

Abstract #13384: Amyloid Clearance And Heterogeneous Downstream Tau Responses After Donanemab: A Three-case Pet Study

Kaiyue xie, Yao li, Li sun*, Haining zhang*.
the first hospital of jilin university, changchun, China.



INTRODUCTION

Donanemab has been approved for the treatment of mild cognitive impairment due to AD and mild AD dementia. Its effect to reduce amyloid protein has been established. However, the extent of amyloid clearance after short-term treatment and its association with downstream tau pathology, cerebral glucose metabolism, and clinical outcomes remain unclear. Therefore, we described the different PET evaluation and clinical changes in three patients with mild AD before and after donanemab treatment.

METHOD

Three middle-aged to elderly patients with mild AD (A+T+N+ by PET) received donanemab after multidisciplinary evaluation and informed consent. Patients were followed for six months. Cognitive assessments and amyloid, tau, and FDG PET imaging were performed at baseline and at 24 weeks to evaluate amyloid burden, tau pathology, and cerebral metabolism. Amyloid-related imaging abnormalities (ARIA) were monitored throughout treatment.

RESULT

Cognitive function remained stable over 24 weeks. No symptomatic amyloid-related imaging abnormalities were observed. Cases A and B (APOE $\epsilon 3/\epsilon 4$) achieved amyloid clearance in Centiloid values (Case A: -25.43 to -12.99; Case B: 51.75 to -15.96). Case A showed tau PET clearance. Case B showed a marked reduction. FDG-PET still showed hypometabolism in selected brain regions. Case C (APOE $\epsilon 3/\epsilon 3$) showed modest amyloid reduction (SUVR 1.56 to 1.51). No change was observed on tau PET or FDG PET. A single asymptomatic microhemorrhage occurred before the fourth infusion in Case C. Treatment was continued. No further ARIA events occurred.

CONCLUSION

These cases show heterogeneous biomarker responses after 24 weeks of donanemab treatment. Two patients achieved amyloid clearance in Centiloid values. Tau PET showed clearance in one case and reduction in another. One patient showed only modest amyloid reduction without downstream changes. All patients remained clinically stable. One asymptomatic microhemorrhage occurred and treatment was continued. These findings suggest variable downstream responses after amyloid removal. Larger studies are needed to confirm these observations.

Table 1. Longitudinal clinical and imaging characteristics of three patients treated with donanemab

Variable	Case A	Case B	Case C
Age, sex	64, male	75, female	71, male
Education (years)	12	9	15
APOE genotype	$\epsilon 3/\epsilon 4$	$\epsilon 3/\epsilon 4$	$\epsilon 3/\epsilon 3$
Clinical stage	MCI due to AD	Mild AD dementia	MCI due to AD
Baseline MMSE	28	25	27
Follow-up MMSE	29	23	29
Δ MMSE	+1	-2	+2
Baseline amyloid (SUVR)	SUVR 0.92	SUVR 1.25	SUVR 1.56
24-week amyloid (SUVR)	SUVR 1.00	SUVR 0.88	SUVR 1.51
Δ amyloid	+0.08	-0.37	-0.05
Visual amyloid status	Negative	Negative	Reduced
Baseline tau PET	Medial temporal uptake	Widespread cortical uptake	Widespread cortical uptake
24-week tau PET	No abnormal uptake	Reduced uptake (residual)	No significant change
Baseline FDG PET	Temporoparietal hypometabolism	Diffuse cortical hypometabolism	Temporoparietal hypometabolism
24-week FDG PET	Persistent hypometabolism	Persistent hypometabolism	Persistent hypometabolism
ARIA	None	None	1 microhemorrhage
Donanemab regimen	Modified titration	Standard titration	Standard titration

*Baseline quantitative amyloid measures in Case A were near the lower threshold for amyloid positivity; visual assessment was therefore used as the primary determinant of amyloid status. Quantitative measures remained within the low range at follow-up despite visually negative amyloid PET findings. Δ indicates change from baseline to 24 weeks. The small SUVR change in Case C may fall within the range of measurement variability.

Figure 1. Amyloid PET imaging before and after donanemab

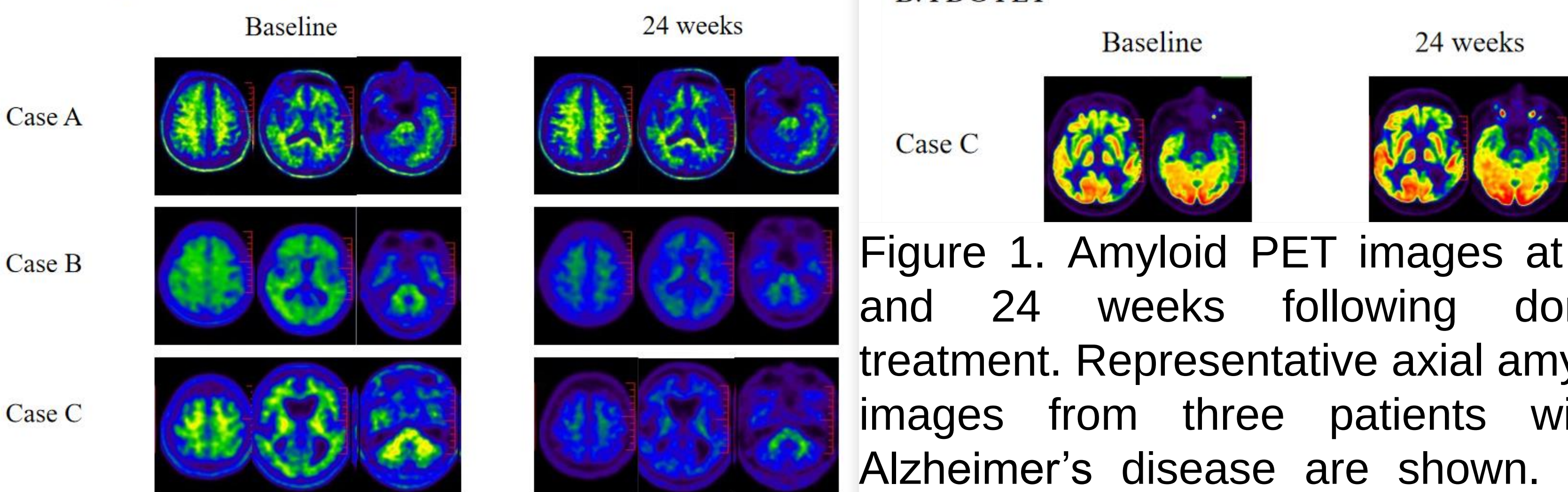
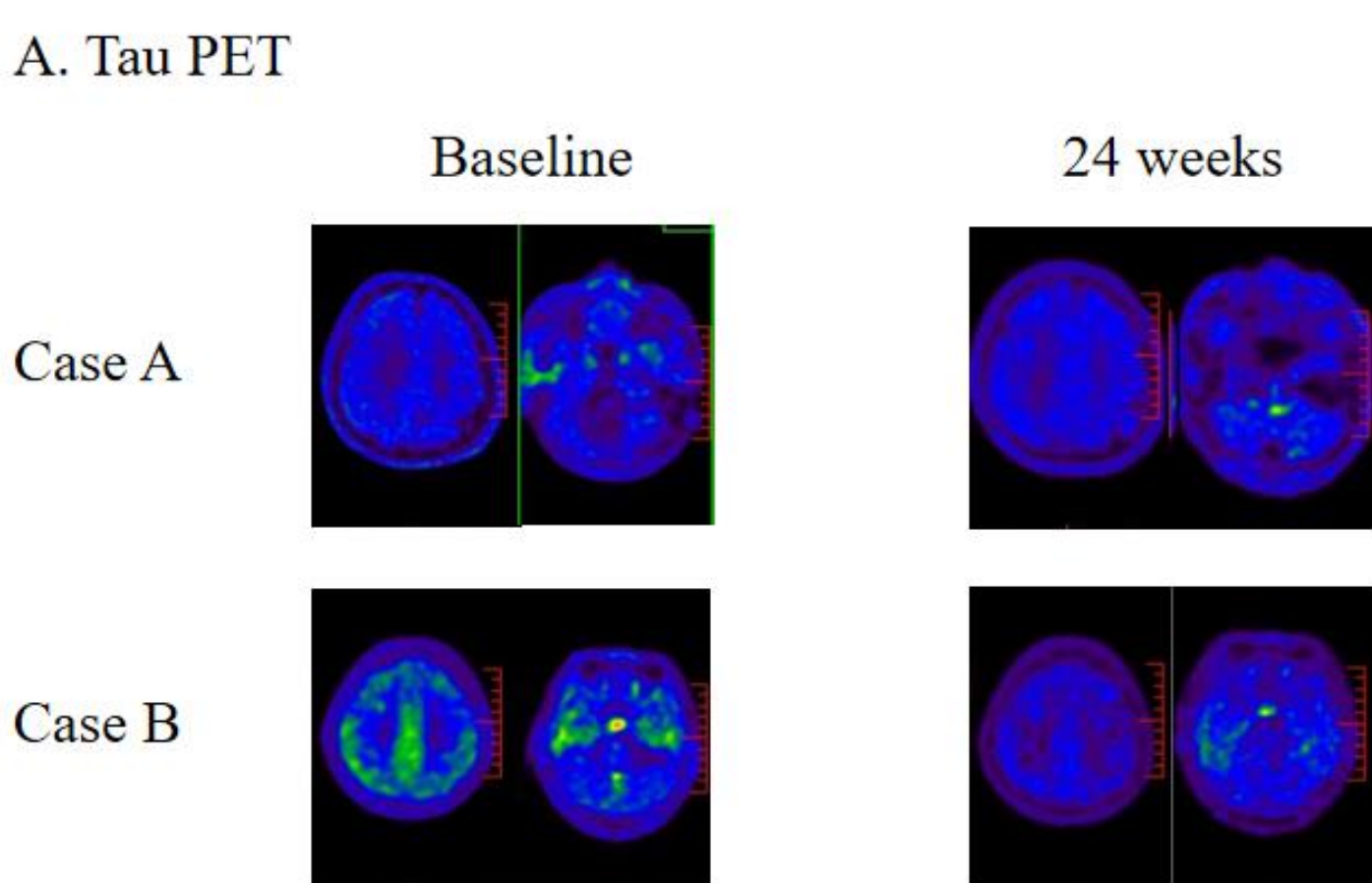


Figure 2. Pre-and Post-Treatment Tau PET and FDG PET imaging



B. FDG PET

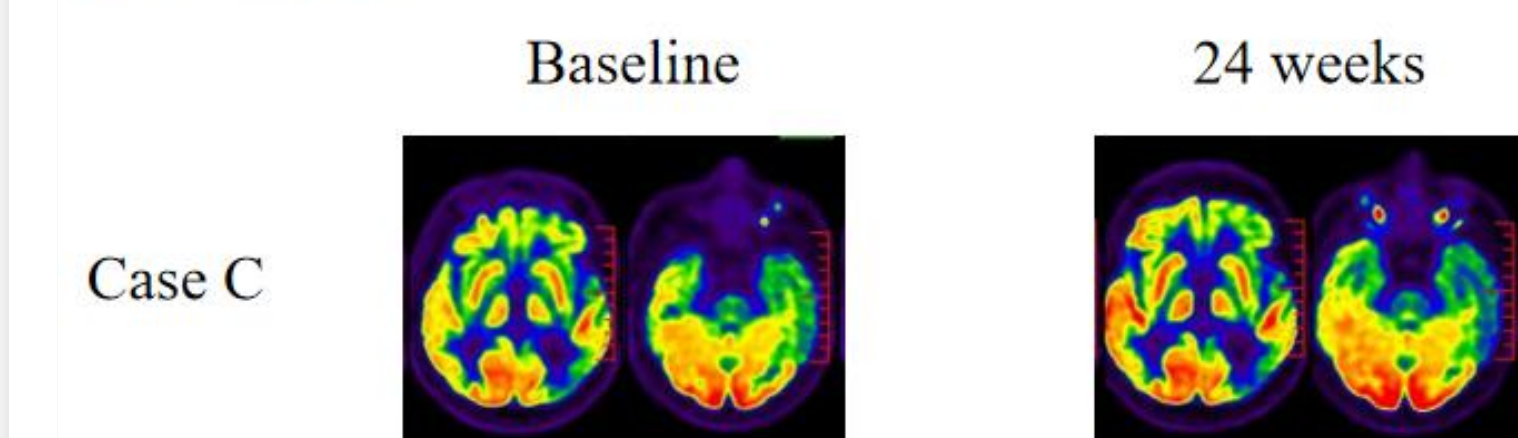


Figure 1. Amyloid PET images at baseline and 24 weeks following donanemab treatment. Representative axial amyloid PET images from three patients with early Alzheimer's disease are shown. Cases A and B achieved visual amyloid clearance, whereas Case C showed reduced amyloid burden. Images are displayed using identical color scales.

Figure 2. Tau PET and FDG PET imaging responses following donanemab treatment. Representative axial tau PET images demonstrate heterogeneous responses across the three cases, whereas FDG PET showed persistent regional hypometabolism at follow-up.