

Differential roles of A β 42/40, p-tau231 and p-tau217 for Alzheimer's trial selection and disease monitoring

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Supplementary Table 1. Uncorrected p-values from Table 1 (Associations of A β status with longitudinal plasma biomarker levels in BioFINDER-1 and WRAP).

	BioFINDER-1 Cognitively unimpaired	BioFINDER-1 Mild cognitive impairment	WRAP Cognitively unimpaired
Plasma biomarkers	uncorrected p-value		
p-tau231	0.946	0.364	0.951
p-tau217	3.1×10^{-14}	0.0002	9.0×10^{-9}
p-tau181	0.033	0.304	0.021
A β 42/40	0.806	0.103	0.317
GFAP	0.049	0.030	0.204
NfL	0.184	0.118	0.228

Supplementary Table 2. Uncorrected p-values from Table 2 (Associations between longitudinal plasma biomarkers and longitudinal mini mental state examination (MMSE), modified Preclinical Alzheimer's Cognitive Composite (mPACC), and cortical thickness of the typical AD signature regions in A β positive cognitively unimpaired participants in BioFINDER-1 and WRAP).

	BioFINDER-1			WRAP		
	MMSE	mPACC	Cortical thickness of the typical AD signature regions	MMSE	mPACC	Cortical thickness of the typical AD signature regions
Plasma biomarkers	uncorrected p-value					
p-tau231	0.179	0.456	0.182	0.491	0.356	0.363
p-tau217	0.0001	0.0001	6.9×10^{-6}	0.0005	1.5×10^{-7}	0.003
p-tau181	0.023	0.158	0.025	0.072	0.159	0.099
A β 42/40	0.910	0.382	0.505	0.734	0.140	0.204
GFAP	0.029	0.112	0.013	0.754	0.745	0.026
NfL	0.053	0.073	0.191	0.264	0.253	0.011

Supplementary Table 3. Associations of plasma biomarkers with CSF A β 42/40 (excluding plasma p-tau values below the detection limit) in BioFINDER-1 (cohort 1).

Plasma biomarkers	AUC, 95% CI	p-value corrected (uncorrected)	AIC
Cognitively unimpaired (Aβ+ / Aβ-, 95/162)			
P-tau231	0.883 (0.844-0.923)	NA	226.8
A β 42/40	0.861 (0.817-0.906)	0.43 (0.43)	237.1
P-tau217	0.800 (0.742-0.858)	0.016 (0.013)	256.2
P-tau181	0.737 (0.675-0.800)	4.0x10 ⁻⁵ (1.6x10 ⁻⁵)	300.0
GFAP	0.727 (0.663-0.792)	0.0001 (2.9x10 ⁻⁵)	324.1
NfL	0.594 (0.524-0.664)	2.3x10 ⁻¹² (4.5x10 ⁻¹³)	338.7
Mild cognitive impairment (Aβ+ / Aβ-, 111/49)			
P-tau231	0.936 (0.895-0.976)	NA	99.2
P-tau217	0.874 (0.814-0.933)	0.10 (0.09)	139.2
P-tau181	0.826 (0.760-0.893)	0.005 (0.004)	153.5
A β 42/40	0.777 (0.689-0.864)	0.001 (0.0007)	163.1
GFAP	0.723 (0.635-0.811)	1.3x10 ⁻⁵ (4.0x10 ⁻⁶)	184.5
NfL	0.512 (0.406-0.617)	2.3x10 ⁻¹² (3.4x10 ⁻¹³)	200.9

Supplementary Table 4. P-values for biomarkers comparisons in Figure 1 excluding plasma p-tau values below the detection limit).

	p-tau231	p-tau217	P-tau181	A β 42/40	GFAP	NfL
Q0 (CL <12) ^a	NA	NA	NA	NA	NA	NA
Q1 (CL 12.0-35.9)	3.0e-09 (3.0e-09)	0.402 (0.402)	0.588 (0.588)	0.0447 (0.0447)	0.550 (0.550)	0.906 (0.906)
Q2 (CL 35.9-71.7)	2.3e-10 (1.4e-10)	4.0e-06 (3.0e-06)	0.0002 (0.0001)	1.0e-08 (7.8e-09)	0.0034 (0.0025)	0.721 (0.541)
Q3 (CL 71.7-95.3)	2.3e-10 (1.7e-10)	6.9e-12 (3.5e-12)	4.4e-10 (2.2e-10)	1.3e-09 (3.2e-10)	3.0e-07 (7.4e-08)	0.140 (0.051)
Q4 (CL >95.3)	2.0e-12 (5.1e-13)	1.1e-17 (2.7e-18)	5.5e-12 (1.4e-12)	1.5e-09 (7.3e-10)	8.0e-06 (4.0e-06)	0.140 (0.070)

^a Reference group

Supplementary Table 5. Associations of A β status with longitudinal plasma biomarker levels (excluding plasma p-tau values below the detection limit) in BioFINDER-1 (cohort 2).

Plasma biomarkers	time $\times$ A β interaction β -estimate	time $\times$ A β interaction p-value corrected (uncorrected)
Cognitively unimpaired		
p-tau231	0.005	0.882 (0.882)
p-tau217	0.260	3.9x10 ⁻¹¹ (3.3x10 ⁻¹²)
p-tau181	0.078	0.008 (0.004)
A β 42/40	0.007	0.841 (0.806)
GFAP	0.028	0.084 (0.049)
NfL	0.035	0.246 (0.184)
Mild cognitive impairment		
p-tau231	-0.073	0.384 (0.304)
p-tau217	0.279	0.001 (0.0005)
p-tau181	0.054	0.395 (0.329)
A β 42/40	-0.076	0.165 (0.103)
GFAP	0.113	0.059 (0.030)
NfL	0.084	0.177 (0.118)

Supplementary Table 6. Associations between longitudinal plasma biomarkers and longitudinal mini mental state examination (MMSE), modified Preclinical Alzheimer's Cognitive Composite (mPACC) and cortical thickness of the typical AD signature regions in A β positive cognitively unimpaired participants (excluding plasma p-tau values below the detection limit) in BioFINDER-1 (cohort 2).

	MMSE		mPACC		Word list delayed recall		Cortical thickness of the typical AD signature regions	
	β -estimate	p-value corrected (uncorrected)	β -estimate	p-value corrected (uncorrected)	β -estimate	p-value corrected (uncorrected)	β -estimate	p-value corrected (uncorrected)
Plasma biomarkers								
p-tau231	-0.099	0.227 (0.189)	-0.021	0.528 (0.481)	0.006	0.867 (0.846)	-0.003	0.246 (0.205)
p-tau217	-0.310	0.001 (0.0002)	-0.124	0.001 (0.0002)	0.094	0.028 (0.005)	-0.012	7.6x10 ⁻⁵ (1.3x10 ⁻⁵)
p-tau181	-0.121	0.182 (0.121)	-0.012	0.528 (0.528)	0.011	0.867 (0.723)	-0.004	0.246 (0.197)
A β 42/40	-0.010	0.910 (0.910)	0.032	0.528 (0.382)	0.014	0.867 (0.700)	0.002	0.505 (0.505)
GFAP	-0.198	0.087 (0.029)	-0.054	0.223 (0.112)	-0.006	0.867 (0.867)	-0.007	0.040 (0.013)
NfL	-0.194	0.107 (0.053)	-0.067	0.220 (0.073)	0.054	0.474 (0.158)	-0.004	0.246 (0.191)