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Detection and Management of Amyloid-Related Imaging Abnormalities During Alzheimer's Disease Treatment

A guide to improving the quality of life in patients with amyloid-related imaging abnormalities

Anti-amyloid monoclonal antibodies are immunotherapeutics approved for the treatment of early-stage Alzheimer's disease (AD)

Treatment with anti-amyloid monoclonal antibodies can[1]:

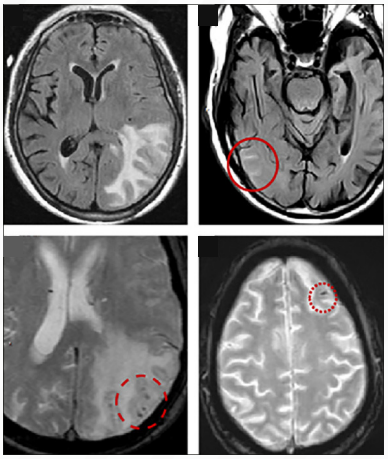
- Slow down disease progression
- Cause side effects known as amyloid-related imaging abnormalities (ARIAs)

ARIAs, as identified by magnetic resonance imaging (MRI), are of two major types[1,8]

Brain edema (ARIA-E)[8]

Swelling in the brain's parenchyma

Narrowing or flattening of the brain's sulci



Parenchymal microhaemorrhages

Hemosiderin deposits along:

- Brain's sulci
- Leptomeninges

Haemorrhage (ARIA-H)[10]

Visible in an MRI with:

- T2-weighted imaging
- Fluid attenuated inversion recovery (FLAIR) imaging

- Susceptibility weighted imaging
- Gradient echo sequence

Image credit: Hampel, H., Elhage, A., Cho, M., Apostolova, L. G., Nicoll, J. A., & Atri, A. (2023). Amyloid-related imaging abnormalities (ARIA): Radiological, biological and clinical characteristics. *Brain*, *146*(11), 4414–4424.

Risk factors for ARIA

- Apolipoprotein E (ApoE) ε4 allele carrier status
- History of cerebral microhaemorrhages
- Antithrombotic use
- Age
- History of stroke
- Hypertension

Estimated 6.1% to 39.3% of ARIA-E cases are symptomatic[2]

Most common ARIA-E symptoms

Headache | Confusion | Vomiting | Visual disturbance | Gait disturbance

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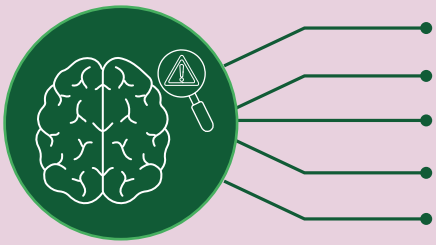
Challenges in clinical detection of ARIA[2]



- Asymptomatic in most cases
- Similarity of MRI findings in cerebral amyloid angiopathy (CAA) and ARIA-H
- Similarity of MRI findings in CAA-related inflammation and ARIA-E
- ARIA-H lesions are difficult to spot due to their small size
- ARIA-H lesions resemble other brain microbleeds

Clinical course of ARIA[8]

ARIA appears during the early course of treatment and tends to decrease with increasing drug exposure

Initial loss of vessel integrity, with reconstitution of vessel wall and resumption of perivascular drainage over continued treatment

ARIA-E: transient in nature with treatment span around 4–12 weeks

Standard MRI protocol for ARIA detection[2]

Scanner field strength

- 1.5 T (minimum)
- 3 T (preferred)

Scan type

- 2D T2* gradient recalled echo or susceptibility weighted imaging (for ARIA-H)
- T2 FLAIR (for ARIA-E)

Echo time

20 ms or higher

Slice thickness

5 mm or less

Computer-aided diagnosis (CAD) can improve ARIA detection[2]

Association between anti-amyloid therapy and ARIA

High ARIA risk during the initial treatment phase[1]

In clinical trials, ARIA incidence correlated with therapeutic dose

Incidence differs with different anti-amyloid therapeutics[2]

ARIA-E resolves within three to four months after drug discontinuation or dose adjustment[2]

Estimated 13.8% to 25.6% ARIA-E recurrence after dose adjustment[2]

ARIA incidence as reported by clinical trials*

Drug	ARIA-E incidence	ARIA-H incidence	Study group	Clinical trial
Aducanumab[10]	35.2%	19.0%	Japanese	EMERGE and ENGAGE
Donanemab[12]	26.7%	22.2%	Japanese	TRAILBLAZER-ALZ 2
Lecanemab[10]	6.2%	14.4%	Asian	Clarity AD
Solanezumab[14]	1.1%	9.1%	Not mentioned	EXPEDITION 1 and EXPEDITION 2

*Not a comparison of drugs (studies may have different inclusion criteria, baseline factors, drug dosage, regimen etc.)

ApoE4 may be less frequent in some Asian populations, like Japanese, but ApoE4 has a stronger association with Alzheimer's risk in these groups[13]

Considerations for anti-amyloid treatment delivery

Patient eligibility

Only a minority of individuals diagnosed with early-stage AD are eligible based on[5]:

- Cognitive score
- Frailty score
- MRI imaging results
- Anticoagulant use

Clinicians should choose the medication based on its efficacy and safety, as well as patient profile

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Strategies for clinical management of ARIA

APOE genotyping or proteotyping[7]

Different *APOE* alleles associated with varying ARIA risk

Appropriate dosing of anti-amyloid therapeutics

Dose titration helps mitigate ARIA risk[8]

Safety monitoring

Ad-hoc MRI scans if ARIA symptoms appear, especially early in treatment[8]

Routine scans to ensure safety (scans recommended before 5th, 7th, and 14th infusions of lecanemab)[7]

Ensuring proper infusion protocols[9]

Establishment of adequate infrastructure

Patient and caregiver education

Transparent communication of anti-amyloid therapy benefits and risks

Collaboration between stakeholders[9]

Establishment of standard MRI protocol for ARIA detection

Collaboration across medical specialties for early AD detection

Collaboration between dementia specialists, radiologists, emergency staff, and geneticists

Role of healthcare providers in the management of ARIA[9]

Neuroradiologists

Trained to detect ARIA on MRI scans

Dementia specialists

Administration of anti-amyloid therapies and monitoring treatment response and safety
Knowledge of efficacy and safety profiles of anti-amyloid therapies

General neurologists, geriatricians, and psychiatrists

Trained to perform clinical and diagnostic assessments to reduce the burden on dementia specialists

Key message

✔ Broader adoption of patient screening and standardized protocols for ARIA detection and management could significantly improve the quality of care for patients with AD during the early treatment phase

References:

1. Doran, S. J., & Sawyer, R. P. (2024). Risk factors in developing amyloid related imaging abnormalities (ARIA) and clinical implications. *Frontiers in Neuroscience*, *18*, 1326784.
2. Hampel, H., Elhage, A., Cho, M., Apostolova, L. G., Nicoll, J. A., & Atri, A. (2023). Amyloid-related imaging abnormalities (ARIA): Radiological, biological and clinical characteristics. *Brain*, *146*(11), 4414–4424.
3. Zimmer, J. A., Ardayfio, P., Wang, H., Khanna, R., Evans, C. D., Lu, M., ... & Sims, J. R. (2025). Amyloid-related imaging abnormalities with donanemab in early symptomatic Alzheimer disease: Secondary analysis of the TRAILBLAZER-ALZ and ALZ 2 randomized clinical trials. *JAMA Neurology*, *82*(5), 461–469.
4. Wang, H., Pan, J., Zhang, M., & Tan, Z. (2025). Re-evaluation of the efficacy and safety of anti-Aβ monoclonal antibodies (lecanemab/donanemab) in the treatment of early Alzheimer's disease. *Frontiers in Pharmacology*, *16*, 1599048.
5. Dobson, R., Patterson, K., Malik, R., Mandal, U., Asif, H., Humphreys, R., ... & Mummery, C. J. (2024). Eligibility for antiamyloid treatment: Preparing for disease-modifying therapies for Alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry*, *95*(9), 796-803.
6. Honig, L. S., Barakos, J., Dhadda, S., Kanekiyo, M., Reyderman, L., Irizarry, M., ... & Sabbagh, M. (2023). ARIA in patients treated with lecanemab (BAN2401) in a phase 2 study in early Alzheimer's disease. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *9*(1), e12377.
7. Cummings, J., Apostolova, L., Rabinovici, G. D., Atri, A., Aisen, P., Greenberg, S., ... & Salloway, S. (2023). Lecanemab: appropriate use recommendations. *The Journal of Prevention of Alzheimer's Disease*, *10*(3), 362–377.
8. Barakos, J., Purcell, D., Suhy, J., Chalkias, S., Burkett, P., Grassi, C. M., ... & Vijverberg, E. (2022). Detection and management of amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with anti-amyloid beta therapy. *The Journal of Prevention of Alzheimer's Disease*, *9*(2), 211–220.
9. Lee, J. H., Jia, J., Ji, Y., Kandiah, N., Kim, S., Mok, V., ... & Chen, C. (2024). A framework for best practices and readiness in the advent of anti-amyloid therapy for early Alzheimer's disease in Asia. *Journal of Alzheimer's Disease*, *101*(1),
10. 1–12.
    Toda, Y., Iwatsubo, T., Nakamura, Y., Matsuda, N., ... & Haeberlein S., Japanese Subgroup Analyses from EMERGE and ENGAGE, Phase 3 Clinical Trials of Aducanumab in Patients with Early Alzheimer's Disease. *The Journal of*
11. *Prevention of Alzheimer's Disease*, *11*(5), 1260–1269.
12. Eli Lilly and Company (n.d.). FDA approves updated label for Lilly's Kisunla (donanemab-azbt) with new dosing in early symptomatic Alzheimer's disease. Retrieved July 09, 2025, from https://investor.lilly.com/node/52581/pdf
13. Sato, S., Hatakeyama, N., Fujikoshi, S., Katayama, S., Katagiri, H., & Sims, J. R. (2024). Donanemab in Japanese Patients with Early Alzheimer's Disease: Subpopulation Analysis of the TRAILBLAZER-ALZ 2 Randomized Trial. *Neurology and Therapy*, *13*(3), 677–695.
14. Chen, C., Katayama, S., Lee, J., Lee, J., Nakagawa, M., Torii, K., Ogawa, T., Dash, A., Irizarry, M., Dhadda, S., Kanekiyo, M., Hersch, S., & Iwatsubo, T. (2025). Clarity AD: Asian regional analysis of a phase III trial of lecanemab in early Alzheimer's disease. *The Journal of Prevention of Alzheimer's Disease*, *12*(5), 100160.

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This Knowledge Hub is supported by Eli Lilly and Eisai Co., Ltd.