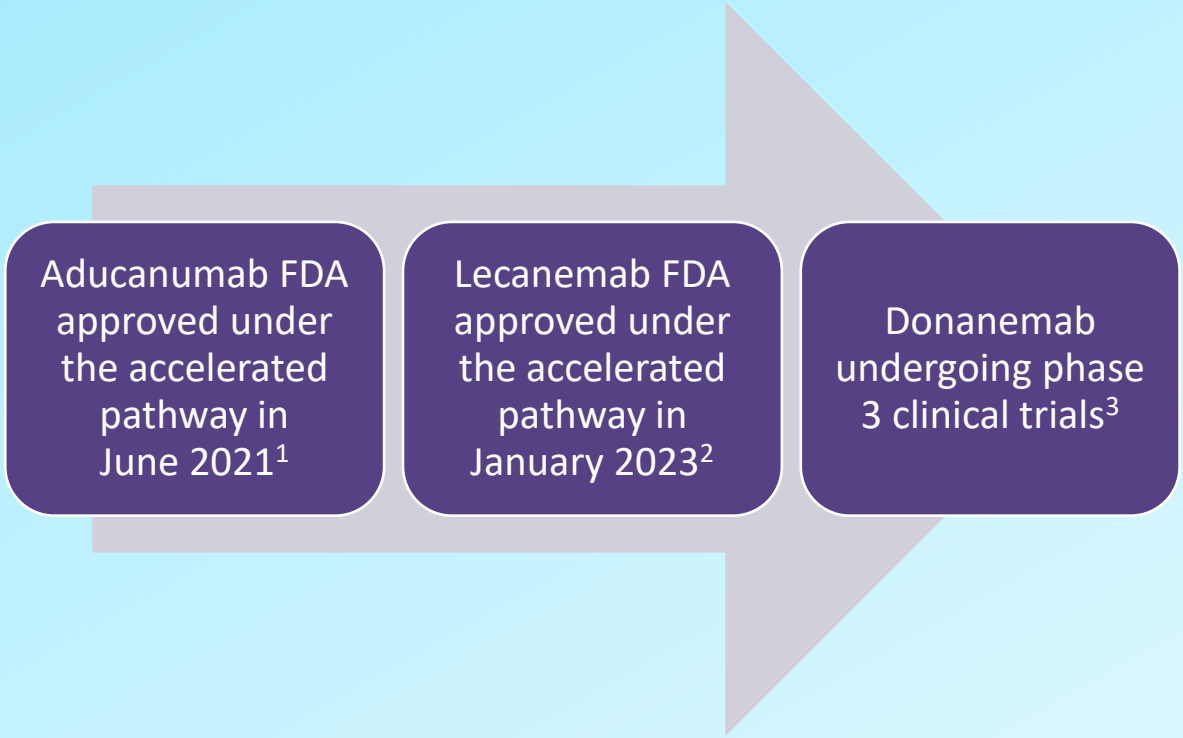
Two Disease-Modifying Therapies for Treating MCI and Mild AD Dementia Are FDA-Approved and One Is in Phase 3 Trials



Anti-Aβ antibodies and amyloid-related imaging abnormalities (ARIA):[4]

- Two types: ARIA-E (edema) and ARIA-H (hemosiderin deposition)
- Typically asymptomatic (74%)
- Symptoms: headaches, loss of coordination, dizziness, visual disturbances, nausea, seizures, disorientation, vomiting, fatigue

MCI, mild cognitive impairment.

1. Cavazzoni P. Updated June 7, 2021. Accessed May 23, 2023. https://www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease; 2. FDA. Published January 6, 2023. Accessed May 23, 2023. https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-disease-treatment; 3. Mintun MA et al. *N Engl J Med.*2021;384:1691-1704; 4. Cummings J et al. *J Prev Alzheimers Dis*. 2021;8:398-410.

ApoE4 Carriers Treated with Anti-Amyloid Antibodies Are at Increased Risk for Both ARIA-E and ARIA-H

	ARIA-E	ARIA-H
Pathophysiology	ARIA-E may be associated with excessive neuroinflammation and saturation of perivascular clearance pathways • Vasogenic edema • Effusion	ARIA-H may be related to vascular amyloid clearance with weakening and rupture of small blood vessels • Microhemorrhages • Superficial siderosis
Risk factors	• Treatment initiation • ApoE4 carriers • Higher dose • >4 microhemorrhages on a baseline MRI	• Age • Cerebrovascular disease • ApoE4 carriers

Withington CG et al. *Front Neurol.* 2022;13:862369.

ARIA-E and ARIA-H Incidence in Anti-Aβ Clinical Trials Indicates Much Higher Frequency of ARIA in ApoE4 Carriers

	Aducanumab (10 mg/kg monthly)[1]	Lecanemab (10 mg/kg every 2 weeks)[2]	Donanemab (1400 mg monthly)[3]
ARIA-E or ARIA-H	425 (41.3%)	193 (21.5%)	51 (38.9%)
ARIA-E	362 (35.2%)	113 (12.6%)	36 (27.5%)
ApoE noncarrier	72/355 (20.3%)	15/278 (5.4%)	4/35 (11.4%)
ApoE3E4	185/515 (35.9%)	52/479 (10.9%)	21/68 (30.9%)
ApoE4E4	105/159 (66.0%)	46/141 (32.6%)	11/25 (44.0%)
ARIA-H	348 (33.8%)	155 (17.3%)	40 (30.5%)
ApoE noncarrier	66/355 (18.6%)	33/278 (11.9%)	no data
ApoE3E4	282/674 (41.8%) (combined)	67/479 (14%)	no data
ApoE4E4		55/141 (39%)	no data

1. Salloway S et al. *JAMA Neurology* 2022;79:13-21; 2. Van Dyck CH et al. *New Engl J Med.* 2023; 388:9-21; 3. Mintun MA et al. *N Engl J Med.* 2021; 384:1691-1704.

Guidelines for Anti-Aβ Antibody Use

	Aducanumab appropriate use[1]	Aducanumab prescribing information[2]	Lecanemab prescribing information[3]
ApoE genotype testing	Discuss with patient, along with risk	Not stated	Consider testing for ApoE4 status to inform the risk of developing ARIA
Amyloid status	Confirm the presence of amyloid beta pathology before initiating treatment	Confirm the presence of amyloid beta pathology before initiating treatment	Confirm the presence of amyloid beta pathology before initiating treatment

1. Cummings J. et al. *J Prev Alz Dis.* 2021;4:398-410; 2. Aduhelm (aducanumab). Package insert. Biogen 2021;
3. Leqembi (lecanemab). Package insert. Eisai and Biogen; 2023.