

Challenges in the Diagnostic Process for Anti-amyloid β Antibody Therapy in Alzheimer's Disease

Mitsuyoshi Tamura¹, Yoshikazu Nakano¹, Kenta Osawa¹, Yoshikazu Chishiki¹, Yutaro Suzuki¹, Kosuke Yamagishi¹, Takuro Horikoshi², Masahiro Mori¹, Shigeki Hirano¹

1) Department of Neurology, Chiba University Graduate School of Medicine, Chiba, Japan

2) Department of Radiology, Chiba University Hospital, Chiba, Japan



Background & Objective

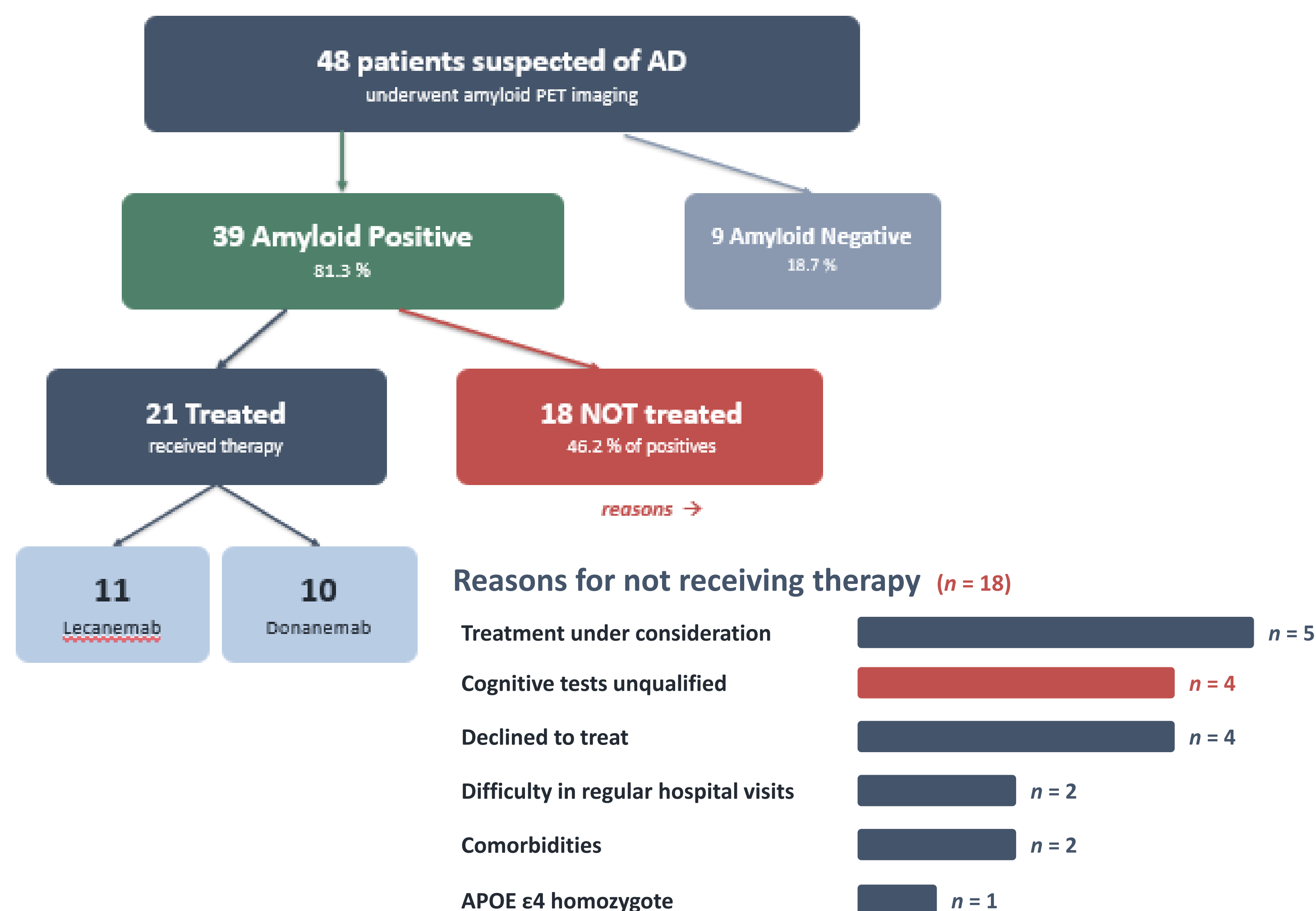
Anti-amyloid β antibody therapies, lecanemab and donanemab, have been available in Japan since 2023 for mild cognitive impairment or dementia due to Alzheimer's disease (AD). Eligibility and monitoring conditions differ by region and by agent; for example, the European Medicines Agency excludes APOE ϵ 4 homozygotes because of the elevated risk of amyloid-related imaging abnormalities, whereas in Japan these patients may be treated under enhanced monitoring, and the two agents differ in their approved disease-severity range and treatment paradigm. However, the diagnostic process imposes a multiple burden on both physicians and patients with dementia. The objective of this study was to clarify the sensitivity of amyloid imaging and to investigate the reasons for not receiving therapy among amyloid-positive patients.

Methods

Participants Consecutive patients who underwent amyloid positron emission tomography (PET) imaging at the Department of Neurology, Chiba University Hospital, from August 2023 to September 2025.

Design Clinical characteristics of amyloid-negative and amyloid-positive patients among dementia patients who underwent PET imaging were retrospectively compared based on information collected from medical records. Among the amyloid-positive patients, the reasons why some did not receive anti-A β antibody therapy were investigated.

Results



Approximately half of amyloid-positive patients did not receive anti-amyloid β antibody therapy. The most common reason for not proceeding was a decline in MMSE score below the eligibility criteria.

Table 1. Baseline characteristics (mean $\pm$ SD unless noted)

	Whole cohort (n = 48)	Amyloid positive group (n = 39)	Amyloid negative group (n = 9)	p-value ^b
Age (years)	70.2 $\pm$ 9.7	69.0 $\pm$ 9.8	75.3 $\pm$ 7.7	0.079
Female, n (%)	23 (47.9)	19 (48.7)	4 (44.4)	1.000
MMSE	24.0 $\pm$ 3.8	23.7 $\pm$ 3.8	25.1 $\pm$ 3.9	0.418
Global CDR ^a	0.68 $\pm$ 0.30	0.70 $\pm$ 0.32	0.61 $\pm$ 0.22	0.455
CDR SoB ^a	3.71 $\pm$ 1.93	3.73 $\pm$ 2.00	3.61 $\pm$ 1.73	0.878
Centiloid scale	54.3 $\pm$ 37.4	68.1 $\pm$ 26.0	-5.4 $\pm$ 7.4	<0.001

^a Global CDR and CDR-SoB available in n = 46 (whole cohort) / n = 37 (AD group). Groups defined by amyloid-PET visual read.

^b AD vs non-AD: Mann-Whitney U test (continuous variables); Fisher's exact test for sex. Bold = p < 0.05.

Discussion

As of June 2026, anti-amyloid- β antibodies are approved in more than 50 countries; in Japan, lecanemab and donanemab are now clinically available¹. Unlike conventional anti-dementia drugs, including cholinesterase inhibitors and memantine, they act on the underlying pathophysiology of AD by removing cerebral amyloid- β ^{2,3}. Real-world implementation, however, faces substantial barriers across four domains:

1 Economic & systemic

Cost-effectiveness is a leading barrier, cited by $\approx$ 55 % of Japanese specialists surveyed⁴.

2 Healthcare infrastructure

Insufficient capacity for amyloid PET, infusion, and the intensive monitoring these therapies require.

3 Safety & AE management

Risk of amyloid-related imaging abnormalities (ARIA), especially in APOE ϵ 4 carriers and patients on anticoagulants⁴. However, the frequency of ARIA seems to be lower in the real-world compared to that of reported clinical trials and when evident, it tends to be mild or asymptomatic. The time spent for explaining ARIA is gradually reducing in clinical practice.

4 Eligibility criteria

Establishing a framework that enables the early detection of AD, along with timely referral to specialists and linkage to appropriate treatment, is necessary. Especially, patients having MMSE 20-23 should proceed to treatment initiation as quickly as possible.

Conclusion

Earlier detection and a faster diagnostic process are pivotal, yet they must be balanced against the difficulty of shared decision-making about these therapies.

1. Eisai Co., Ltd. / Eli Lilly and Company. News releases on global regulatory approval status of lecanemab and donanemab; 2026.

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