



# Discordance of plasma pTau-217 levels with amyloid PET and CSF biomarkers in subjects with cognitive decline: a single center study

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## Background

Detection of cerebral  $\beta$ -amyloid plaques ( $A\beta^*$ ) is essential for the diagnosis and therapeutic management of Alzheimer's disease (AD). Although amyloid PET and CSF biomarkers offer high diagnostic accuracy in early AD, their invasiveness, cost and limited availability restrict widespread implementation. Plasma phosphorylated tau at threonine 217 (pTau-217) has emerged as a promising blood-based biomarker for AD.

## Aim

To evaluate the diagnostic performance of plasma pTau-217 in comparison with CSF biomarkers and amyloid PET imaging in patients with cognitive impairment in routine clinical practice.

## Methods

Seventy-one patients (mean age: 65.3 years, F/M=0.9/1) referred to our Memory Clinic for cognitive evaluation were prospectively enrolled. AD diagnosis was established through clinical assessment, supported by CSF biomarker profiling and amyloid PET imaging. pTau-217 levels were quantified using the LUMIPULSE<sup>®</sup> G1200 platform on K2-EDTA plasma. A double-threshold model was employed to stratify patients into high-, intermediate- and low-risk categories. The optimal cut-off value for pTau-217 was defined between 0.22 and 0.34, based on literature (1)

## Results

pTau-217 levels were below the lower cut-off value in 35 patients, higher than the upper cutoff in 26 patients; 13% patients had an intermediate level (Figure 2). Plasma pTau-217 demonstrated high concordance with both PET and CSF findings. Agreement with amyloid PET positivity was 87% and with CSF  $A\beta^*$  status was 95%. Mean level of pTau-217 in CSF +/- and amy-PET +/- are shown in Figure 1. No correlation was found between pTau-217 levels and renal function (serum creatinine and glomerular filtration rate). Within the amyloid-positive group, there was a significant correlation between higher pTau-217 levels and younger age (PET  $A\beta^*$  patients, Spearman's rho = -0.5260, p = 0.0143; CSF- $A\beta^*$  patients, Spearman's rho = -0.7223, p = 0.0001).

Eleven patients showed discordant pTau217 with PET- or CSF- $A\beta$  findings: three patients were pTau-217 negative and CSF positive, all with CAA pathology. Eight patients were pTau-217/PET $A\beta^*$ , three of whom were diagnosed with cerebral amyloid angiopathy, suggesting the potential influence of non-parenchymal amyloid pathology on PET interpretation.

## Conclusion

In this real-world clinical cohort, plasma pTau-217 demonstrated robust diagnostic performance and substantial agreement with CSF and PET biomarkers. These findings support its clinical utility as a non-invasive, cost-effective, and scalable tool in the diagnostic work-up of patients with cognitive impairment. Discordant cases highlight the complexity of AD diagnosis, AD-copathology and different dynamic of amyloid concentrations in different compartments. A comprehensive diagnostic framework—considering comorbid conditions and the possible application of a dual-threshold for pTau-217—may enhance diagnostic precision in challenging cases.

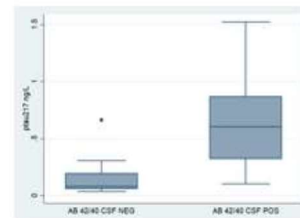


Fig 1: correlation between ptau217 levels and CSF Ab findings

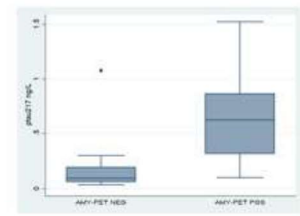


Fig 2: correlation between ptau217 levels and PET Ab findings

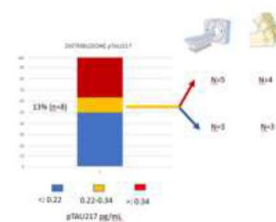


Fig 3: distribution of p-tau 217 levels

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