



IST-NDDP: An Istanbul-Based Real-World Data Platform for Neurodegenerative Disease Research and Biomarker Validation

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Istanbul Cohort provide diversity for biomarker studies with CSF or blood biomarker confirmed cases

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Two major areas dominate Alzheimer’s disease (AD) research: biomarker development and therapeutic strategies, both requiring rigorous longitudinal evaluation for robustness, reliability, and safety. However, drug trials remain challenged by biomarker validity, coexisting pathologies, and population diversity. The IST-NDDP has extensive biomarker expertise through JPND/BIOMARKAPD, the ADDIA-Horizon 2020, and TUBİTAK-supported standardization of blood- and CSF-based AD biomarkers using SIMOA and RT-QuIC [1-5]. Anticipating FDA-approved AD therapies in Turkey by 2026, the platform aims to establish a regulatory-grade biomarker registry and longitudinal database.	Preanalytical procedures, including LP, CSF collection, handling, and storage, were conducted in accordance with SOPs. The unit performs CSF core biomarker and neurofilament light chain (NfL) analyses using ELISA (Fujirebio, Umman Diagnostic), and measures blood pTau217 (ALZpath) and NfL/GFAP using SIMOA technology. Second-generation CSF prion RT-QuIC is conducted with an in-house-produced prion peptide. IUC-INS actively participates in the UGOT QC Program (University of Gothenburg-DxA-GBSC, formerly AAQC) and the Prion RT-QuIC Ring Trial (University of Göttingen). Development of a homebrew α-synuclein seed amplification assay (aSyn-SAA) is ongoing and expected to be completed in 2026.	The center had evaluated more than 6,500 patients with neurodegenerative disorders. Of these, 2,538 cases—including AD, MCI, PPA, atypical dementia, VaD, CJD, FTD, DLB, PDD, PD, CBS, and PSP—were recruited from a single center (IU-IFM), forming the Istanbul Cohort. Blood, CSF, and DNA samples were available for 1,465 cases, enabling CSF core biomarker-based diagnostic confirmation. In a subset of cases, biomarker cutoffs were concordant with the literature for AD versus healthy controls: CSF Aβ1-42, 811 pg/ml (0.96/0.93); CSF pTau181, 52.5 pg/ml (0.89/0.87); CSF tTau, >378.5 pg/ml (0.92/0.83); CSF pTau181/Aβ42, >0.066 (0.97/0.98); serum NfL, >19.05 pg/ml (0.72/0.43); serum GFAP, >120.85 pg/ml (0.80/0.59); plasma pTau217, >0.39 pg/ml (0.90/0.90). CSF prion RT-QuIC showed 0.97/0.96 sensitivity/specificity in 33 CJD versus 71 non-CJD cases.	The Istanbul Cohort enabled the identification of novel CSF (STUB1/CHIP, PCK2) biomarkers and evaluation of emerging technologies (SIMOA, NULISA), yielding candidate blood biomarkers (CXCL1, SNAP25, TREM1, β-synuclein, TEK). Its nationwide infrastructure supports real-world data collection and comprehensive biomarker assessment, enhancing diversity and rigor in AD biomarker research and clinical trials.	[1] Sordu P, Alaylioglu M, Samanci B, Bulu E, Gulec ZEK, Bilgic B, et al. Cerebrospinal fluid HSP90AA1, HSPA4, and STUB1/CHIP levels in Alzheimer’s disease, mild cognitive impairment, and frontotemporal dementia. J Alzheimers Dis. 2025;13872877251329540. [2] İlhan N, Sahin E, İldiz S, Samancı B, Sordu P, Alaylioglu M, et al. The CSF Levels of Mitochondrial Phosphoenolpyruvate Carboxykinase 2 as a Novel Biomarker in Alzheimer’s Disease. Mol Neurobiol. 2025;63:98. [3] İlhan N, Keskin E, Sahin E, Alaylioglu M, Samancı B, Camoglu T, et al. The mRNA Expression Levels of General Transcription Factors Altered in Alzheimer Cases Possibly Due to Amyloid Beta 1-42 Exposure. Noro Psikiyatr Ars. 2026;63:341-9. [4] Gezen H, Alaylioglu M, Sahin E, Swann O, Veleva E, Guven G, et al. Unravelling the plasma proteome: Pioneering biomarkers for differential dementia diagnosis. Alzheimers Dement. 2025;21:e70162. [5] Delaby C, Ladang A, Martinez-Yriarte J, Zecca C, Logroschino G, Körtvelyessy P, et al. Clinical use and reporting of neurofilament quantification in neurological disorders: A global overview. Alzheimers Dement. 2025;21:e70343.
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What we can provide... is diversity				ALZHEIMER’S ASSOCIATION AAIC>26