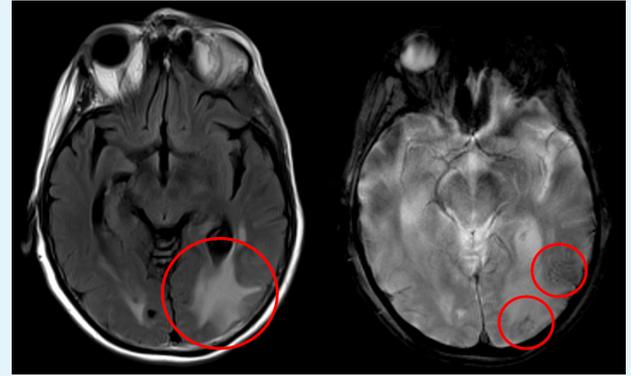


WHAT IS ARIA?

Amyloid-related imaging abnormalities, also known as “**ARIA**”, are MRI abnormalities typically associated with the use of monoclonal antibodies that remove amyloid plaque in patients with Alzheimer’s disease (AD)¹⁻³

ARIA is subdivided into **ARIA-E** (edema/effusion) or **ARIA-H** (hemosiderin/hemorrhage)^{2,3}

ARIA-E and -H may occur **concurrently**² as shown here: parenchymal edema + microhemorrhages⁵



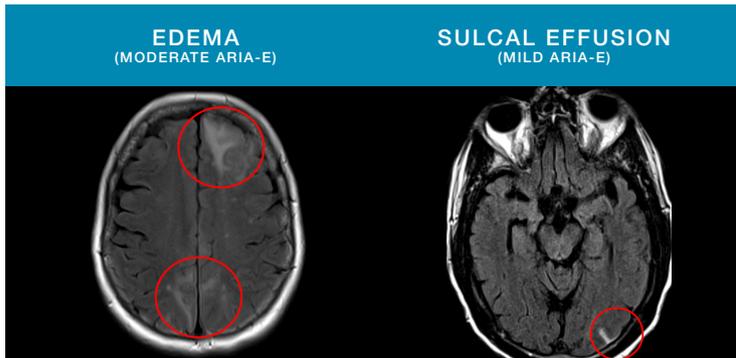
MRI images data on file



ARIA MRI FINDINGS INCLUDE²⁻⁵:

- **Parenchymal vasogenic edema** (ARIA-E)
- **Sulcal effusion** (ARIA-E)
- **Superficial siderosis** (ARIA-H)
- **Cerebral microhemorrhages** (ARIA-H)
- **Intracerebral hemorrhage** (also termed macrohemorrhages)

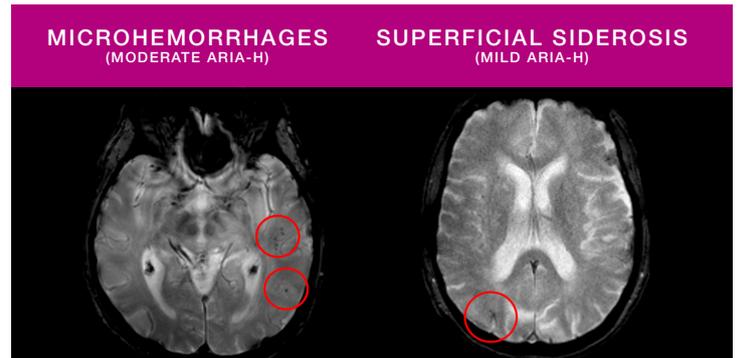
ARIA-E (EDEMA/EFFUSION)



MRI images data on file

Parenchymal edema or sulcal hyperintense abnormalities detected on FLAIR sequences^{3,5}

ARIA-H (HEMOSIDERIN/HEMORRHAGE)



MRI images data on file

Microhemorrhages, superficial siderosis and/or rare lobar intracerebral hemorrhage observed as hypointense abnormalities detected on T2*GRE sequences^{3,5}

HYPOTHESIZED PATHOPHYSIOLOGY OF ARIA

ARIA is a consequence of the presence of amyloid in cerebral blood vessel walls (cerebral amyloid angiopathy [CAA]), which can cause **spontaneous ARIA**.⁴ The increased occurrence of ARIA-E seen with treatments that remove amyloid plaques is thought to be due to the removal and disruption of amyloid in blood vessel walls.⁴ Other mechanisms are also hypothesized⁶

Aggregation of toxic amyloid β ($A\beta$) species in the brain contributes to AD pathogenesis³

After the introduction of monoclonal antibodies that removes amyloid plaques, amyloid deposits begin to clear leading to increased vascular permeability⁶

This loss of vascular integrity may be thought of as a transient exacerbation of the effects of CAA⁵. The leakage of fluid could give rise to an increased signal detected on FLAIR images (ARIA-E), while leakage of red cells would result in ARIA-H^{4,6}

Limited evidence suggests that with repeated immunization and continued $A\beta$ clearance, the integrity of vessels and efficiency of clearance can improve and risk of ARIA decreases⁷

CLINICAL MANIFESTATIONS OF ARIA



In most cases, ARIA-E and ARIA-H are **asymptomatic**^{1,4}



The symptoms of **ARIA-E** are transient and nonspecific, and include headache, confusion, nausea, vomiting, visual disturbance, neuropsychiatric symptoms, dizziness, fatigue, or gait disturbances.^{1,4} **ARIA-H** cases are generally asymptomatic¹



Infrequently, severe neurological symptoms (e.g., encephalopathy, focal neurological symptoms, seizures, and status epilepticus) occur, and may require hospitalization and specific treatments (e.g., intensive care, corticosteroids, antiepileptics)^{1,4,8}



Most cases of ARIA-E occur early in the treatment course and decrease with increased duration of exposure⁴

ARIA MAIN RISK FACTORS

APOE ε4 carrier status, treatment with **monoclonal antibodies that remove amyloid plaque**, and **pretreatment history of microhemorrhages** are risk factors for ARIA-E and ARIA-H^{4,5}



APOE ε4 carrier status^{1,4,5}



Number of pre-treatment microhemorrhages^{4,5}



Treatment with monoclonal antibodies that remove amyloid plaque^{4,5}

TREATMENT-RELATED ARIA OVERVIEW



Most cases of ARIA-E and ARIA-H are **asymptomatic** and usually recognized as **incidental** ARIA during follow-up evaluation on MRI^{1,6}



Most cases of ARIA-E occur **early in the treatment** course and decrease with increased duration of exposure.^{1,8} ARIA-E and -H may occur concurrently²



Most cases of **ARIA-E** resolve completely. Depending on the severity, treatment may continue, be interrupted or discontinued until resolution.^{5,10-12} Some cases may require specific treatments and even hospitalization¹



In past clinical trials, **ARIA-E** resolved radiographically over time, whereas **ARIA-H** can remain visible on subsequent imaging⁴

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ABBREVIATIONS:

APOE ε4, ε4 allele of the Apolipoprotein E gene; Aβ, amyloid beta; AD, Alzheimer's disease; ARIA, amyloid-related imaging abnormalities (includes ARIA-E and H); ARIA-E, ARIA-edema/effusion; ARIA-H, ARIA-hemosiderin/hemorrhage; FLAIR, fluid-attenuated inversion recovery; GRE, gradient recalled-echo; MRI, magnetic resonance imaging; SWI, susceptibility weighted imaging.

For additional information on ARIA, scan here:



www.UnderstandingARIA.com