

Preliminary Head-to-head Comparison Of Longitudinal Tau-PET Performance Of Flortaucipir And MK6240 In The HEAD Study

#10889

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MK6240 showed greater sensitivity in CU Aβ+, detecting significant accumulation across Braak ROIs where Flortaucipir did not.

INTRODUCTION

Tau-PET tracers are used to identify and monitor tau pathology progression in Alzheimer's disease (AD). However, different tracers exhibit distinct binding properties across the brain, which may affect their utility as outcome measures in clinical trials. Here, we provide a preliminary head-to-head comparison of the longitudinal performance of Flortaucipir and MK6240 in the same individuals.

METHODS

We longitudinally assessed 214 individuals [11 young, 119 cognitively unimpaired (CU; 17.6% Aβ+), 67 cognitively impaired (CI; 64.2% Aβ+)] with head-to-head Flortaucipir and MK6240 (18-month follow-up). Individuals receiving anti-amyloid therapies between time points were excluded. SUVRs were calculated using the inferior cerebellar gray matter as the reference region. Rates of change were calculated as follow-up minus baseline divided by time in years. Effect sizes and sample size estimates were calculated for a hypothetical clinical trial (25% drug effect, 80% power, α=0.05).

RESULTS

No significant tau accumulation was observed in young or Aβ- groups (Fig.1A,C; Fig.2). In CU Aβ+, voxel-wise analyses revealed medial temporal lobe tau accumulation with both tracers, but only MK6240 detected significant accumulation in Braak I-II and III-IV ROIs (Fig.1B, Fig.2). In CI Aβ+, both tracers demonstrated widespread cortical accumulation and significant change in Braak III-IV and V-VI (Fig.1D, Fig.2). Overall, MK6240 showed higher accumulation rates and larger effect sizes across brain regions and clinical groups, resulting in substantially smaller sample size requirements for clinical trials (Fig.3).

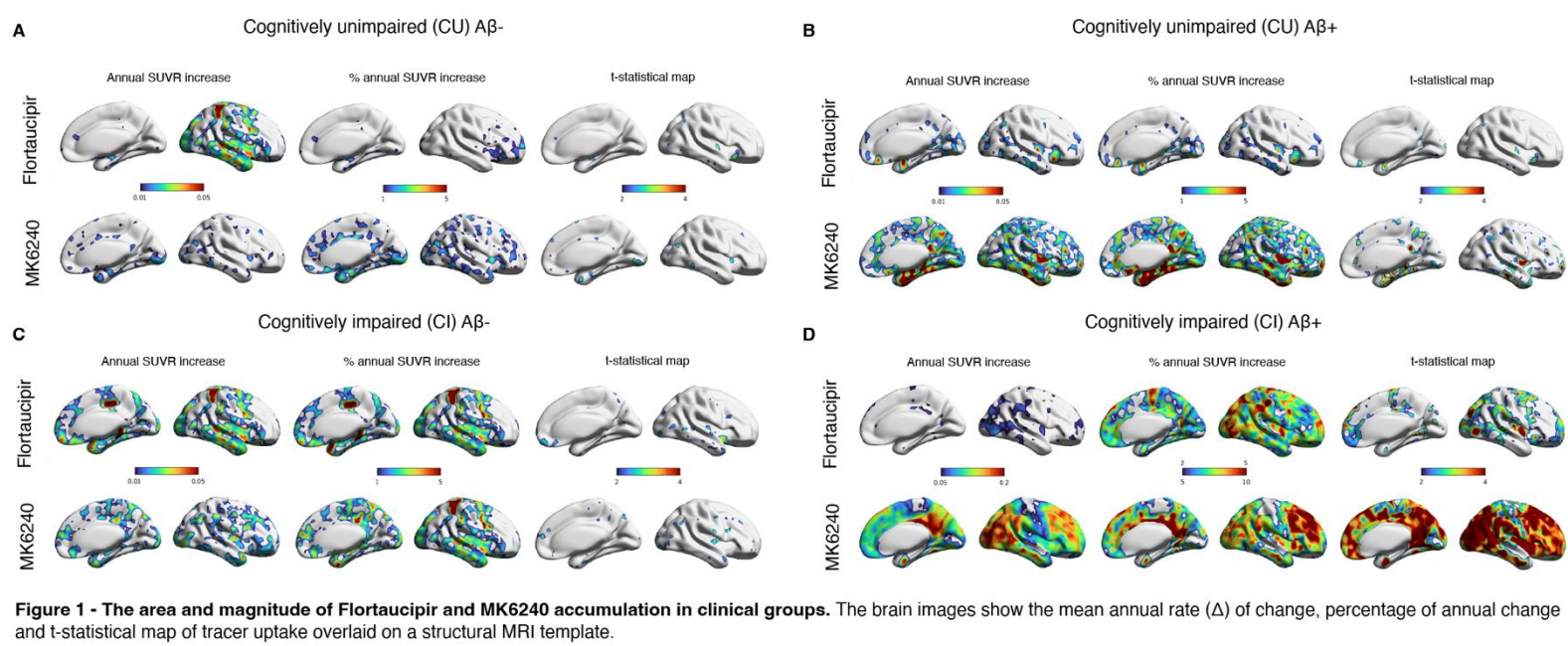


Figure 1 - The area and magnitude of Flortaucipir and MK6240 accumulation in clinical groups. The brain images show the mean annual rate (A) of change, percentage of annual change and t-statistical map of tracer uptake overlaid on a structural MRI template.

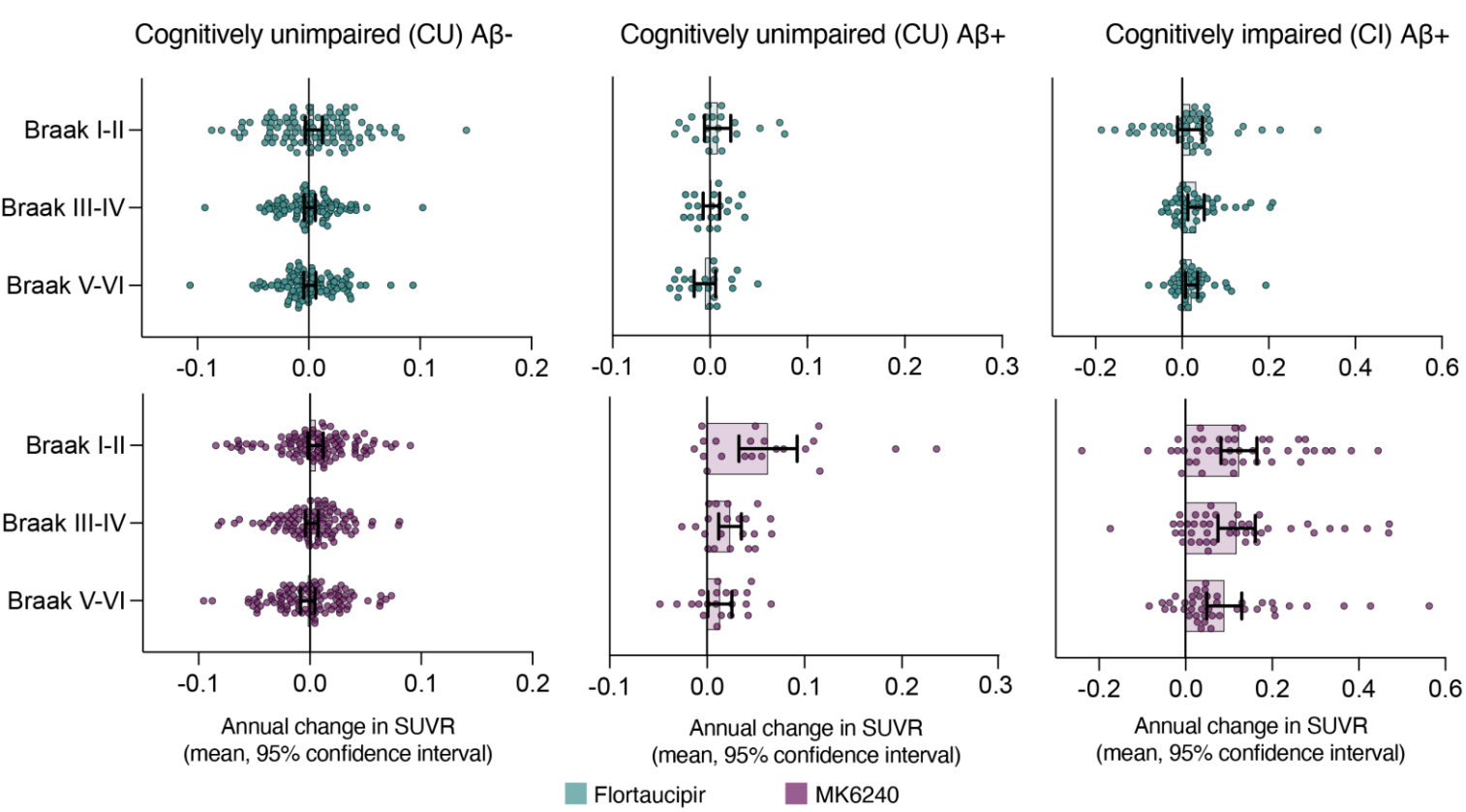


Figure 2 - Annual change in SUVR across Braak regions in clinical groups. Bars show the mean annual rate of change, and confidence intervals that do not cross the zero line indicate a statistically significant tau accumulation.

ROIs	CU Aβ+ (n = 21)				CI Aβ+ (n = 43)			
	Flortaucipir		MK6240		Flortaucipir		MK6240	
	Effect size	Sample size	Effect size	Sample size	Effect size	Sample size	Effect size	Sample size
MTL	0.25	NS	0.95	277	0.18	NS	0.84	354
Temporal neocortex	0.15	NS	0.84	356	0.54	853	0.84	357

Figure 3 - Effect size and sample size calculation (per arm) for a hypothetical clinical trial using Flortaucipir or MK6240. MTL: medial temporal lobe. NS: mean annual change was not significant.

CONCLUSIONS

Our preliminary data demonstrate that both tracers detect annual tau accumulation, particularly in CI Aβ+. However, MK6240 showed greater sensitivity in CU Aβ+, detecting significant accumulation across Braak ROIs where Flortaucipir did not. MK6240's larger effect sizes translate into smaller sample sizes, potentially requiring fewer participants for clinical trial recruitment.



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