa-Saito⁴ Kensaku Kasuga^{1,5} Naoto Takenoshita⁶ Satomi Kubota⁷
Yasuko Kuroha⁸ Kenji Ishii² Meiko Hamada³ Nobuo Sanjo^{3,9} Kinya Ishikawa³ Hisashi Nojima⁴ Jo Kamada⁴ Katsumi Aoyagi⁴ Soichiro Shimizu⁶
Hidetomo Murakami⁷ Tetsuya Takahashi⁸ Osamu Onodera¹ Takeshi Iwatsubo^{10,11} Masahito Yamada^{3,9} Takanori Yokota³ Atsushi Iwata² Takeshi Ikeuchi¹

¹Brain Research Institute, Niigata University, Niigata, Japan, ²Tokyo Metropolitan Institute for Geriatrics and Gerontology, Tokyo, Japan, ³Institute of Science Tokyo, Tokyo, Japan, ⁴FUJIREBIO INC., Tokyo, Japan
⁵Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, Aichi, Japan, ⁶Tokyo Medical University, Tokyo, Japan, ⁷Showa Medical University, Tokyo, Japan
⁸NHO Nishiniigata Chuo Hospital, Niigata, Japan, ⁹Kudanzaka Hospital, Tokyo, Japan, ¹⁰National Institute of Neuroscience, National Center of Neurology and Psychiatry, Tokyo, Japan, ¹¹The University of Tokyo Hospital, Tokyo, Japan.

Objective

- ✓ To evaluate the real-world diagnostic performance and clinical applicability of plasma p-tau217 [1-3] in a multicenter Japanese memory clinic cohort.

Methods



- ✓ Plasma and cerebrospinal fluid (CSF) biomarkers were measured using the LUMIPULSE G1200® system (Fujirebio, Japan).
- ✓ Amyloid pathology (A+) was determined by visual assessment of amyloid PET (local read) and/or CSF Aβ42/40 ratio (< 0.067 [4]).
- ✓ 1-point cutoffs were defined using the Youden index, and a 2-point cutoff approach [5] was applied to achieve ≥90% sensitivity and specificity.
- ✓ The study was approved by the institutional review board of Niigata University (2023-0087).

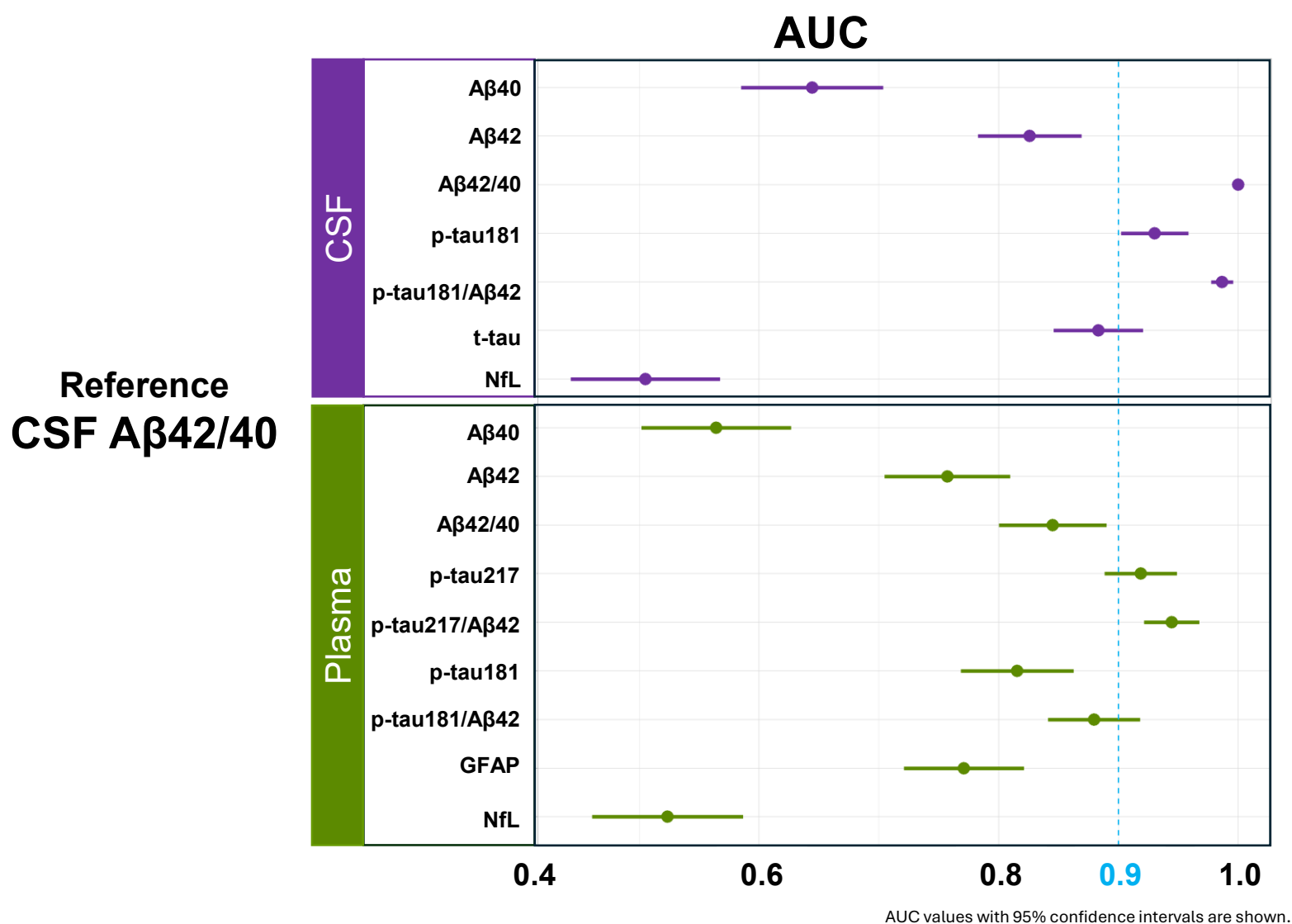
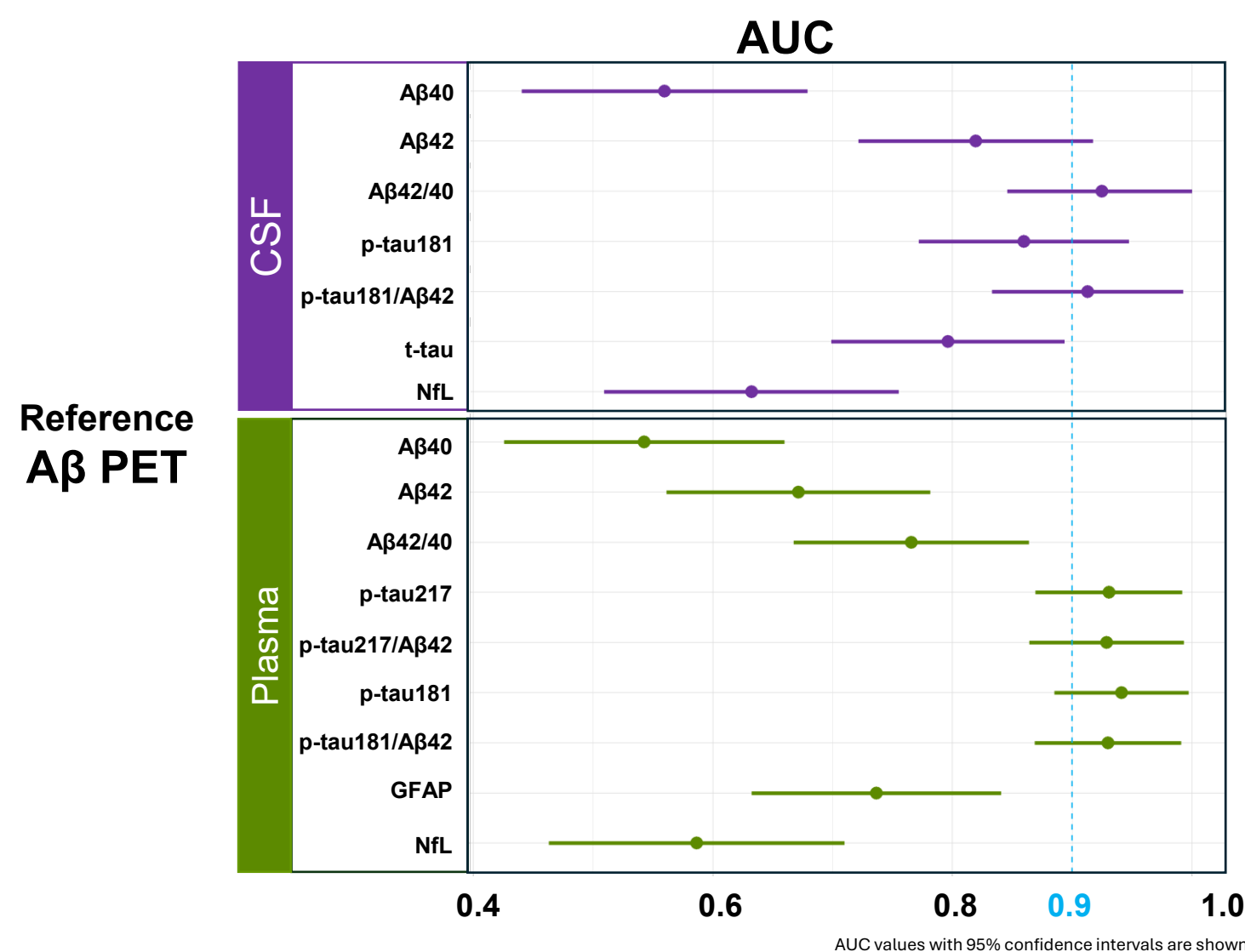
Results

1. Demographics

	ALL N = 332	CU n = 98	MCI n = 61	ADD n = 61	non-ADD n = 112	p-value*
Age	73 [63, 79]	74 [62, 79]	73 [68, 79]	66 [56, 76]	74 [68, 80]	<0.01
Female, n (%)	167 (50%)	41 (42%)	37 (61%)	34 (56%)	55 (49%)	0.100
MMSE	25 [21, 28]	28 [26, 30]	27 [24, 28]	21 [17, 23]	23 [17, 27]	<0.001
APOE ε4 alleles, n (%)						<0.001
0	227 (68%)	74 (76%)	33 (54%)	34 (56%)	86 (77%)	
1	90 (27%)	24 (24%)	24 (39%)	19 (31%)	23 (21%)	
2	15 (4.5%)	0 (0%)	4 (6.6%)	8 (13%)	3 (2.7%)	
Amyloid positivity (%)						
PET A+	58%	20%	88%	89%	7.7%	<0.001
CSF A+	41%	13%	66%	87%	27%	<0.001

Data are shown in median [Q1, Q3]; n (%).
*Kruskal-Wallis rank sum test; Pearson's Chi-squared test

2. Diagnostic performance of plasma biomarkers



3. Determination of cutoff values

1-point cutoffs

Biomarker	Cutoff	Sen (%)	Spe (%)	OPA (%)	NPV (%)	PPV (%)
p-tau217 (pg/mL)	0.212	84 (77, 89)	91 (86, 94)	88 (84, 91)	89 (84, 93)	87 (80, 92)
p-tau217/Aβ42	0.007	90 (84, 94)	88 (83, 92)	89 (85, 92)	93 (88, 96)	84 (77, 89)

Abbreviations: AUC, area under the curve; Sen, sensitivity; Spe, specificity; OPA, overall percent agreement; NPV, negative predictive value; PPV, positive predictive value.

2-point cutoffs

Cutoff determination	Biomarker	Cutoffs High Low	Sen (%)	Spe (%)	OPA (%)	NPV (%)	PPV (%)	Intermediate zone (%)
Sen 90% Spe 90%	p-tau217 (pg/mL)	0.247 0.134	90 (84, 95)	90 (84, 94)	90 (86, 93)	93 (88, 96)	87 (79, 92)	15
	p-tau217/Aβ42	0.00700 0.00613	90 (83, 94)	90 (85, 94)	90 (86, 93)	93 (88, 96)	87 (80, 91)	3
FDA-approved cutoff	p-tau217/Aβ42	0.00738 0.00370	98 (94, 100)	89 (83, 93)	93 (89, 96)	98 (95, 100)	88 (81, 92)	20

Abbreviations: AUC, area under the curve; Sen, sensitivity; Spe, specificity; OPA, overall percent agreement; NPV, negative predictive value; PPV, positive predictive value.

- ✓ Analyses were performed in participants with a consistent amyloid status based on amyloid PET and/or CSF Aβ42/40 (n=324), excluding 8 PET–CSF discordant cases.
- ✓ 1-point cutoffs were defined using the Youden index, whereas 2-point cutoffs were set to achieve at least 90% sensitivity and 90% specificity.

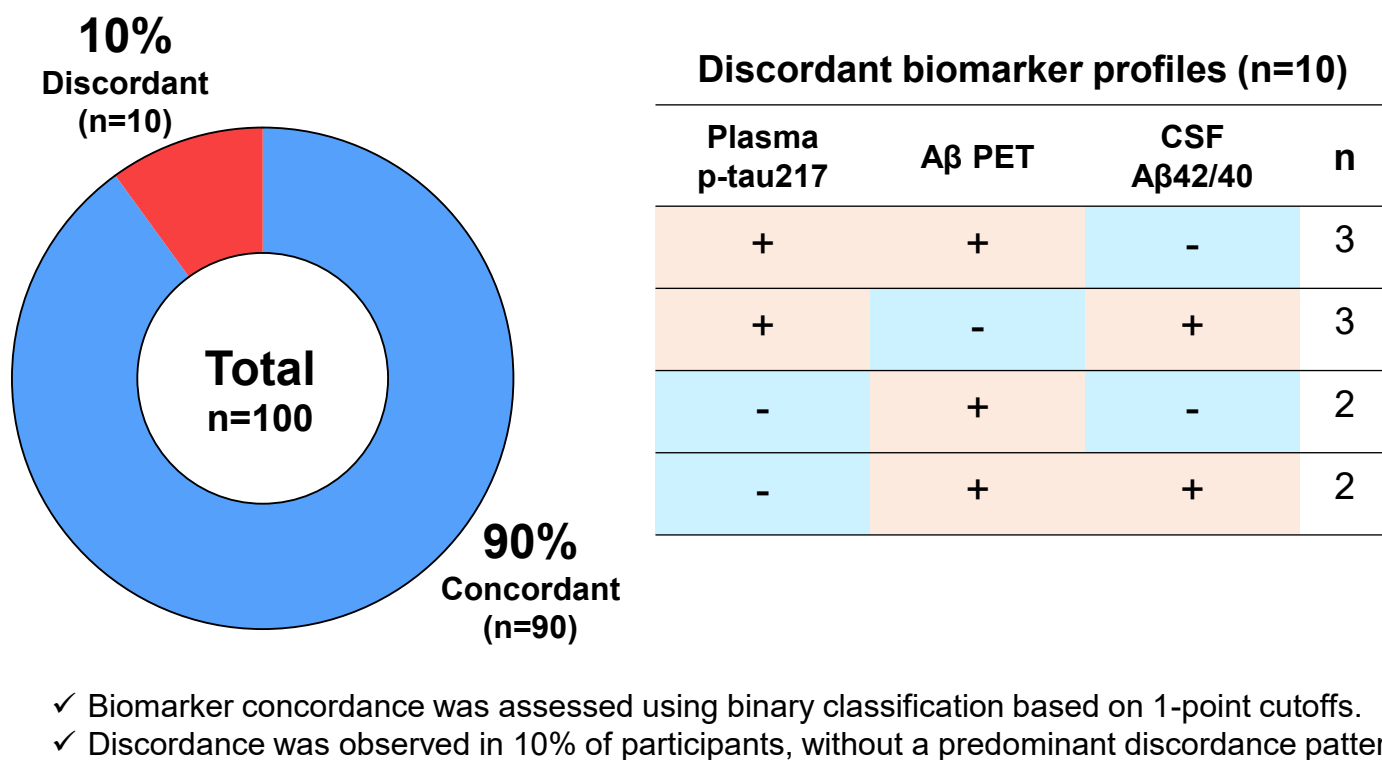
4. Application of 2-point cutoffs and biomarker discordance in participants with plasma p-tau217, Aβ PET, and CSF data (n=100)

A. Classification and amyloid positivity using 2-point cutoffs

Biomarker	Classification (%)	Amyloid positivity (%)	
		Aβ PET	CSF Aβ42/40
p-tau217	Positive	51	94
	Intermediate	9	89
	Negative	40	7
p-tau217/Aβ42	Positive	58	95
	Intermediate	2	50
	Negative	40	7
p-tau217/Aβ42 (FDA-approved cutoff)	Positive	58	95
	Intermediate	9	22
	Negative	33	6

- ✓ Analysis included 100 participants with plasma, amyloid PET and CSF available.

B. Biomarker concordance and discordance using 1-point cutoffs



Conclusions

- ✓ Plasma p-tau217 demonstrated high diagnostic performance for detecting Aβ pathology in a Japanese multicenter, real-world memory-clinic cohort.
- ✓ Further studies are needed to evaluate biological confounders, such as renal dysfunction [6], and to better characterize biomarker-discordant cases.

References

- Schöll M, et al. *J Prev Alzheimers Dis*. 2025.
- Barthélemy NR, et al. *Nat Med*. 2024.
- Palmqvist S, et al. *JAMA*. 2024.
- Nojima H, et al. *Ann Clin Transl Neurol*. 2022.
- Brum WS, et al. *Nat Aging*. 2023.
- Yun J, et al. *JAMA Neurol*. 2026.

Conflict of Interest:

The presenter has received research support from
FUJIREBIO INC.
Presenter: Takanobu Ishiguro