

DAY 4 ABSTRACT 1

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Incidence and symptomatology of ARIA

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Background: To summarize available evidence on ARIAs from randomized clinical trials (RCTs) testing anti- β -amyloid mAbs in patients with AD and to provide a comprehensive update about risk factors, clinical correlates, and implications for withholding and reinitiating treatment.

Method: A literature search of MEDLINE/PubMed, Embase, and Cochrane Library and a search of ClinicalTrials.gov were conducted through September 15, 2021. Publications describing RCTs, secondary analyses of RCT data, and case reports of ARIAs were included. Strengths of clinical data were graded according to the Oxford Centre for Evidence-Based Medicine.

Result: Twenty-two RCTs, 11 secondary analyses of RCTs, and 1 case report, including in total 15 508 adult patients (8483 women [54.7%]; mean [SD] age, 69.6 [8.3] years) were selected for inclusion. Signal alterations that included parenchymal edema and sulcal effusion leading to transient hyperintensities on fluid-attenuated inversion recovery and T2-weighted sequences were termed ARIA-E, whereas those consisting of hemosiderin deposits, including parenchymal microhemorrhages and leptomeningeal superficial siderosis, were termed ARIA-H. Apolipoprotein E (ApoE) ϵ 4 genotype was the main risk factor for both ARIA types; ARIA-E incidence was further associated with treatment dose, affecting the 55% of ApoE ϵ 4 carriers in the high-dose aducanumab treatment group. Both ARIA types manifested early during study course, and symptomatic cases accounted for the 6.1% to 39.3% of ARIA-E cases at higher treatment doses across RCTs, whereas ARIA-H cases were generally asymptomatic. Most ARIA-E cases resolved with treatment withholding, although corticosteroid administration was required anecdotally. ARIA-E recurrence after dose reinitiation or adjustment varied from 13.8% to 25.6% across RCTs.

Conclusion: Evidence suggests that ARIAs are frequent, mostly asymptomatic collateral events of amyloid-modifying therapies, highlighting the need for standardized clinical and neuroradiological management protocols in real-world clinical settings.