Recent Advances in the Treatment of Alzheimer's Disease

Biography

Professor Takeshi IWATSUBO is a Professor of Neuropathology at the Graduate School of Medicine, The University of Tokyo. He also serves as the Director of the National Institute of Neuroscience, National Center of Neurology and Psychiatry, and the Chairman of the Japan Society for Dementia Research. Trained as a neurologist and neuropathologist, Iwatsubo has contributed to the studies of human neurodegenerative disorders, especially Alzheimer's and Parkinson's disease, using multidisciplinary approaches. He demonstrated that Aβ42 is the initially deposited species in senile plaque amyloid, elucidated the process of γ-secretase complex formation and identified phosphorylated α-synuclein as a component of Lewy bodies. He has been the Principal Investigator of the Japanese AD Neuroimaging Initiative (J-ADNI) and currently serves as the PI of the Japanese Trial Ready Cohort for Prevention of Alzheimer's Disease (J-TRC). He was awarded the MetLife Award for Medical Research (2008) and the Potamkin Prize (2012).

Abstract

Recent clinical trials of disease-modifying therapies (DMT) for early Alzheimer's disease (AD), especially those for anti-amyloid β (Aβ) antibody drug have been successful, opening up a new era for AD therapies. Notably, these positive outcomes of AD DMT trials have largely depended on molecular imaging and fluid biomarkers, underscoring the needs of markers that surrogate the clinical and pathophysiological progression of AD. Longitudinal observational studies as represented by AD Neuroimaging Initiative (ADNI) in the North America, as well as the Japanese ADNI, have contributed greatly towards the goal of very early treatment at the prodromal and preclinical AD stages by delineating the early natural course of AD and facilitating the development of biomarkers. We have demonstrated that the clinical and biomarker profiles of prodromal AD in J-ADNI were remarkably similar to those in North American ADNI, supporting the harmonization in global clinical trials. Although the A4 study, the initial secondary prevention trials in preclinical AD, did not meet the primary endpoint, it has elucidated the natural history of preclinical AD and established a clinical platform for DMT trials in preclinical AD, on which a number of new trials are underway. To make these preclinical AD trials successful, trial ready cohorts (TRC) of preclinical and prodromal AD, are being established in the US and Japan. J-TRC launched in 2019 is comprised of a webstudy followed by an on-site study, so far having recruited ~14100 and ~687 participants, respectively. Biomarker studies in J-TRC have shown that combinations of plasma Aβ42-related biomarkers and p-tau217 are potent in the prediction of Aβ-PET positivity and may be instrumental in the prescreening for clinical trials of DMTs for preclinical and prodromal AD. These clinical activities will pave the way toward the development of AD therapies targeting its very early stages.