

Evaluation of the clinical performance of p-tau217 in plasma using the analytical platform cobas-8000 for the study of Alzheimer's Disease

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INTRODUCTION	METHODS	RESULTS
Automated immunoassays have been developed to quantify biomarkers in plasma, with the aim of reducing invasive tests, hospital costs, diagnostic time, and facilitating the selection of candidates for disease-modifying treatments. In this context, p-tau217 has demonstrated high diagnostic sensitivity (Se) and specificity (Sp). Latest recommendations suggest establishing a lower cut-off with high Se and negative predictive value (NPV) ≥90%, and a higher cut-off with high Sp and positive predictive value (PPV) ≥90%, while maintaining an indeterminate zone <15–30% of individuals. This strategy enables ruling out or confirming AD-related pathology with high probability. For this purpose, we evaluated the diagnostic performance of the Elecsys®Phospho-Tau217 immunoassay.	A retrospective study was conducted on 81 patients with cognitive impairment from the neurology department, classified as non-AD (Aβ-) (n=27) and AD (Aβ+) (n=54) based on CSF p-tau181/Aβ(1-42) ratio (<0.023) and clinical evaluation. Aβ+ patients were subclassified using the Global Deterioration Scale (GDS) into GDS3 (n=30) and GDS4 (n=24) (Table1). EDTA-K2 samples were collected and stored at -80°C until analysis. Plasma p-tau217 was measured by electrochemiluminescence using the Elecsys®Phospho-Tau217 assay on the Cobas-8000-e801 platform (Roche Diagnostics®). Statistical analyses included group comparisons and ROC analysis; AUC, Se, Sp, PPV, and NPV were calculated for the proposed cut-offs.	ROC analysis yielded an AUC of 0.9822. The cut-offs identified with the highest Se and Sp were <0.262 pg/mL (NPV 100%) and >0.386 pg/mL (PPV 97.8%) (Table2), with an indeterminate zone of 13.6%. CONCLUSIONS Quantification of p-tau217 in plasma allows for a robust classification of patients in Aβ- or Aβ+. Establishing stricter cut-off values could optimize the NPV/PPV, although it would increase the proportion of indeterminate results. Therefore, it would be advisable to verify the cut-off values in independent cohorts in clinical practice. The Elecsys®Phospho-Tau217 assay is presented as a valid tool for incorporation into the clinical laboratory in the study of AD.

	Aβ- (n=27)	Aβ+ (n=54)		p-value
		GDS3 (n=30)	GDS4 (n=24)	
Sex(M,%)	14(51.85%)	13(43.33%)	6(25%)	0.140
Age(years)	70.56 ± 10.31	77.33 ± 6.95	74.04 ± 8.81	0.017
CFS p-tau181/Aβ42	0.013±0.007	0.0765±0.058	0.085±0.050	<0.001
Plasma p-tau217(pg/ml)	0.211±0.066	0.750±0.559	1.030±0.341	<0.001

Table1. Demographics and biomarker concentrations from the study cohort. Age is presented as mean ± SD; biomarkers as median (IQR).

		Se(%)	Sp(%)	YI	PPV(%)	NPV(%) _a	Diagnostic agreement(%)	Indeterminate zone (%)	FP (%)	FN (%)
Cut-off (pg/mL)	0.262	100	88.89	0.889	94.7	100	85.2	13.6	0.9	-
	0.386	85.19	96.30	0.815	97.8	74.3				

Table2. Representative plasma p-tau217 cutoffs and their corresponding diagnostic performance.

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