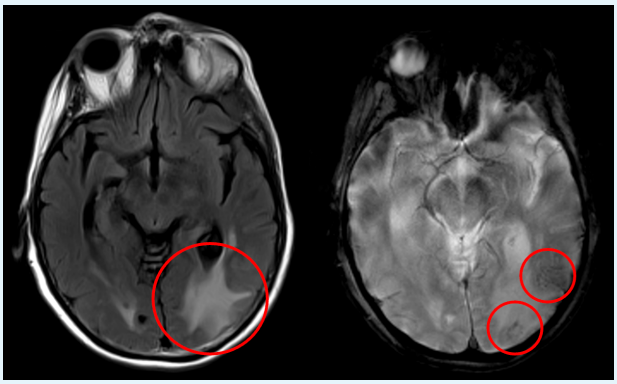
Introduction to ARIA

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 separately or **concurrently**[2] as shown here: parenchymal edema + microhemorrhages[5]

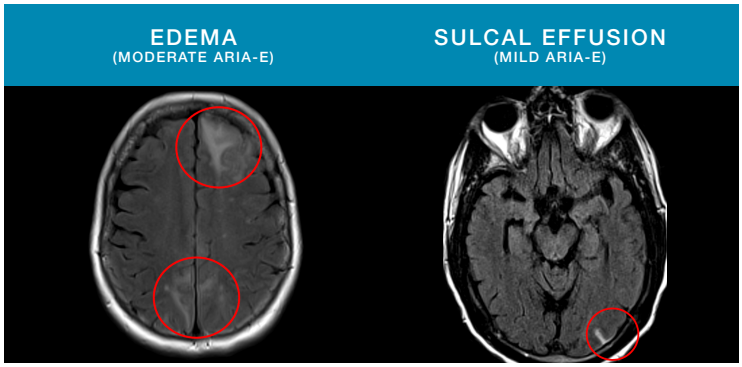


MRI images data on file

ARIA MRI FINDINGS INCLUDE[2-5]:

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

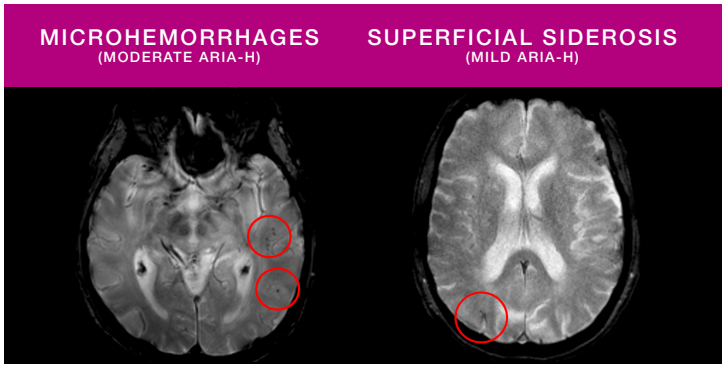
ARIA-E (EDEMA/EFFUSION)



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 can also be seen with treatments that remove amyloid plaque and is thought to be due to the removal and disruption of amyloid in blood vessel walls.[4] Other mechanisms are also hypothesized[6]

Aggregation of toxic amyloid β (Aβ) species in the brain contributes to AD pathogenesis[3]

After the introduction of monoclonal antibodies that removes amyloid plaque, amyloid deposits begin to clear leading to increased vascular permeability[6]

This loss of vascular integrity may be thought of as a transient exacerbation of the effects of CAA[5]. The leakage of fluid could give rise to increased fluid related signal detected on FLAIR images (ARIA-E), while leakage of red cells could result in ARIA-H[4,6]

Limited evidence suggests that with repeated immunization and continued Aβ clearance, the integrity of vessels and efficiency of clearance improves and the risk of ARIA decreases[7]

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 asymptomatic[1]

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 admission, corticosteroids, antiepileptics)[1,4,8]

Most cases of ARIA-E occur early in the treatment course and decrease with increased duration of exposure[4]

ARIA can be serious and life-threatening[12]

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 routine 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 separately or concurrently[2]

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 hospitalization[1]

In past clinical trials, **ARIA-E** resolved radiographically over time, whereas **ARIA-H** can remain visible on subsequent imaging[4]

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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.ca

Eisai hhc human health care