

SHORT REPORT

Lecanemab in symptomatic PSEN1 p.Met233Val early-onset Alzheimer's disease: Neuroimaging safety, regional amyloid-PET dynamics, and longitudinal plasma biomarkers

Min-Young Noh^{1,2}  | Wonjae Sung^{1,2}  | Hyunkee Kim^{1,2}  | Bugyeong Son²  |
 Young-Eun Kim³  | Yun Young Choi⁴ | David M. Holtzman^{5,6,7}  | Seung Hyun Kim^{1,2} 

¹Department of Neurology, College of Medicine, Hanyang University, Seoul, Republic of Korea

²Cell Therapy Center, Department of Neurology, Hanyang University Seoul Hospital, Seoul, Republic of Korea

³Department of Laboratory Medicine, College of Medicine, Hanyang University, Seoul, Republic of Korea

⁴Department of Nuclear Medicine, Hanyang University Medical Center, Hanyang University College of Medicine, Seoul, Republic of Korea

⁵Department of Neurology, Hope Center for Neurological Disorders, Knight Alzheimer's Disease Research Center, Washington University School of Medicine, St. Louis, Missouri, USA

⁶Knight Washington University Alzheimer Disease Research Center, Washington University in St Louis, St Louis, Missouri, USA

⁷Hope Center for Neurological Disorders, Washington University in St Louis, St Louis, Missouri, USA

Correspondence

David M. Holtzman, Department of Neurology, Knight Washington University Alzheimer Disease Research Center, Hope Center for Neurological Disorders, Washington University in St Louis, St Louis, MO 63110, USA.

Email: holtzman@wustl.edu

Seung Hyun Kim, Address: Director of Cell Therapy Center, Department of Neurology, College of Medicine, Hanyang University, 222-1, Wangsimni-ro, Seongdong-gu, Seoul, 04763, Republic of Korea.

Email: kimsh1@hanyang.ac.kr

Funding information

Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea, Grant/Award Number: RS-2024-00348451

Abstract

Introduction: The presenilin 1 (PSEN1) p.Met233Val variant is a Dominantly Inherited Alzheimer Network–Trials Unit (DIAN-TU)–eligible autosomal-dominant Alzheimer's disease (ADAD) variant for which lecanemab response data are unavailable.

Methods: A 34-year-old symptomatic PSEN1 p.Met233Val carrier (APOE ε3/ε3) was prospectively followed through 26 lecanemab infusions over 12 months, with serial magnetic resonance imaging (MRI), amyloid positron emission tomography (PET), and plasma biomarkers.

Results: No amyloid-related imaging abnormalities occurred. Composite Centiloid increased modestly (+7.2), masking regional divergence: basal ganglia (−24.5) and medial temporal cortex (−22.1) declined, whereas posterior cortical regions accrued amyloid. Plasma amyloid beta (Aβ) 42/40 rose to 122% by T22, with concurrent decreases in phosphorylated tau at threonine 217 (p-tau217), p-tau181, neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP). Global Clinical Dementia Rating (CDR) score remained 0.5; caregiver reports noted improvements in spasticity, dystonia, and affective features.

Discussion: Lecanemab demonstrated neuroimaging safety and evidence of biological target engagement in this symptomatic PSEN1 p.Met233Val ADAD carrier. These longitudinal neuroimaging and plasma biomarker findings may help inform interpretation of treatment responses in genetically defined ADAD.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2026 The Author(s). *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring* published by Wiley Periodicals LLC on behalf of Alzheimer's Association.

KEYWORDS

amyloid-related imaging abnormalities (ARIA), autosomal-dominant Alzheimer's disease, Centiloid, Dominantly Inherited Alzheimer Network–Trials Unit (DIAN-TU), lecanemab, plasma biomarkers, presenilin 1 (PSEN1) p.Met233Val, regional amyloid positron emission tomography

Highlights

- This is the first 12-month lecanemab characterization in a symptomatic PSEN1 p.Met233Val carrier.
- There were no ARIA across 26 biweekly infusions in this APOE $\epsilon 3/\epsilon 3$ ADAD case.
- A reduction in basal ganglia (−24.5 CL) and medial temporal (−22.1 CL) amyloid was observed.
- Sustained plasma A β 42/40 elevation with downstream tau and NfL decreases was observed.
- Composite Centiloid (+7.2) masks regional divergence; the region level matters.

1 | BACKGROUND

Autosomal dominant Alzheimer's disease (ADAD) caused by pathogenic variants in presenilin 1 (*PSEN1*) is characterized by near-complete penetrance, very early onset, and a causal relationship between amyloid beta ($A\beta$) accumulation and neurodegeneration.¹ Among *PSEN1* variants, the p.Met233Val variant (exon 7; ATG→GTG) is associated with very early onset and a pleiotropic phenotype, including spasticity, cerebellar signs, and psychiatric features that precede overt dementia.^{2,3} Residue 233 lies at the substrate-binding pore of γ -secretase,⁴ consistent with gain-of-function amyloid beta ($A\beta$) 42 overproduction that can elevate plasma A β 42/40 ratios above thresholds typically observed in sporadic Alzheimer's disease (AD).⁵

Lecanemab, a humanized antibody targeting soluble $A\beta$ protofibrils,⁶ has demonstrated clinical benefit in early sporadic AD,⁷ and the Dominantly Inherited Alzheimer Network–Trials Unit (DIAN-TU) has opened anti-amyloid treatment arms to ADAD carriers.⁸ However, beyond a single brief case report involving the related p.Met233Thr variant,⁹ no published lecanemab response data exist for the *PSEN1* p.Met233Val variant despite its formal DIAN-TU eligibility. Two specific uncertainties remain: whether the microvascular vulnerability associated with aggressive *PSEN1* variants¹⁰ translates into elevated amyloid-related imaging abnormalities (ARIA) risk and whether the regional pattern of amyloid response in a high-production ADAD variant mirrors the whole-brain pattern seen in sporadic AD or instead shows region-specific divergence.

We present a prospective 12-month single-case characterization of a 34-year-old *PSEN1* p.Met233Val variant carrier treated with 26 lecanemab infusions at 2-week intervals, focusing on three observational anchors: (i) neuroimaging safety, (ii) regional amyloid-PET dynamics, and (iii) concurrent plasma biomarker profiling. We present this as a descriptive case report; no causal inference is made.

2 | METHODS

This prospective single case was approved by the Hanyang University Hospital Institutional Review Board (IRB) (HYUH IRB 2024-02-003-003) and conducted per the Declaration of Helsinki; the patient gave written informed consent for publication. A 34-year-old symptomatic man carrying heterozygous pathogenic *PSEN1* c.697A > G, p.Met233Val (pathogenic in ClinVar and Alzforum; APOE $\epsilon 3/\epsilon 3$) was enrolled on September 25, 2024. He received 26 lecanemab infusions at 2-week intervals under stepwise dose escalation (200 mg $\times$ 2, 500 mg $\times$ 2, then 10 mg/kg), following the Korean lecanemab practical guide.¹¹ The first infusion (T_1) was given on March 13, 2025; at the March 3, 2026 data cut-off, 26 infusions were complete and treatment ongoing (timeline, Figure 1A). Baseline assessment included Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) global score and sum of boxes (CDR-SB), and neurological examination. Baseline amyloid positron emission tomography (PET) (18 F-florbetaben) was performed 154 days before treatment; follow-up PET occurred 343 days after initiation. Composite and seven-region Centiloid (CL) values (frontal, posterior cingulate cortex [PCC]–precuneus, lateral temporal, lateral parietal, medial temporal, occipital, and basal ganglia, with hemispheric partitioning) were referenced to the standard Centiloid scale.¹² ARIA-monitoring magnetic resonance imaging (MRI) (FLAIR and hemorrhage-sensitive sequences, dual neuroradiologist review) was performed at the sixth, 13th, and 26th infusions. Plasma at eight time points (T-enroll, T_0 , T_1 , T_3 , T_5 , T_7 , T_{13} , T_{22}) was analyzed in duplicate on a Simoa HD-X analyzer (Quanterix) for A β 40, A β 42, phosphorylated tau at threonine 181 (p-tau181), p-tau217, neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP).^{13–15} Trajectories are presented descriptively as percentage of T_0 (absolute values, Table S1). Analyses used Python 3.11 and GraphPad Prism 10.

RESEARCH IN CONTEXT

- 1. Systematic review:** We searched PubMed and Google Scholar through April 2026 for lecanemab treatment response in PSEN1 carriers. Apart from a brief report involving the related *p*.Met233Thr variant, no longitudinal imaging or plasma biomarker data have been published for the PSEN1 *p*.Met233Val variant, a DIAN-TU-eligible mutation, before forthcoming DIAN-TU NexGen read-outs.
- 2. Interpretation:** This study provides the first 12-month longitudinal characterization of lecanemab response in symptomatic PSEN1 *p*.Met233Val early-onset AD. Although composite Centiloid increased modestly, region-level amyloid-PET revealed divergent responses, including reductions in the basal ganglia and medial temporal cortex. Plasma A β 42/40 elevation was accompanied by concurrent decreases in downstream tau, neurodegeneration, and glial biomarkers. Across 26 infusions, lecanemab was neuroimaging-safe, with no ARIA, and global CDR remained stable at 0.5, despite the minimal change in CDR-SB.
- 3. Future directions:** These observations may serve as useful reference data for future DIAN-TU and related ADAD studies, particularly for symptomatic carriers with substantial baseline amyloid burden. They support the incorporation of region-level amyloid-PET dynamics and longitudinal plasma biomarker profiling alongside composite measures, as these approaches may capture treatment-related biological and clinically relevant signals – including changes in motor tone and affective features – that are not fully reflected by global CDR or composite Centiloid outcomes alone.

3 | RESULTS

3.1 | Baseline phenotype, 12-month safety, and clinical stability

The patient presented with a decade-long history of dysarthria followed by progressive gait disturbance. Examination showed predominant upper motor neuron features, including lower-limb spasticity (Modified Ashworth Grade 2), brisk reflexes, sustained ankle clonus, and focal upper-limb dystonic posturing, with reduced facial expressivity and blunted affect that the caregiver reported as preceding cognitive decline. Baseline cognition was MMSE 21, global CDR 0.5, and CDR-SB 2, consistent with very mild impairment at the dementia threshold and characteristic of *p*.Met233Val.^{2,3} All 26 infusions were completed without interruption. Protocolized MRI after the sixth, 13th, and 26th infusions showed no ARIA-edema (ARIA-E) or ARIA-

hemorrhage (ARIA-H), with modest progression of cortical atrophy (grade 1 to 2; Figure S1). Across T₁ to T₂₂, global CDR stayed at 0.5, CDR-SB 2.0 to 2.5, and MMSE declined modestly (21 to 19) (Figure 1C). From around the second to fourth infusion, serial clinical and concordant caregiver observations noted reduced lower-limb spasticity and tone, improved dystonic posturing, and greater facial expressivity, spontaneous speech, and social engagement, sustained throughout but reported descriptively, without causal inference.

3.2 | Regional amyloid-PET divergence masked by composite

Baseline PET showed disproportionately prominent striatal deposition relative to cortex (Figure 1B); follow-up showed visually reduced striatal uptake. Composite Centiloid rose from 86.26 to 93.49 (Δ +7.23 CL over 497 days), obscuring marked regional divergence (Table 1, Figure S2). The basal ganglia, with the highest baseline burden (193.2 CL), declined by -24.5 CL (-12.7%); the medial temporal cortex fell from 15.6 to -6.5 CL (Δ -22.1 CL; standardized uptake value ratio 1.11 to 0.97). Conversely, PCC-precuneus rose +13.9 CL (+16.9%) and lateral parietal +11.3 CL (+34.0%); frontal, lateral temporal, and occipital regions were stable. Medial temporal asymmetry reversed from right-predominant to near-symmetric (index -0.93 to +0.22).

3.3 | Sustained plasma target engagement and downstream reductions

Plasma A β 42/40 rose after the first infusion (T₁, 104% of T₀) to 122% by T₂₂ (Figure 1D; raw values, Table S1), consistent with sustained engagement of the soluble compartment. The absolute ratio (~ 0.23 to 0.28) is expected for PSEN1 carriers from γ -secretase gain of function⁵ and reflects pharmacodynamic engagement, not threshold crossing. Downstream markers decreased relative to T₀ (Figure 1E,F): p-tau217 to $\sim 80\%$ by T₂₂ (-20%), p-tau181 to $\sim 94\%$ (nadir $\sim 78\%$ at T₇), NfL to $\sim 79\%$, and GFAP to $\sim 88\%$ (after an early T₁ to T₃ rise). Thus, by T₂₂, all four downstream markers were reduced, coinciding temporally with sustained A β 42/40 elevation and basal ganglia and medial temporal PET reduction, though the single-case design precludes mechanistic inference.

4 | DISCUSSION

This case offers three observations from ~ 12 months of ongoing lecanemab in aggressive PSEN1 ADAD. First, lecanemab was neuroimaging-safe across 26 infusions in a symptomatic *p*.Met233Val carrier with severe baseline amyloid burden, with no ARIA. Post-codon-200 PSEN1 variants carry severe leptomenigeal A β and microbleed susceptibility,¹⁰ although APOE $\epsilon 3/\epsilon 3$ confers a lower-risk stratum,⁷ PSEN1-associated cerebral amyloid angiopathy (CAA) risk is APOE-independent. Recently reported 6-month DIAN-TU NexGen

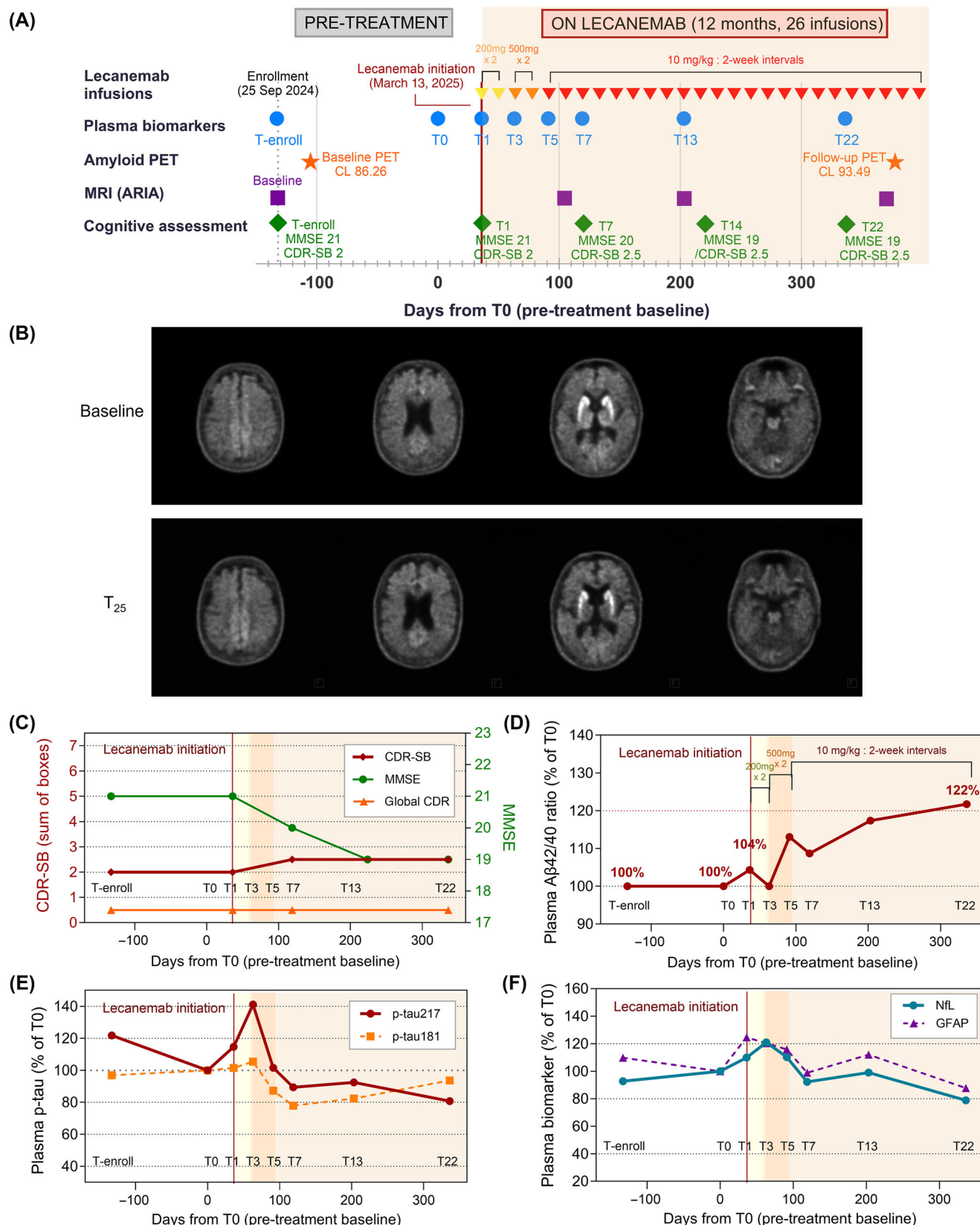


FIGURE 1 Integrated longitudinal characterization of lecanemab response in a young symptomatic *PSEN1* p.Met233Val variant carrier. (A) Study timeline. Enrollment occurred at T-enroll, 19 weeks before lecanemab initiation. Baseline PET, MRI, and cognitive assessment were performed before treatment. Lecanemab was initiated at T₁ on March 13, 2025, using a stepwise dose-escalation protocol: 200 mg × 2, 500 mg × 2, then 10 mg/kg every 2 weeks. Surveillance MRI for ARIA monitoring (squares) was performed at baseline and after the sixth, 13th, and 26th infusions. Cognitive assessments (diamonds; MMSE/CDR-SB shown at each time point) were performed at T-enroll, T₁, T₇, T₁₄, and T₂₂, and plasma sampling was collected at eight time points (T-enroll, T₀, T₁, T₃, T₅, T₇, T₁₃, T₂₂). Follow-up PET was performed at T₂₅ (CL 93.49). (B) Axial

TABLE 1 Regional amyloid-PET Centiloid and SUVR trajectories (baseline vs follow-up).

Region	CL (2024)	CL (2026)	Δ CL	% change	CL/year	SUVR (2024)	SUVR (2026)
Basal ganglia	193.23	168.71	-24.52	-12.7%	-18.02	2.27	2.11
Medial temporal	15.63	-6.51	-22.14	-141.7%	-16.27	1.11	0.97
Occipital	38.30	39.13	+0.83	+2.2%	+0.61	1.26	1.26
Lateral temporal	25.82	27.41	+1.59	+6.2%	+1.17	1.18	1.19
Frontal	54.18	57.20	+3.02	+5.6%	+2.22	1.36	1.38
Lateral parietal	33.13	44.40	+11.27	+34.0%	+8.28	1.23	1.30
PCC-precuneus	82.31	96.18	+13.87	+16.9%	+10.19	1.55	1.64
Composite	86.26	93.49	+7.23	+8.4%	+5.31	1.29	1.32

Note: Lecanemab exposure covered the final 343 days (0.94 year). Inter-scan interval: 497 days (1.36 years).

Abbreviations: CL, Centiloid; PCC, posterior cingulate cortex; SUVR, standardized uptake value ratio.

data ($N = 97$ symptomatic ADAD; ARIA-E 20.6% overall, 13.9% in $\epsilon 4$ non-carriers) confirm elevated ARIA risk in ADAD without variant stratification¹⁶; the absence of ARIA here across 26 infusions is therefore noteworthy. The clinical phenotype, dominated by spasticity, dystonic posturing, and pyramidal and pseudobulbar features out of proportion to cognition, aligns with the post-codon-200 transmembrane-domain spectrum linked to spastic paraplegia and severe CAA, and variant location influences progression.¹⁶ The striatal-predominant baseline burden is a recognized *PSEN1* hallmark.^{2,3,17,18}

Second, regional amyloid-PET was heterogeneous. Striatal-predominant retention is a characteristic *PSEN1* imaging feature, distinct from the cortical-predominant pattern of sporadic AD.¹⁹ Despite a +7.2 CL composite increase, the basal ganglia (193 CL baseline) declined -24.5 CL and the medial temporal cortex -22.1 CL, while PCC-precuneus and lateral parietal continued to accrue. This may reflect γ -secretase gain-of-function sustaining *A β 42* overproduction⁵ that locally outpaces clearance, lecanemab's preferential engagement of soluble protofibrils over fibrillar plaque,⁶ and regional antibody-penetration variation. The modest composite response is consistent with PK/PD modeling predicting slower reduction at younger ages,²⁰ relevant for this 34-year-old. Critically, basal ganglia clearance is invisible at the composite level, so region-level quantification may capture treatment effects in aggressive ADAD that the composite reads as progression. The basal ganglia and medial temporal reductions also

align temporally with the observed motor and affective improvements, which is hypothesis-generating but not attributable to treatment.

Third, sustained *A β 42/40* elevation with concurrent decreases in *p*-tau217 (-20%), *p*-tau181, NfL (-21%), and GFAP (-12%) provides a within-subject pattern in which target engagement and downstream tau, neurodegeneration, and glial markers move consistently with an amyloid-directed response. Notably, plasma *p*-tau217 exhibited a transient increase immediately after treatment initiation before subsequently declining. One possible explanation is transient mobilization of soluble tau species or an acute biological response accompanying rapid amyloid remodeling rather than worsening neurodegeneration. Overall, the subsequent trajectories of plasma *p*-tau217 and *p*-tau181 were consistent with amyloid-driven biological change.¹⁴ The downstream reductions oppose the rising NfL and GFAP expected from ADAD natural history.¹⁵ Continued posterior cortical accrual despite plasma engagement suggests soluble and fibrillar compartments may respond divergently within one individual. Future studies or clinical trials in *PSEN1* variants with prominent pyramidal, extrapyramidal, cerebellar, and neuropsychiatric features should include longitudinal standardized scales to objectively capture these non-cognitive clinical domains, alongside cognitive, imaging, and fluid biomarker outcomes.¹⁸

This study has several limitations. As a single open-label case, all observations are descriptive and cannot establish treatment efficacy or causality. Tau PET and cerebrospinal fluid biomarkers were

amyloid-PET images at baseline and follow-up. Baseline PET was performed in October 2024 before treatment initiation, and follow-up PET was performed at T₂₅, in February 2026, after approximately 11 months of lecanemab treatment. Composite Centiloid increased from 86.26 to 93.49. Four representative axial slices are shown for each time point, from superior to inferior levels, demonstrating persistent amyloid positivity and prominent striatal tracer retention characteristic of ADAD. Full regional quantification is provided in Table 1 and Figure S2. (C) Cognitive trajectories across the on-treatment interval, showing CDR-SB, MMSE, and global CDR. (D) Longitudinal plasma *A β 42/40* ratio across eight time points. (E) Longitudinal plasma *p*-tau217 and *p*-tau181 and (F) longitudinal plasma NfL, GFAP. Biomarker values in panels (D)–(F) are expressed as percentages relative to the T₀ baseline. The x-axis in all panels is referenced to T₀, defined as the pre-treatment baseline. The vertical line in panels (C)–(F) indicates lecanemab initiation at T₁, and the shaded pre-treatment interval denotes the 154-day gap between baseline PET and treatment initiation. ARIA, amyloid-related imaging abnormalities; *A β* , amyloid beta; CDR, Clinical Dementia Rating; CDR-SB, Clinical Dementia Rating Sum of Boxes; CL, Centiloid; GFAP, glial fibrillary acidic protein; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging; NfL, neurofilament light chain; PET, positron emission tomography; *p*-tau, phosphorylated tau; SUVR, standardized uptake value ratio; T-enroll, enrollment time point; T₀ to T₂₅, longitudinal study time points (T₀ = pre-treatment baseline; T₁ = first lecanemab infusion; subscripts denote infusion number).

unavailable, and baseline amyloid-PET was performed 154 days before treatment initiation, limiting direct assessment of treatment-related amyloid changes. Although serial plasma biomarkers provided dense longitudinal monitoring, the findings require validation in larger ADAD cohorts.

In conclusion, in this young symptomatic *PSEN1* p.Met233Val carrier, 12 months of lecanemab was neuroimaging-safe with sustained plasma target engagement. Regional amyloid-PET diverged, with basal ganglia and medial temporal reductions alongside posterior accrual, together with downstream biomarker decreases and preserved CDR. Although no causal or efficacy inference can be drawn from a single case, this dense longitudinal profile suggests that lecanemab can engage amyloid biology in *PSEN1* p.Met233Val ADAD and may generate regional and biomarker signals not captured by composite amyloid or global cognitive measures alone. This case highlights the importance of region-level amyloid quantification, longitudinal plasma biomarker profiling, and standardized assessment of non-cognitive motor and neuropsychiatric features in future DIAN-TU and related ADAD studies.

AUTHOR CONTRIBUTIONS

M.-Y.N.: Conceptualization, methodology, investigation, writing – original draft. W.S., H.K., B.S.: Investigation, data curation. Y.-E.K.: Methodology (genetic and laboratory analysis). Y.Y.C.: Methodology (neuroimaging analysis), formal analysis (amyloid-PET regional Centiloid quantification). D.M.H.: Conceptualization (supporting), review and editing, supervision (supporting). S.H.K.: Conceptualization, supervision, writing – review and editing, funding acquisition. All authors discussed the results and commented on the paper.

ACKNOWLEDGMENTS

The authors are grateful to the patient and his family for their participation in this study. We also thank the nursing and PET imaging staff at Hanyang University Hospital for their support of this prospective characterization. This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center (KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (RS-2024-00348451).

CONSENT STATEMENT

Written informed consent was obtained from all participants.

CONFLICT OF INTEREST STATEMENT

M.-Y.N., W.S., H.K., B.S., Y.-E.K., Y.Y.C., and S.H.K. declare no competing interests. D.M.H. has equity in and is on the scientific advisory board of C2N Diagnostics; is on the scientific advisory boards of Denali, Genentech, Acta, Cajal, and Cajal Therapeutics; and consults for Pfizer, Roche, Switch Therapeutics, and Annexon. Author disclosures are available in the [Supporting Information](#).

ORCID

Min-Young Noh  <https://orcid.org/0000-0002-2746-0686>

Wonjae Sung  <https://orcid.org/0000-0002-4637-5890>

Hyunkee Kim  <https://orcid.org/0000-0003-3824-6930>

Bugyeong Son  <https://orcid.org/0009-0004-5372-5248>

Young-Eun Kim  <https://orcid.org/0000-0002-4082-7630>

David M. Holtzman  <https://orcid.org/0000-0002-3400-0856>

Seung Hyun Kim  <https://orcid.org/0000-0001-9644-9598>

REFERENCES

1. Liu H, Marsh TW, Shi X, et al. The landscape of autosomal-dominant Alzheimer's disease: global distribution and age of onset. *Brain*. 2025;148(7):2429–2440.
2. Houlden H, Crook R, Dolan RJ, McLaughlin J, Revesz T, Hardy J. A novel presenilin mutation (M233V) causing very early onset Alzheimer's disease with Lewy bodies. *Neurosci Lett*. 2001;313(1–2):93–95.
3. Appel-Cresswell S, Guella I, Lehman A, Foti D, Farrer MJ. *PSEN1* p.Met233Val in a complex neurodegenerative movement and neuropsychiatric disorder. *J Mov Disord*. 2018;11(1):45–48.
4. Zhou R, Yang G, Guo X, Zhou Q, Lei J, Shi Y. Recognition of the amyloid precursor protein by human gamma-secretase. *Science*. 2019;363(6428):eaaw0930.
5. Petit D, Fernandez SG, Zoltowska KM, et al. Abeta profiles generated by Alzheimer's disease causing *PSEN1* variants determine the pathogenicity of the mutation and predict age at disease onset. *Mol Psychiatry*. 2022;27(6):2821–2832.
6. Johannesson M, Soderberg L, Zachrisson O, et al. Lecanemab demonstrates highly selective binding to abeta protofibrils isolated from Alzheimer's disease brains. *Mol Cell Neurosci*. 2024;130:103949.
7. van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9–21.
8. Bateman RJ, Li Y, McDade EM, et al. Safety and efficacy of long-term gantenerumab treatment in dominantly inherited Alzheimer's disease: an open-label extension of the phase 2/3 multicentre, randomised, double-blind, placebo-controlled platform DIAN-TU trial. *Lancet Neurol*. 2025;24(4):316–330.
9. Pan A, Cao R, Ling X, Zou J, Bi W. Efficacy of lecanemab in early-onset Alzheimer's disease with a novel *PSEN1* (p.Met233Thr) mutation: a case report. *Neurol Sci*. 2025;47(1):21.
10. Ringman JM, Sachs MC, Zhou Y, Monsell SE, Saver JL, Vinters HV. Clinical predictors of severe cerebral amyloid angiopathy and influence of APOE genotype in persons with pathologically verified Alzheimer disease. *JAMA Neurol*. 2014;71(7):878–883.
11. Jeon SY, Wang SM, Roh HW, et al. Practical guide of the Korean association for geriatric psychiatry to anti-amyloid monoclonal antibody therapy for Alzheimer's disease: focused on lecanemab. *J Korean Med Sci*. 2025;40(28):e215.
12. Klunk WE, Koeppe RA, Price JC, et al. The centiloid project: standardizing quantitative amyloid plaque estimation by PET. *Alzheimers Dement*. 2015;11(1):1–15 e11–14.
13. Schindler SE, Bollinger JG, Ovod V, et al. High-precision plasma beta-amyloid 42/40 predicts current and future brain amyloidosis. *Neurology*. 2019;93(17):e1647–e1659.
14. Palmqvist S, Janelidze S, Quiroz YT, et al. Discriminative accuracy of plasma phospho-tau217 for Alzheimer disease vs other neurodegenerative disorders. *JAMA*. 2020;324(8):772–781.
15. Hofmann A, Hasler LM, Lambert M, et al. Comparative neurofilament light chain trajectories in CSF and plasma in autosomal dominant Alzheimer's disease. *Nat Commun*. 2024;15(1):9982.
16. Zhou J, Llibre-Guerra J, Clifford D, et al. Safety of lecanemab during 6-month treatment in the DIAN-TU-001 trial. *Alzheimers Dement*. 2025;21 (Suppl 5): e105304 doi:10.1002/alz70859_105304
17. Benzinger TL, Blazey T. Regional variability of imaging biomarkers in autosomal dominant Alzheimer's disease. *Proc Natl Acad Sci U S A*. 2013;110(47):E4502–4509.

18. Schultz SA, Shirzadi Z, Schultz AP, et al. Location of pathogenic variants in PSEN1 impacts progression of cognitive, clinical, and neurodegenerative measures in autosomal-dominant Alzheimer's disease. *Aging Cell*. 2023;22(8):e13871.
19. Qin Q, Fu L, Wang R, et al. Prominent striatum amyloid retention in early-onset familial Alzheimer's disease with PSEN1 mutations: a pilot PET/MR study. *Front Aging Neurosci*. 2021;13:732159.
20. Wildsmith KR, Benzinger TLS, Gordon BA, et al. Lecanemab in DIAD: 6-month amyloid PET results from the DIAN-TU-001 trial. *Alzheimers Dement*. 2025;21(1):e70859 doi:[10.1002/alz70859_105303](https://doi.org/10.1002/alz70859_105303)

How to cite this article: Noh M-Y, Sung W, Kim H, et al. Lecanemab in symptomatic PSEN1 p.Met233Val early-onset Alzheimer's disease: Neuroimaging safety, regional amyloid-PET dynamics, and longitudinal plasma biomarkers. *Alzheimer's Dement*. 2026;18:e70468. <https://doi.org/10.1002/dad2.70468>

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.