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Sysmex Corporation
Eisai Co., Ltd.

Sysmex Presents Academic Report in Effort to Create a Simple Blood Test to Diagnose Alzheimer's Disease

The Content Presented at the International Conference on Alzheimer's & Parkinson's Diseases: (AD/PD™ 2022)

Sysmex Corporation (HQ: Kobe, Japan; Chairman and CEO: Hisashi Ietsugu; hereafter, "Sysmex") and Eisai Co., Ltd. (Headquarters: Tokyo; CEO: Haruo Naito; hereafter, "Eisai") are aiming to leverage their individual technologies and expertise in the creation of next-generation diagnostic agents that may aid in early diagnosis of dementia, treatment selection, and regular confirmation of treatment efficacy. Sysmex and Eisai have a non-exclusive comprehensive agreement for the creation of novel diagnostic agents for the dementia area.

Sysmex and Eisai announced today that an oral presentation on the use of the HISCL™ Automated Immunoassay System in the clinical evaluation of the plasma $A\beta_{1-42}/A\beta_{1-40}$ ratio was delivered at the International Conference on Alzheimer's & Parkinson's Diseases (AD/PD™ 2022) held in Barcelona, Spain from March 15 to 20 2022.

Presentation title	Fully Automated Plasma Beta-Amyloid Immunoassays Predict Amyloid Pathology Defined by Amyloid PET
Authors	Kazuto Yamashita[1], Masao Miura[1], Shunsuke Watanabe[1], Kengo Ishiki[1], Yuji Arimatsu[2], Yasuhiro Irino[1], Toshiko Kubo[3], Kei Hagino[2], Kota Nagai[4], David Verbel[5], Akihiko Koyama[6], Shobha Dhadda[7], Hayato Niiro[8], Shigeki Iwanaga[1], Toshiyuki Sato[1], Tomokazu Yoshida[9], Atsushi Iwata[10] [1]Central Research Laboratories, Sysmex Corporation, Kobe, Japan; [2]Business Incubation Division, Sysmex Corporation, Kobe, Japan; [3]Sysmex R&D Center Americas, Mundelein, Illinois, USA; [4]Japan and Asia Clinical Development Department, Eisai Co., Ltd., Japan; [5]Biostatistics, Eisai Inc., Woodcliff Lake, NJ, USA; [6]Translational Science, Eisai Inc., Woodcliff Lake, NJ, USA; [7]Biostatistics and Project Operations, Eisai Inc., Woodcliff Lake, NJ, USA; [8]Medical Affairs Division, Sysmex Corporation, Kobe, Japan; [9]Sysmex Corporation, Kobe, Japan; [10]Department of Neurology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan
Type of presentation	Virtual, On-Demand Oral

Overview of presentation	Accumulation of β-amyloid peptide (Aβ) (amyloid pathology) in the brain is a hallmark of Alzheimer's disease (AD). Several clinical trials on disease-modifying therapies (DMTs) targeting Aβ have been conducted. The US Food and Drug Administration has recently granted accelerated approval for an anti-amyloid antibody for early AD. Given this background, there is an increasing need for simple, cost-effective diagnostic methods of detecting amyloid pathology in the brain. Our group previously reported that amyloid PET status was correlated with $A\beta_{1-42}$/ $A\beta_{1-40}$ ratio in plasma (hereafter, "plasma Aβ ratio") and that amyloid pathology in the brain could potentially be predicted using blood biomarkers.[*1] Our research has focused on the plasma Aβ ratio using clinical specimens. In this presentation, we conducted a clinical evaluation of the plasma Aβ ratio measured using the HISCL Automated Immunoassay System (Sysmex) in comparison with amyloid PET status determined by the Centiloid method[*2] in 180 patients (Discovery Study) and 191 patients (Validation Study) clinically diagnosed with mild AD or mild cognitive impairment. (Results) ✓ In the Discovery Study, the plasma Aβ ratio was significantly lower in the Amyloid PET positive group as compared to the negative group and it predicted amyloid PET status with high accuracy: sensitivity 97.5%, specificity 80.8%, AUC = 0.93 (0.90 – 0.97). ✓ In the Discovery Study, the plasma Aβ ratio and Centiloid unit (CL) were significantly correlated with a Spearman rank correlation coefficient[*3] of -0.75 ($P<0.001$), and this indicates that our assay could be indicative of the amount of Aβ accumulation in the brain. Also, we observed inconsistency in several patients, who had a positive plasma Aβ ratio and a negative CL. This inconsistency has also been found in other studies and it was reported that it represented an increased risk of conversion to PET positive as compared to Aβ ratio negative subjects.[*4] Our results suggest that the plasma Aβ ratio measured using the HISCL Automated Immunoassay System could potentially indicate presence of amyloid pathology in the brain at an earlier stage when it was not detectable by PET. Since measurement of plasma $A\beta_{1-42}$ and $A\beta_{1-40}$ in the HISCL is fully automated immunoassay that is less invasive and more accessible, it may contribute to the diagnosis of AD in routine clinical practice. We believe that the plasma Aβ can contribute to early diagnosis, of AD, treatment selection and monitoring of treatment effect.

[Notes**]**

*1 The 18th R&D Meeting (2021, Sysmex)

*2 Klunk WE et al, *Alzheimer's Dementia* (2014)

*3 Shows significant correlation between data from 2 quantitative data distributions. In the present analysis, we calculated Spearman's rank correlation coefficients, which indicate correlations between rank data.

*4 Schindler SE et al, *Neurology*, 93, e1647-e1659 (2019)

Contacts for inquiries

IR & Corporate Communication Sysmex Corporation Tel：+81-(0)78-265-0500	Public Relations Department Eisai Co., Ltd. Tel：+81-(0)3-3817-5120 Eisai Inc. (US) Tel：+1-201-753-1945 Libby_Holman@eisai.com