Tau PET Results From The Phase 2b Auτonomy Trial Evaluating Posdinemab In Early Alzheimer's Disease

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Presenting Author

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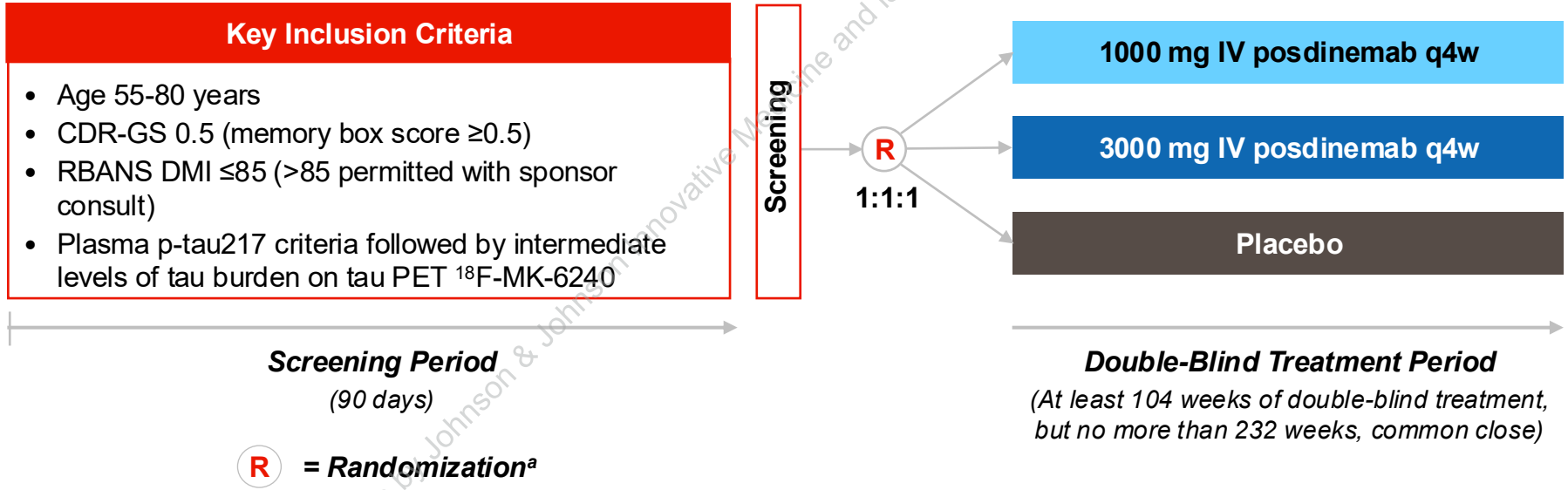
Disclosures

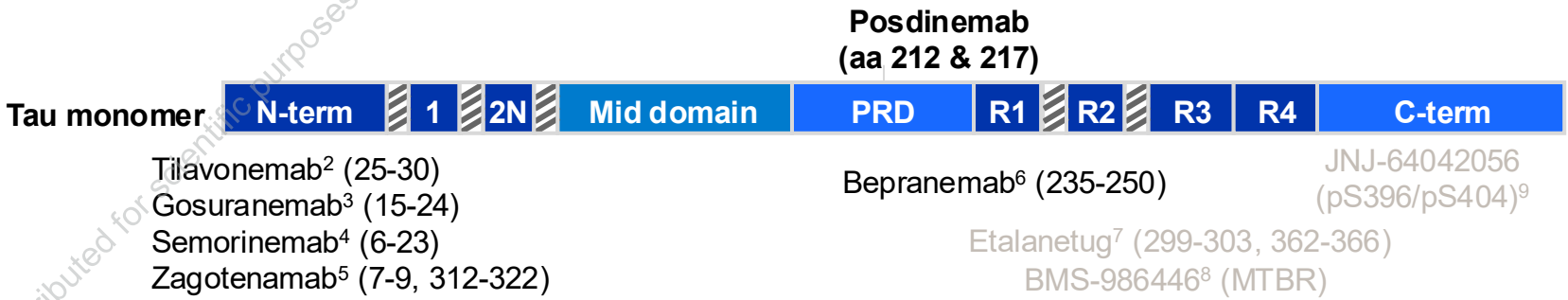
Ziad S. Saad

- Employee of Johnson & Johnson and may hold stock and stock options

INTRODUCTION – The Autonomy phase 2b trial showed posdinemab did not slow clinical decline in early Alzheimer's disease.[1] Here, we present additional tau PET results

- **Posdinemab** (JNJ-63733657), an IgG1 anti-phosphorylated tau (p-tau) monoclonal antibody that targets mid-domain tau (including p-tau217) did not slow tau spread or clinical decline as hypothesized in the Autonomy trial (NCT04619420)[1]
- Tau PET measures intracellular tau neurofibrillary tangles (NFT), a key pathology in Alzheimer's disease



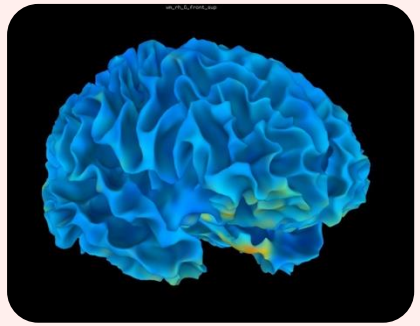


1. Cohen et al. Results from the phase 2b Autonomy trial of anti-p-tau monoclonal antibody posdinemab for early Alzheimer's disease. Oral presented at: International Conference on Alzheimer's and Parkinson's Diseases; March 2026; Copenhagen, Denmark. 2. Yanamandra K, et al. *Neuron*. 2013;80(2):402-414. 3. Bright J, et al. *Neurobiol Aging*. 2015;36(2):693-709. 4. Teng E, et al. *JAMA Neurol*. 2022; 79(8):758-767. 5. Fleisher AS, et al. *Neurology*. 2024;102(5):e208061. 6. Albert M, et al. *Brain*. 2019;142(6):1736-1750. 7. Roberts M, et al. *Acta Neuropathol Commun*. 2020;8(1):13. 8. van Dyck CH, et al. *Alzheimers Dement*. 2025;20(Suppl 8):e094677. 9. ClinicalTrials.gov. Identifier: NCT06544616. Available at: https://clinicaltrials.gov .
[a]Randomization was stratified by geographic region (North America, Europe, Australia, and Japan) and baseline tau burden on tau PET (Braak 4 ROI z-score ≤ or >4.62). CDR-GS, Clinical Dementia Rating Global Score; DMI, Delayed Memory Index; IV, intravenous; p-tau217, tau phosphorylated at amino acid residue 217; q4w, every 4 weeks; R, randomization; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; ROI, region of interest; tau PET, tau positron emission tomography.

METHODS – Tau PET was used for precision selection of participants and analysis of treatment effect on tau pathology[1]

Very low tauopathy

(Inferior temporal lobe ROI z-score ≤1)

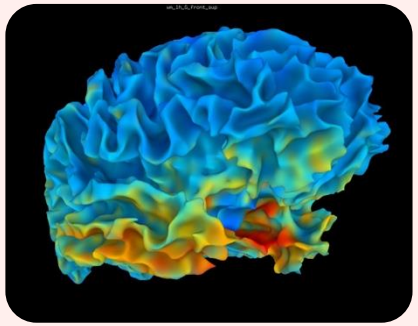


Absent/minimal pathology
Too little clinical change

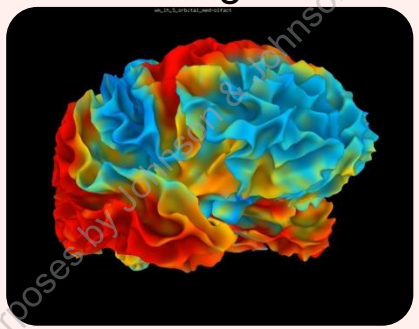
Autonomy inclusion range

(Inferior temporal lobe ROI z-score >1)

Low burden



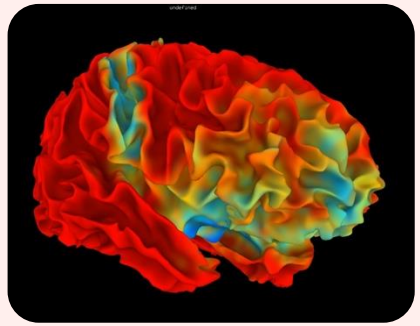
High burden



Presence of pathology and likely to progress
Most likely to benefit?

Widespread

(Each of Braak 4, 5 and 6 ROI z-score >5)



Advanced pathology and fast progression
Too late to slow tau spread?

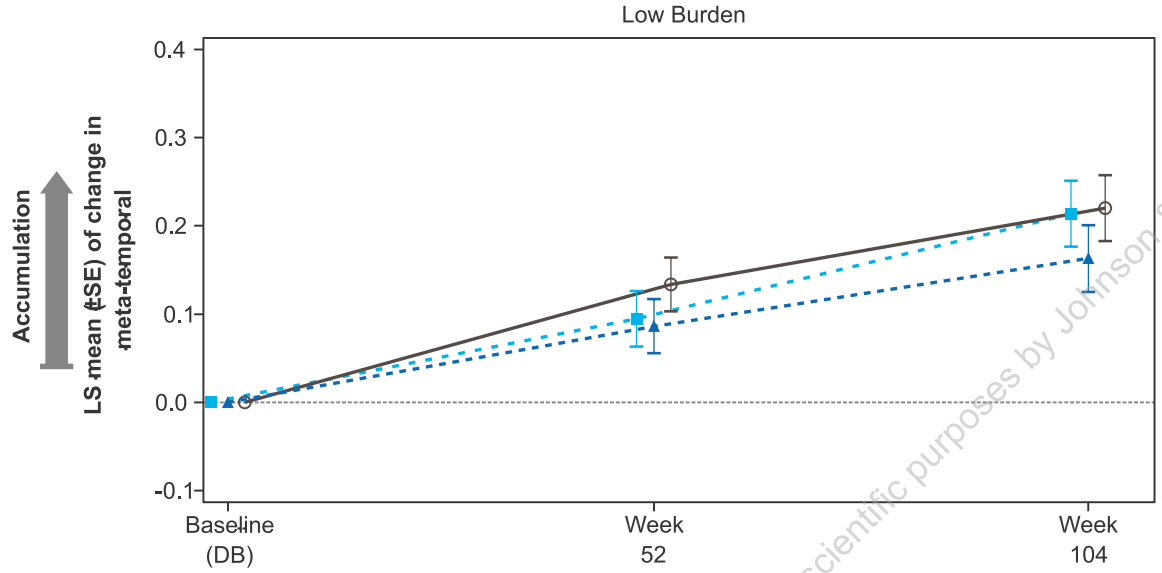
- Stratification by low vs high tau burden by tau PET: Braak 4 ROI z-score ≤4.62 vs >4.62, respectively
- Change-from-baseline in tau PET at Week 104 was a secondary endpoint

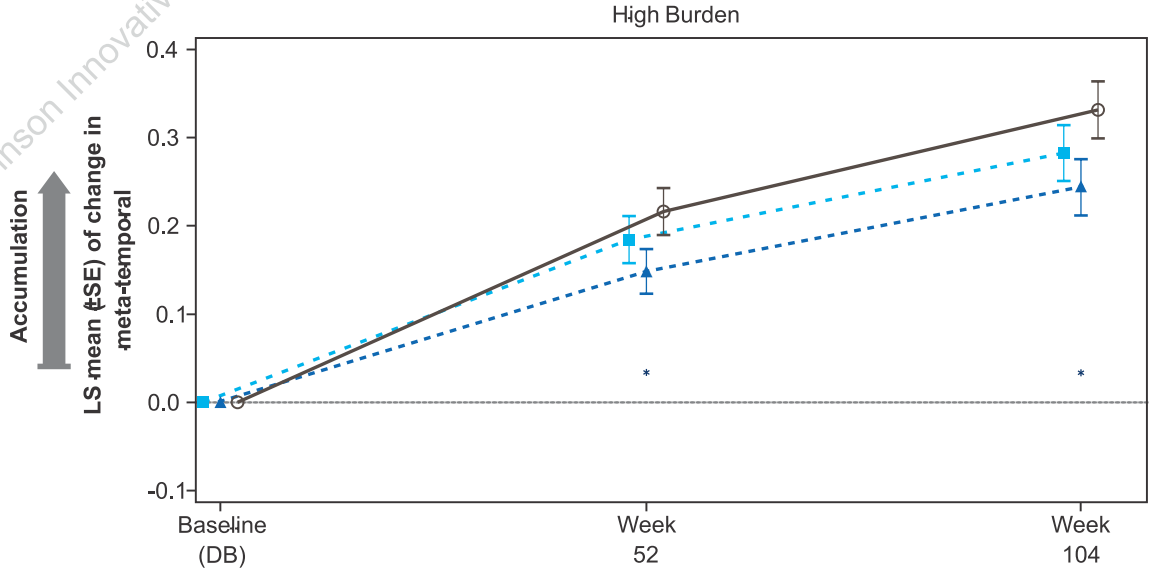
1. Wong J, Wang T, Datta R, et al. Tau positron emission tomography analysis methods for the quantification of tau spread in preclinical and early Alzheimer's disease. Alzheimer's Dement. 2026;22:e71573.
Z-score reference population was cognitively normal amyloid negative older individuals.
PET, positron emission tomography; p-tau217, tau phosphorylated at amino acid residue 217; ROI, region of interest; SD, standard deviation.

RESULTS – Posdinemab modestly slowed NFT accumulation in the meta-temporal region, with slowing in the high tau burden subgroup nominally significant at 3000 mg

- Analyses included 520 participants: posdinemab 1000 mg (n=170), 3000 mg (n=175), and placebo (n=175)

LS mean change over time in meta-temporal ROI SUVR by baseline tau burden on tau PET (low vs high, Braak 4 ROI z-score ≤4.62 vs >4.62)





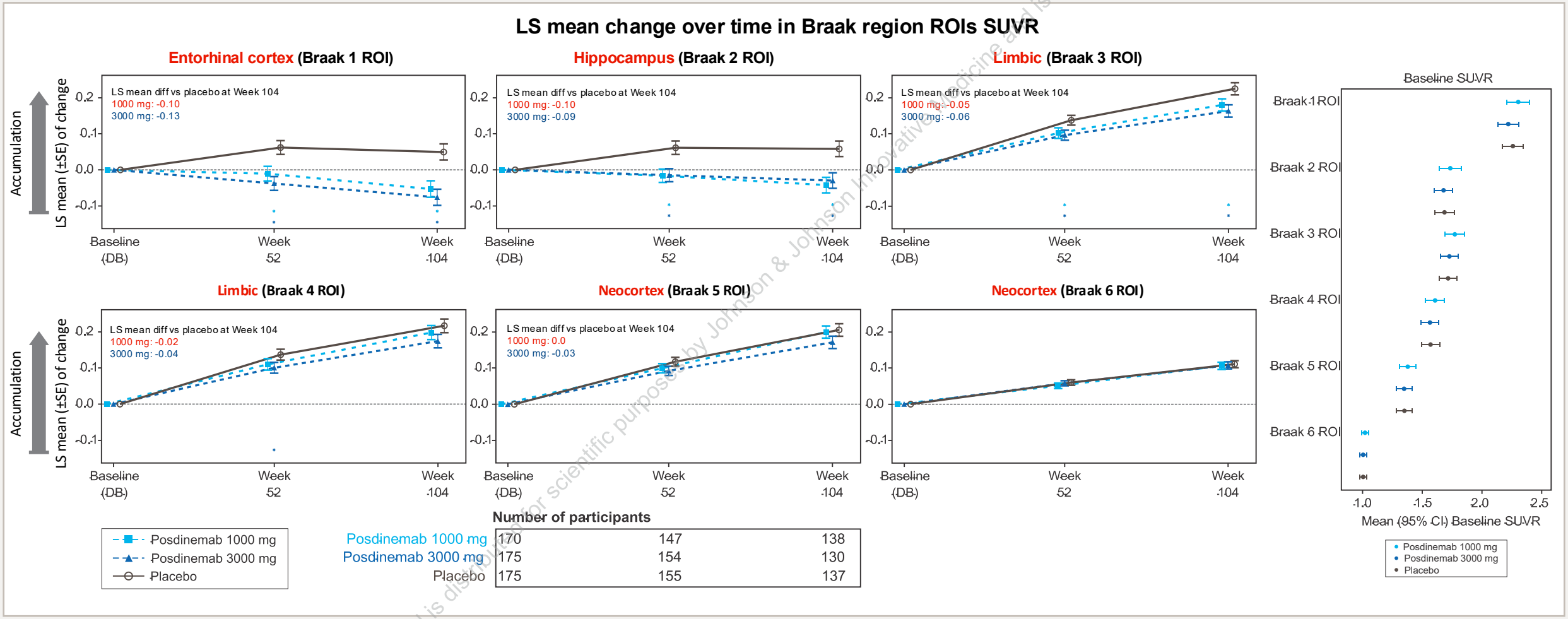
Number of participants	Baseline (DB)	Week 52	Week 104
Posdinemab 1000 mg	75	63	58
Posdinemab 3000 mg	76	63	56
Placebo	77	65	57

Number of participants	Baseline (DB)	Week 52	Week 104
Posdinemab 1000 mg	95	84	80
Posdinemab 3000 mg	99	91	74
Placebo	98	90	80

Posdinemab 1000 mg Posdinemab 3000 mg Placebo

*indicates nominal p-value for posdinemab 3000 mg versus placebo <0.05. LS mean change from baseline, SE, and p-value are derived using MMRM.
DB, double-blind; LS, least squares; MMRM, mixed model for repeated measures; NFT, neurofibrillary tangles; ROI, region of interest; SE, standard error; SUVR, standardized uptake value ratio.

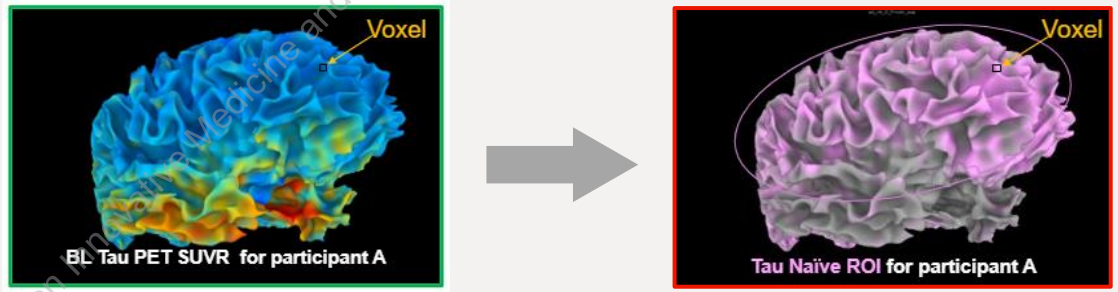
RESULTS – NFT accumulation was slowed (and even reduced below baseline) in brain regions affected earliest in AD but not in later affected regions



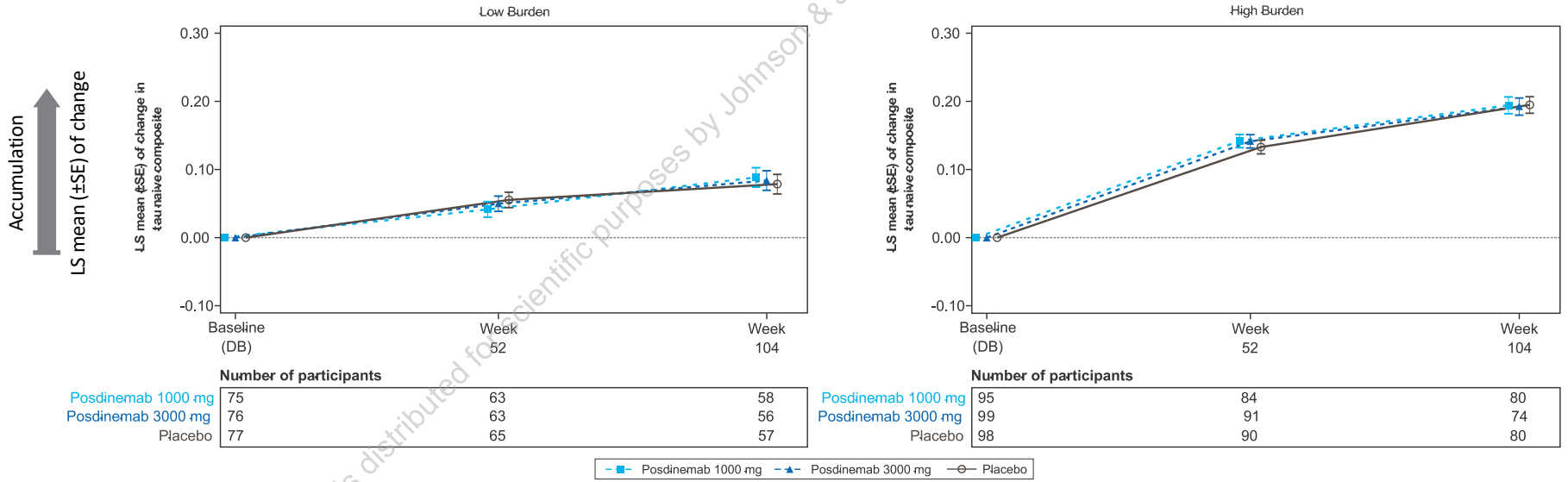
*indicates nominal p-value for posdinemab 1000 or posdinemab 3000 mg versus placebo <0.05. LS mean change from baseline, SE, and p-value are derived using MMRM.
DB, double-blind; LS, least squares; MMRM, mixed model for repeated measures; ROI, region of interest; SE, standard error; SUVR, standardized uptake value ratio, tau PET, tau positron emission tomography.

RESULTS – Posdinemab did not impact the spread of tau PET as measured by tau naïve ROI in the high or low tau burden subgroups

- Tau naïve ROI was designed to measure the spread of tau, detecting new NFT accumulation by tau PET in brain regions where SUVR was within 1 SD of cognitively normal amyloid-negative controls at baseline[1]



LS mean change over time in the tau naïve composite ROI SUVR by baseline tau burden on tau PET



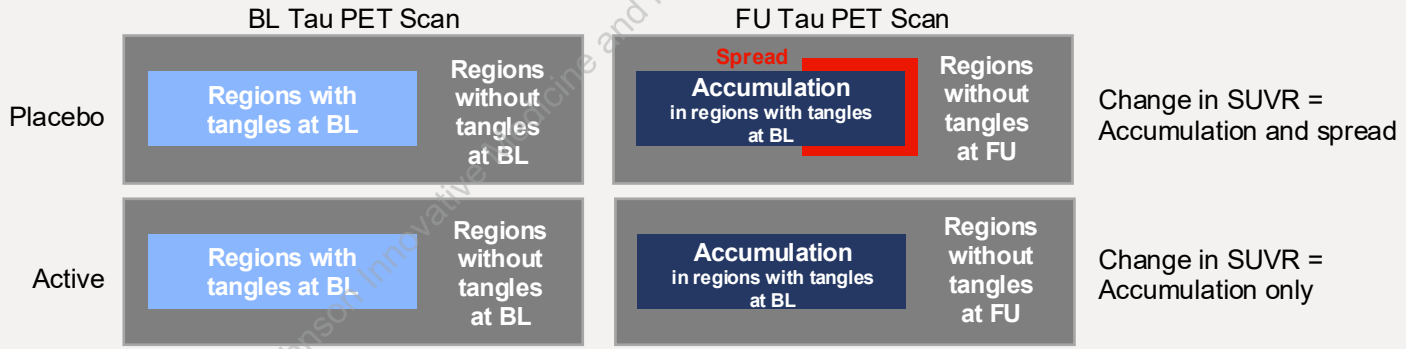
1. Wong J, Wang T, Datta R, et al. Tau positron emission tomography analysis methods for the quantification of tau spread in preclinical and early Alzheimer's disease. Alzheimer's Dement. 2026;22:e71573.

Note: LS mean change from baseline and SE are derived using MMRM.

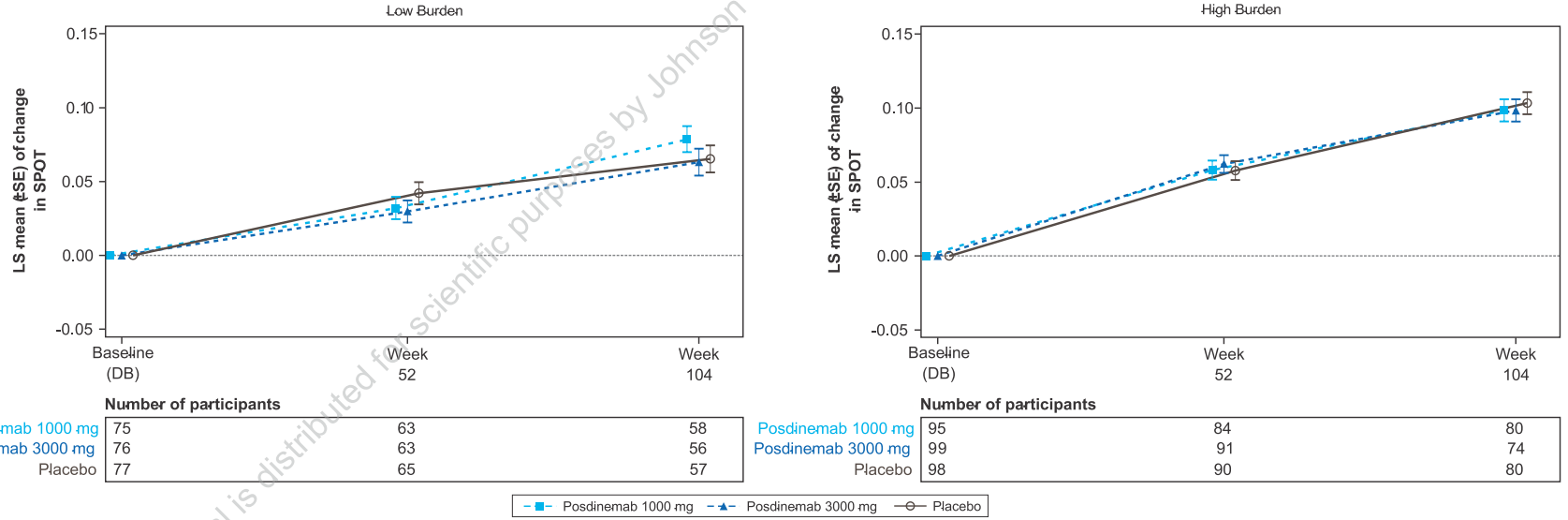
DB, double-blind; LS, least squares; MMRM, mixed model for repeated measures; NFT, neurofibrillary tangles; ROI, region of interest; SE, standard error; SUVR, standardized uptake value ratio; tau PET, tau positron emission tomography.

RESULTS – Similarly, posdinemab did not impact the spread of tau PET as measured by SPOT in the high or low tau burden subgroups

- The SPOT approach measures spread by computing the change in the fraction of cortex where voxels have elevated uptake, using tracer-specific SUVR threshold of 1.2[1]



LS mean change over time in SPOT volume over cerebral cortex ROI by baseline tau burden on tau PET



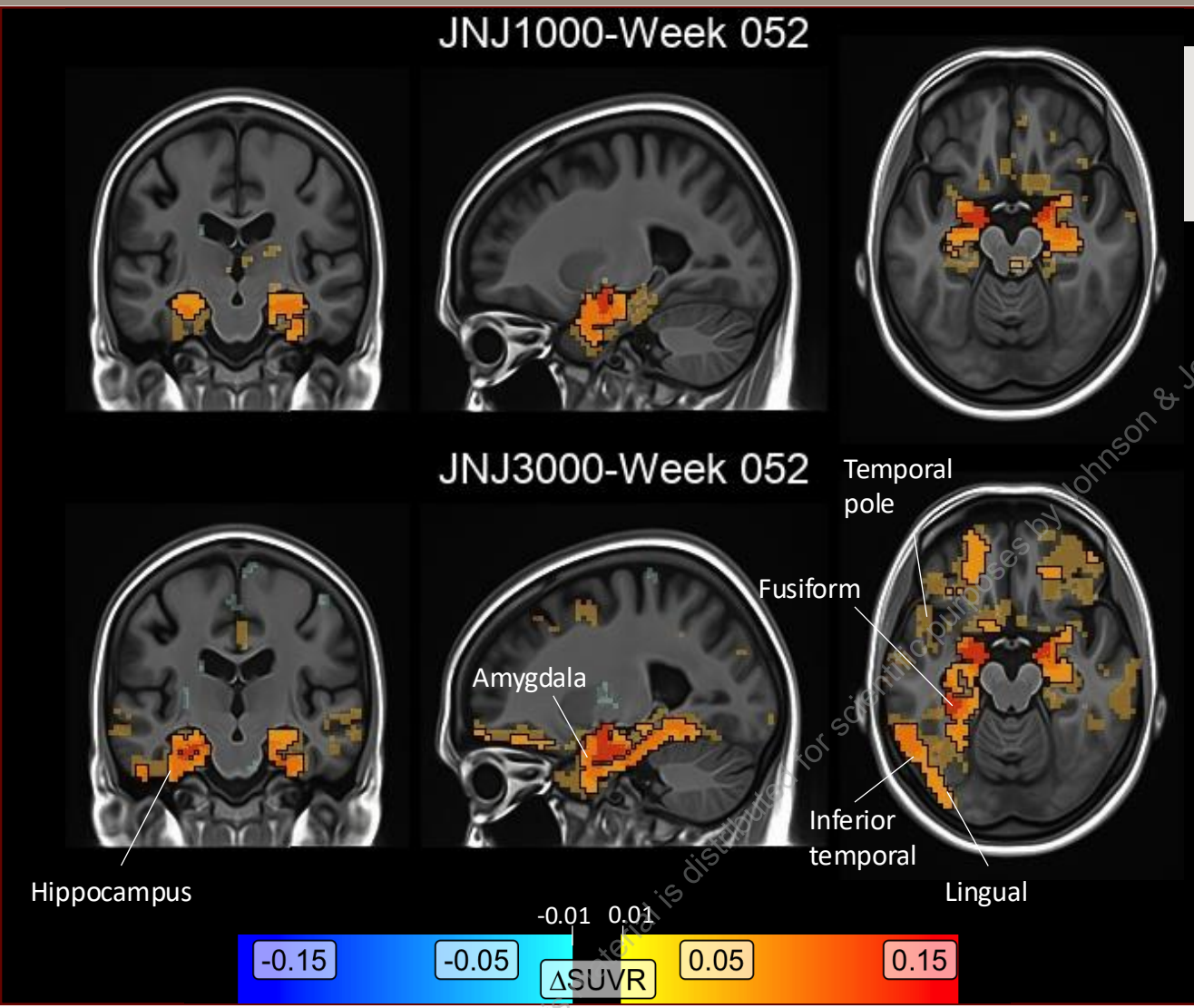
1. Wong J, Wang T, Datta R, et al. Tau positron emission tomography analysis methods for the quantification of tau spread in preclinical and early Alzheimer's disease. Alzheimer's Dement. 2026;22:e71573.

Note: LS mean change from baseline and SE are derived using MMRM.

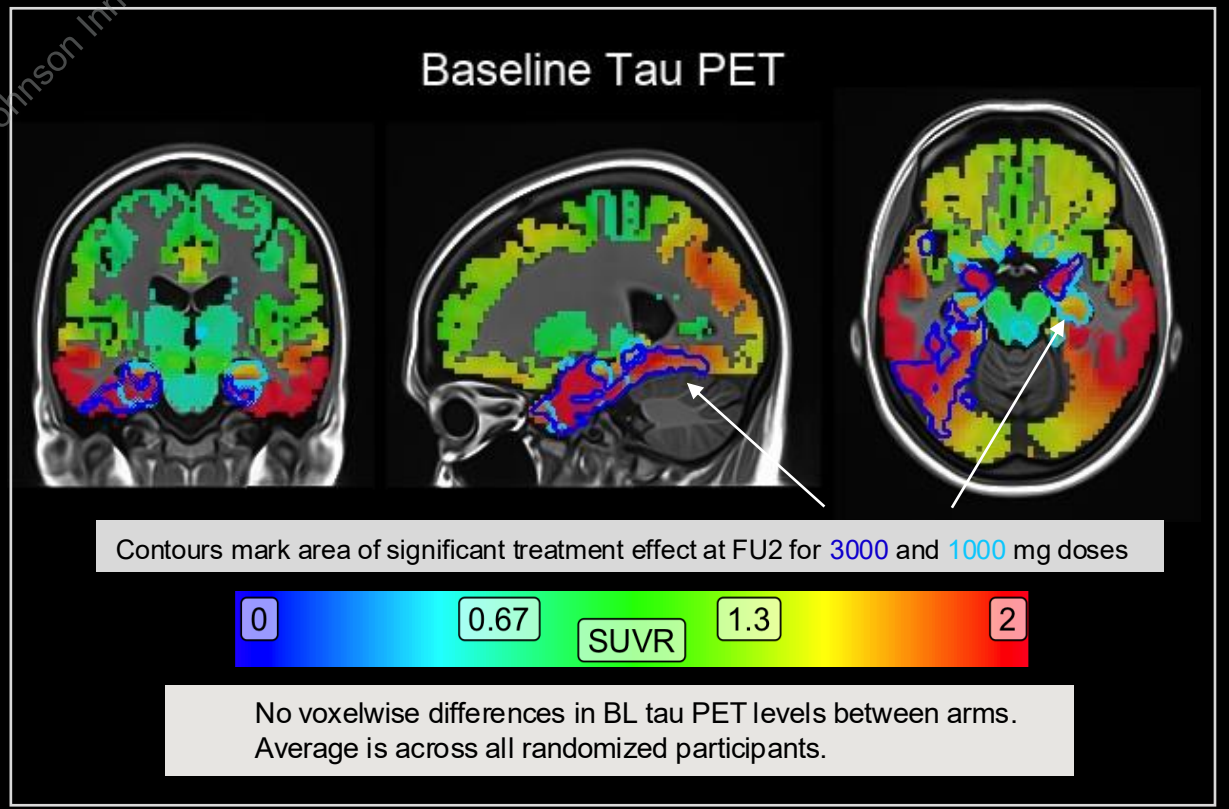
BL, baseline; DB, double-blind; FU, follow-up; LS, least squares; MMRM, mixed model for repeated measures; ROI, region of interest; SE, standard error; SPOT, spatial progression of tauopathy; SUVR, standardized uptake value ratio; tau PET, tau positron emission tomography.

RESULTS – In the aggregate, the areas of significant treatment effect on tau PET:

- Increased over time
- Were greater at the higher dose
- Co-located with regions of elevated SUVR at baseline



- Contoured regions denote areas of significant treatment effects (FWE < 0.05)
- Translucent areas denote voxels with nominal treatment effects (uncorrected p < 0.05)
- Treatment effect models included BL tau PET, age and sex as covariates



BL, baseline; FWE, family-wise error; NFT, neurofibrillary tangles; SUVR, standardized uptake value ratio; ; SUVR, standardized uptake value ratio; tau PET, tau positron emission tomography.

CONCLUSIONS

- **Posdinemab did not slow clinical decline or the spread of tau NFTs. However, results confirmed that NFT accumulation can be slowed by an anti-tau monoclonal antibody, particularly in earlier AD regions with higher tau burden**
- **Tau PET findings suggest that NFT accumulation can be modulated by an antibody targeting extracellular tau. This is consistent with observations in the Phase 2 trial of bepranemab, another mid-domain tau targeting monoclonal antibody[1]**
- **This finding is contrary to our prior expectation that posdinemab would have greatest slowing of NFT formation in unaffected regions. These tau PET results suggest that NFT formation and dissolution is a dynamic process**

1. Maguire RP, et al. Tau positron emission tomography results from TOGETHER, a double-blind, placebo-controlled Phase II study of bepranemab in prodromal–mild Alzheimer's disease. *Alzheimers Dement*. 2025 Dec 25;21(Suppl 5):e099279.
NFT, neurofibrillary tangles; PET, positron emission tomography.

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