Dec. 8th, 2025

Sysmex Corporation

【Overview presentation】

The 18th Clinical Trials on Alzheimer's Disease conference (CTAD)

High diagnostic performance of the random-access HISCL-5000 pTau217, Aβ42 and Aβ40 plasma assays for detecting amyloid pathology across the Alzheimer's disease clinical continuum.

Authors	Inge Verberk[1], Daniel Antwi-Berko[1], Thomas Claessen[2], Hans Heijst[1], Azzam Aladdin[1], Yuko Sasaki Mori[3], Roman Boeer[4], Argonde Van Harten[2], Charlotte Teunissen[1] [1]Neurochemistry Laboratory, Laboratory Medicine, Amsterdam UMC - Amsterdam (Netherlands) [2]Alzheimer Center Amsterdam, Neurology, Amsterdam UMC - Amsterdam (Netherlands) [3]Sysmex R&D Center Europe GmbH - Hamburg (Germany) [4]Neurochemistry Laboratory, Laboratory Medicine, Amsterdam UMC - Hamburg (Germany)
Overview presentation	**Background** Blood-based biomarkers for Alzheimer's disease (AD) are on the verge of clinical implementation. Particularly plasma phosphorylated (p-)tau217 or pTau217 over amyloid-beta (Aβ)42 ratio are considered ready for use in clinical and trial settings to screen for presence of cerebral amyloid pathology (*i.e.*, (A(myloid)+ status). To facilitate clinical uptake, robust assays on fully automated random access instruments are required. These random access technologies offer essential flexibility, accessibility and scalability in comparison to batch-based technologies. Sysmex developed assays for pTau217, Aβ42 and Aβ40 quantification on their random-access Automated Immunoassay System HISCL™-5000 / HISCL-800. Here, we sought to clinically validate these assays for their potential to diagnose cerebral amyloid pathology across the clinical AD continuum.

	Methods From the Amsterdam Dementia Cohort, we selected plasma samples of 50 cases with subjective cognitive decline (SCD) who were A- (Controls; 40% female, median 65 [interquartile range (IQR) 61–69] years), of 50 cases with SCD who were A+ (SCD A+; 40%F, 66 [61–71] years), of 50 cases with mild cognitive impairment (MCI) who were A- (MCI A-; 40%F, 67 [61–72] years), of 50 cases with MCI who were A+ (MCI A+; 40%F, 68 [61–71] years), and of 50 cases with dementia who were A+ (AD-dem; 40%F, 67 [62–70] years). A-status was based on cerebrospinal fluid analyses of core-1 AD biomarker. Samples were measured by HISCL-5000 in duplicates for the markers pTau217, Aβ42 and Aβ40. As a benchmark, the same samples were also measured with Lumipulse pTau217, Aβ42 and Aβ40 assays. All measurements were performed in the first freeze-thaw cycle and according to manufacturer's instructions. Mann-Whitney U tests with Benjamini-Hochberg correction for multiple testing and ROC-AUC analyses were conducted. **Results** Across the samples, average coefficients of variation (CV) of duplicate measurements reflecting the repeatability precision of the HISCL-5000 assays were 3.3% for pTau217, 1.4% for Aβ42 and 1.4% for Aβ40. Plasma pTau217 levels measured with HISCL-5000 were significantly increased in the A+ groups (SCD A+, MCI A+, AD-dementia) compared to the A- groups (Controls, MCI A-; all $p<0.001^{FDR}$), with no difference between Controls and MCI A-, and further a stepwise increase in levels was observed across the syndromal A+ stages: from Controls to SCD A+ (%change of median: +188%, $p^{FDR}<0.001$), from SCD A+ to MCI A+ (+43%, $p^{FDR}=0.001$) and from MCI A+ to AD dementia (+114%, $p^{FDR}<0.001$). Similar findings were obtained when pTau217 is measured with Lumipulse, albeit with a slightly lower %change of the median in the comparison Control to SCD A+ (i.e., +119% instead of +188%). Plasma Aβ42/40 ratio measured with HISCL-5000 was significantly decreased in the SCD A+, MCI A+

Sysmex Corporation
1-5-1 Wakinohama-Kaigandori, Chuo-ku, Kobe 651-0073,Japan
Tel 81-78-265-0500 Fax 81-78-265-0524

	and AD dementia groups compared to the Controls and the MCI A- group (all: p^{FDR}<0.001; range %change of median A+ versus A- groups: -7.8% – -10.2%), whereas there was no difference in levels between the A+ groups. Similar findings were observed when Aβ42/40 levels were measured with Lumipulse. HISCL-5000 group differences observed for pTau217 alone were highly similar to group differences observed for pTau217/Aβ42 ratio, except that discrimination between A+ and A- in the SCD stage was enhanced (median %change 220% for the pTau217/Aβ42 ratio compared to +188% for pTau217 alone). Expressed as ROC-AUCs, across all syndromal stages, HISCL-5000 pTau217 discriminated A+ from A- with AUC=0.92 (95%CI: 0.89–0.96), HISCL-5000 pTau217/Aβ42 with AUC=0.93 (95%CI: 0.89–0.96) and HISCL-5000 Aβ42/A40 with AUC=0.80 (95%CI: 0.74–0.86). ROC-AUCs for Lumipulse measurements were similar to those obtained for HISCL-5000 measurements for pTau217 and pTau217/Aβ42 ratio (both DeLong's p > 0.155), whereas ROC-AUC was higher for HISCL-5000 Aβ42/40 ratio compared to Lumipulse Aβ42/40 ratio (DeLong's p: 0.02, ΔAUC: 0.08). Zooming in onto the SCD stage (Controls vs SCD A+), HISCL-5000 pTau217 had AUC=0.90 (95%CI: 0.84 – 0.96), pTau217/Aβ42 ratio had AUC=0.91 (95%CI: 0.85–0.97) and Aβ42/40 ratio had AUC=0.74 (95%CI: 0.63–0.84). AUCs obtained with Lumipulse for these same markers were comparable (All DeLong's p >0.05), but AUC of pTau217/Aβ42 tended to be higher for HISCL-5000 compared to Lumipulse (DeLong's p=0.506; Δ0.05). **Conclusions** We have clinically validated the HISCL-5000 pTau217, Aβ42 and Aβ40 assays, and found them fit for purpose to identify cerebral amyloid pathology across the clinical AD continuum. Robust clinical assays on random-access instruments will streamline diagnostic decision making in dementia care.
Session	Poster, 07. CLINICAL TRIALS: BIOMARKERS INCLUDING PLASMA - P197

Sysmex Corporation
1-5-1 Wakinohama-Kaigandori, Chuo-ku, Kobe 651-0073,Japan
Tel 81-78-265-0500 Fax 81-78-265-0524