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Integrating Disease-Modifying Therapies and Management of Amyloid-Related Imaging Abnormalities in Early Alzheimer's Care

Updated Guidance for Specialist Clinicians in the Asia-Pacific

Patient Selection for Disease-Modifying Therapies (DMTs)[1,2,3]

Key evaluation criteria

- Age
- Diagnosis and assessed severity of cognitive impairment
- Confirmed amyloid pathology
- Neuroimaging results
- Apolipoprotein E (*APOE*) genotype
- Anticoagulant use*

Final treatment plan based on:

- Risk-benefit analysis
- CARE–Connect: build a shared understanding of the diagnosis

*Lecanemab is not recommended in patients requiring anticoagulants; thrombolytics should be avoided with lecanemab and donanemab

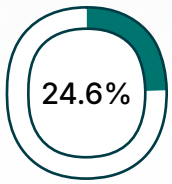
- *APOE* ε4 homozygotes carry the highest risk of amyloid-related imaging abnormalities (ARIA)[1,4]
  - Some regulators, including the European Union (EU), the United Kingdom, and Taiwan, exclude them from treatment
  - The US and most Asia-Pacific (APAC) appropriate use recommendations (AURs) advise genotyping and counselling not exclusion
- Magnetic resonance imaging (MRI) findings may exclude a significant proportion of amyloid-positive patients
- Over 30% of otherwise AUR-eligible patients in a Korean memory clinic were excluded on MRI findings—mainly vascular lesions, including cortical infarcts, lacunar infarcts, and Fazekas grade 3 white matter hyperintensities[2]

Real-World Eligibility in an Asia-Pacific Memory Clinic[2*]

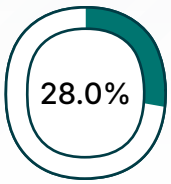
2,726 patients attending a Korean memory clinic

1,005 amyloid-positive patients with MRI and clinical dementia rating data

Eligible for:



Lecanemab



Donanemab

(9.1% and 10.3% of the initial sample)

In the Korean cohort, microhaemorrhages were counted on susceptibility-weighted imaging (SWI), which was the routine sequence in Korean centres at the time, whereas Clarity AD used T2-weighted gradient-recalled echo (GRE). SWI detects substantially more microhaemorrhages than T2* GRE, so the 24.6%/28.0% eligibility estimates are likely conservative relative to trial-based counting. In Korea, lecanemab has been in routine use since late 2024, while donanemab is not. LQB agents are non-reimbursed, and out-of-pocket cost is the dominant barrier to treatment

Insights from a Retrospective Study of Eligibility for Anti-Amyloid Treatment[5]

517 patients attending community memory services

32% patients potentially eligible for triaging

500 patients attending specialist clinics

14% patients potentially eligible for anti-amyloid treatment

- Specialist clinics with advanced testing facilities recommend a narrower eligible pool for triaging than community services
- Although many patients attending memory clinics may be referred for DMT triaging, only a minority are likely suitable for treatment

Additional Considerations for Eligibility

- Transport access to:
  - Infusion centres
  - Centres/clinics for patient monitoring
- Care partner for treatment support

- Healthcare infrastructure varies across APAC, potentially constraining access to positron emission tomography (PET)/MRI scans, cerebrospinal fluid (CSF) biomarker analysis, and *APOE* ε4 testing[6]
  - A 2023 ASNR international neuroradiologist practice survey found that less than half of respondents (39.4%) had specific MRI protocols in place for Alzheimer's disease (AD) therapeutics imaging[11]
- Plasma phosphorylated-tau 217 (p-tau$_{217}$) performs comparably to CSF p-tau$_{217}$ and may reduce the need for lumbar punctures[7]
- The first plasma p-tau$_{217}$/Aβ$_{1-42}$ ratio test was cleared by the FDA in May 2025, with comparable assays already available in Japan, the UK, and China[8]

Fostering Collaboration and Shared Understanding[6]

Primary care physicians must communicate clearly and manage expectations by educating and counselling patients and caregivers

Geriatricians, neurologists, and psychiatrists support early diagnosis and collaborative decision-making in early AD

Building the Individual Monitoring Plan[4]

When assessing risk of ARIA, clinicians must consider:

APOE genotyping

Baseline microhaemorrhage count

Anticoagulant and antiplatelet use (increases haemorrhage risk)

CARE–Align: match monitoring burden to patient and care partner goals[3]

APOE ε4 Status in APAC Populations

APOE ε4 is less frequent in Asia than in Europe and North America[9]

However, the *APOE* ε4 allele carries a higher AD risk in East Asian populations[10]

MRI Surveillance Schedule[11]

Baseline brain MRI: ideally, 3–6 months before initiating therapy; up to 12 months acceptable if negative for microhaemorrhages

Repeat MRI: if 1–4 baseline microhaemorrhages on a scan 7–12 months before initiation (interval progression may affect treatment eligibility or later be counted as ARIA-H)

4 to 5 routine MRI scans/year: during the first year of DMT

Specific schedule varies by anti-amyloid antibody[11]

- Lecanemab: before the 3rd, 5th, 7th, and 14th infusions, with a further scan recommended around week 52
- Donanemab: before the 2nd, 3rd, 4th, and 7th infusions

Japan's specific guidance for ARIA during anti-amyloid antibody treatment[12]

Lecanemab: baseline brain scans within a year prior to treatment and scheduled routine MRI monitoring before the 3rd, 5th, 7th, and 14th doses, and subsequently every 6 months

- Additional, monthly MRI scans recommended for patients developing ARIA continued until resolution of ARIA-E and stabilisation of ARIA-H
- Any new symptom should prompt an unscheduled MRI, regardless of the assigned risk label[11,13]
- Monitoring beyond the routine schedule should align with patient needs
- Microhaemorrhage counts are sequence-dependent; SWI detects more than the T2*-weighted GRE. Use standardised axial T2* GRE with appropriate echo time (TE) across serial scans

The Real-World Infusion-and-Review Loop

AURs allow continued dosing under closer review for anti-amyloid therapies including:

Lecanemab[4] | Donanemab[14]

The Clarity AD Asian regional analysis of lecanemab in patients with early AD from Japan, South Korea, and Singapore showed 24% slowing of decline in Clinical Dementia Rating at 18 months (no statistical significance in subgroup analysis), with lower ARIA-E, ARIA-H, and infusion reaction rates than the overall trial population[3]

Mild Asymptomatic ARIA[11,15]

- Mild ARIA-E: one location < 5 cm
- Mild ARIA-H*: ≤ 4 new treatment-emergent microhaemorrhages, OR a single focal area of superficial siderosis

Moderate or Symptomatic ARIA[11,15]

- Moderate ARIA-E: one location 5–10 cm, or multiple locations each < 10 cm
- Moderate ARIA-H*: 5–9 new treatment emergent microhaemorrhages OR two focal areas of superficial siderosis

Pause treatment until ARIA-E resolves and ARIA-H is stable

Severe or Recurrent ARIA[11,15]

- Severe ARIA-E: one or more locations > 10 cm
- Severe ARIA-H*: ≥ 10 new treatment-emergent microhaemorrhages OR more than two focal areas of superficial siderosis
- Any macrohaemorrhage (> 1 cm) is severe ARIA-H

Expert guidance recommends discontinuation of anti-amyloid therapies for severe ARIA-H; labelling advises suspension, with clinical judgement on whether to resume or stop permanently[11]

Important Considerations During Infusion

Neuroradiology reports
Ensure neuroradiology reports reach the physician before scheduled infusions

Emergency pathways
Clinical protocols must explicitly define emergency pathways for patients with anti-amyloid therapy

Designated coordinator
Designate a clinical coordinator to track the calendar[16]
- Initial screening
- Biological confirmation and tests
- ARIA surveillance
- Infusion management

CARE–Reframe[3]
- Present ARIA as an expected, manageable event not treatment failure
- Educate patients and caregivers on ARIA symptoms and their impact on the therapy schedule[17]

*ARIA-H thresholds are counts of treatment-emergent microhaemorrhages and are therefore sequence-dependent

Importance of Ongoing Disease Management

Treatment completion differs by agent

- Donanemab: dosing may be stopped once PET confirms amyloid clearance[14]
- Lecanemab: treatment continues into maintenance dosing rather than stopping at clearance[3]
- Safety-driven discontinuation: severe or recurrent ARIA[15]

Premature discontinuation[16]

- Discontinuation of DMT may lead to amyloid reaccumulation; the clinical consequences are not yet established
- PET-based stopping criteria come from trial design and are hard to replicate in routine care
- Where amyloid PET is not accessible, treatment duration rests on clinical judgement and shared decision-making

Shared decision-making

Treatment and monitoring plans must carefully consider:

- Risk-benefit
- ARIA risk
- Monitoring burden

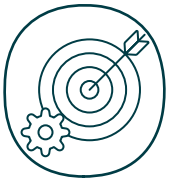
Assessing capacity to consent

- Cognitive decline in AD may leave patients unable to give informed consent
- Consent norms may vary markedly across different countries in APAC
- A pre-consent checklist to confirm eligibility before consent is recommended[1]

Importance of Early Consensus

Multidisciplinary AD teams must explicitly define criteria for continuing, adjusting, and discontinuing DMT

Goal-Setting Checklists for Treatment



- **Slowing disease progression**[1]
  Complete remission or reversal of cognitive deficits may be impractical
- **Amyloid clearance goals**
  Substantial early clearance may significantly slow cognitive decline[1]

Communication Strategies[8]

CARE–Explain

- Where treatment is not recommended, maintain trust through open, honest communication with patients and caregivers
- Written or visual aids can aid communication

Key Messages

- Real-world DMT use needs clear patient screening, appropriate treatment and monitoring schedules, and well-defined goals and decision-making frameworks
- Antibody therapy decisions require careful clinical judgment, clear communication, and a patient-centred approach[1]
- The CARE framework—Connect, Align, Reframe, Explain—links patient selection, ARIA monitoring, and treatment delivery into one integrated APAC pathway[8]

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