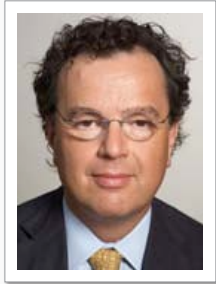


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Anti-hypertensive drugs for the treatment of Alzheimer's disease

Current FDA-approved Alzheimer's disease (AD) treatments have modest symptomatic effects, and do not significantly modify disease course. In a population-based sample of incident AD, we observed that use of β -adrenergic antagonists was associated with slower functional decline. Our data combined with other epidemiologic data suggest the potential therapeutic effect of β -adrenergic antagonists in AD patients. One agent that passed the screen was carvedilol, a β -adrenergic antagonist FDA-approved for several cardiac indications. In two transgenic mouse models of AD, chronic oral administration of carvedilol decreased brain monomeric and oligomeric β -amyloid content, attenuated cognitive deterioration, and improved basal neuronal transmission in the brain. Additionally, carvedilol may beneficially affect vascular risk factors for AD by stabilizing blood pressure and improving brain perfusion since it's an approved treatment for hypertension and congestive heart failure and has been shown to be neuroprotective in brain ischemia models. We're clinically exploring a target dose of 25 mg daily of carvedilol to 50 AD patients in a 6-month randomized, placebo-controlled, double-blind, single-site trial, with change in episodic recall as the primary outcome and biomarker change and safety/tolerability as secondary measures. If we observe significant improvements in clinical outcomes, we will propose a definitive trial of carvedilol in AD. If we observe changes only in biomarker outcomes, this will inform further studies of similar treatment mechanisms. Should carvedilol prove to be effective in AD, it has advantages over novel agents in human trials since it has a well-characterized, generally well-tolerated safety profile and is available as a generic drug.

Biography

Dr. Giulio Maria Pasinetti's research on lifestyle factors and metabolic co-morbidities influencing clinical dementia, neurodegeneration and Alzheimer's disease has made him a top expert in his field. He has received over 30 grants and published over 160 groundbreaking research articles. Dr. Pasinetti is a Professor of Neurology, Psychiatry, Neuroscience, and Geriatrics and Adult Development, and is Director of the Brain Institute Center of Excellence for Novel Approaches to Neurotherapeutics at Mount Sinai School of Medicine. He also serves as Director of the Basic and Biomedical Research and Training, Geriatric Education and Clinical Center at the Bronx Veterans Affairs Medical Center.

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