Intracellular tau deposition is a key pathologic feature of Alzheimer’s disease (AD) and other neurodegenerative disorders. Several positron emission tomography (PET) tracers targeting tau have been discovered and tested in humans. [[18F]F]PI-2620 is a novel tau PET-tracer with a high binding-affinity for pathological tau that accumulates in regions of tau pathology. The ability of [[18F]F]PI-2620 to measure the spatial distribution of tau pathology in AD was demonstrated previously. Elenbecestat is a small-molecule inhibitor of BACE that is currently being evaluated in two global Phase 3 studies (MissionAD1 and MissionAD2). In these studies, a two-year, 50 mg once-a-day course of elenbecestat in patients (age 50 to 85) who have biomarker-confirmed MCI due to AD/progressive AD or mild AD dementia will be compared to placebo. Change from baseline on the CDR-SB at the 2-year time point serves as the primary outcome; The trial also assesses exploratory outcomes such as change on amyloid PET, hippocampal volume and functional connectivity fMRI, and CSF biomarkers.

The objective of this study was to evaluate tau deposition at baseline using [[18F]F]PI-2620 PET tracer in beta-amyloid positive patients with MCI or mild AD dementia from a sub-study of the elenbecestat Mission AD program.

**Methods**

- Cerebellar cortex was used as reference region (vermis and anterior cerebellar grey matter contiguous to the vermis was excluded).
- Individual MRI-based subregions including hippocampus (HC), parahippocampus (PHC) and fusiform gyrus were further investigated.

**Results**

- 45 beta-amyloid positive subjects were recruited into the TAU PET substudy and underwent [[18F]F]PI-2620 PET examination
- Mean age was 76 ± 7 yrs


- Of the 45 subjects studied, 27 subjects were Tau PET positive (60%) 13 subjects had obvious [[18F]F]PI-2620 neocortical accumulations extending from the mesial-temporal cortex (see Figure 1).

**Additional images**

- Subject #1
- Subject #2
- Subject #3
- Subject #4
- Subject #5

**Quantitative analysis of [[18F]F]PI-2620 uptake in MRI-based subregions**

- A) Hippocampus
- B) Parahippocampus
- C) Fusiform gyrus

**Conclusions**

- [[18F]F]PI-2620 accumulation was observed in 60% of the studied subjects with MCI due to AD, mild AD dementia. 44% of the apparent tau positive cases had isolated mesial temporal uptake consistent with early disease.
- The presented analysis is preliminary. Enrolment into the substudy and further analyses are continuing
- Longitudinal evaluation of these cases together with the beta-amyloid-positive but tau negative cases will provide important insights into development of tau pathology and is expected to provide insights into the selection of an ideal cohort for therapeutic interventions

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