Multi-tracer PET monitoring of an immunomodulatory therapy in 4R tauopathy: Evaluating a novel drug's impact on glial function and protein pathology

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The prevalence of neurodegenerative diseases (ND), including Alzheimer's disease (AD) and tauopathies, is projected to rise significantly by 2050 due to global aging. Chronic neuroinflammation, driven by glial activation in response to protein aggregation, is a key factor in disease progression. Immunomodulatory therapies targeting glial dysfunction offer a promising approach to mitigate tauopathy and other ND pathologies. This study evaluates the efficacy of GV1001 in the PS19 tauopathy mouse model, employing an early-intervention biomarker strategy. Molecular and neuroimaging techniques are used, including serial PET with [^{18}F]DPA-714 to measure microglial activation, [^{18}F]F-DED for astrocytic reactivity, and [^{18}F]PI-2620 to quantify tau aggregation. CSF biomarkers such as sTREM2 (inflammation) and neurofilament light chain (NfL, neurodegeneration) are also analyzed. GV1001 is administered chronically over five months. PET imaging monitors longitudinal treatment effects, while postmortem analyses include immunohistochemistry and biochemical assays comparing treated mice with placebo and non-transgenic controls. Preliminary results reveal subtle, brain region-specific changes in tracer uptake, suggesting early therapeutic effects on glial responses and tau pathology.
This study highlights the potential of monitoring immunomodulatory strategies to address the complex interplay between chronic neuroinflammation and protein aggregation in ND. The integration of PET imaging and fluid biomarkers underscores the utility of non-invasive tools for evaluating disease-modifying therapies. If validated, these findings could inform the development of glia-targeted treatments for AD and related tauopathies, bridging the gap between preclinical research and clinical application.

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