



Anti-Amyloid Therapy Safety in the Real World

A Comparison Between Lecanemab and Donanemab Across Three Institutions

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BACKGROUND

- CLARITY-AD and TRAILBLAZER-ALZ2/ALZ6 showed a combined amyloid-related imaging abnormality (ARIA) rate of 21.5% for lecanemab and 29-36% for donanemab.^{1,2}
- Infusion-related reactions (IRRs) were higher (25.8%) for lecanemab compared to donanemab (9%)
- Relative safety of the two FDA-approved AATs, lecanemab and donanemab is not well characterized in real-world clinical practice.

OBJECTIVE

To compare real-world rates of ARIA, IRRs, and treatment discontinuation between patients treated with lecanemab and donanemab across three institutions

METHODS

Design. Prospective rolling enrollment cohort across three institutions — two academic (Univ. of Kansas; Univ. of Washington) and one private (Abington Neurological Associates) — over 3 years.

Patients. Early-stage AD patients (biomarker confirmed) initiating lecanemab or donanemab, followed from first infusion.

Outcomes. ARIA (ARIA-E, ARIA-H, combined) for full cohort+≥6 months; grade ≥2 IRRs; and treatment discontinuation.

Analysis. χ^2 test and multivariable logistic regression via R (v4.5.2). Additional sensitivity analyses including diagnosis and APOE-e2-carriership as well as restricting cohort to those treated >6mo performed. Models:

- Outcome ~ Drug + e4/e4 + site
- IRR ~ Drug + e4/e4 + diagnosis

COHORT OVERVIEW

N=651

patients · 3 sites

71.4%

lecanemab (n=465)

15.2%

any ARIA (full cohort)

17.3%

any ARIA (≥6 months)

3.4%

symptomatic ARIA

76.5%

treated ≥6 months

Donanemab n = 186 (28.6%) · lecanemab-predominant cohort

REFERENCES

- van Dyck CH, et al. Lecanemab in early AD. N Engl J Med. 2023;388:9–21.
- Sims JR, et al. Donanemab (TRAILBLAZER-ALZ 2). JAMA. 2023;330:512–527.

RESULTS

COHORT BY SITE

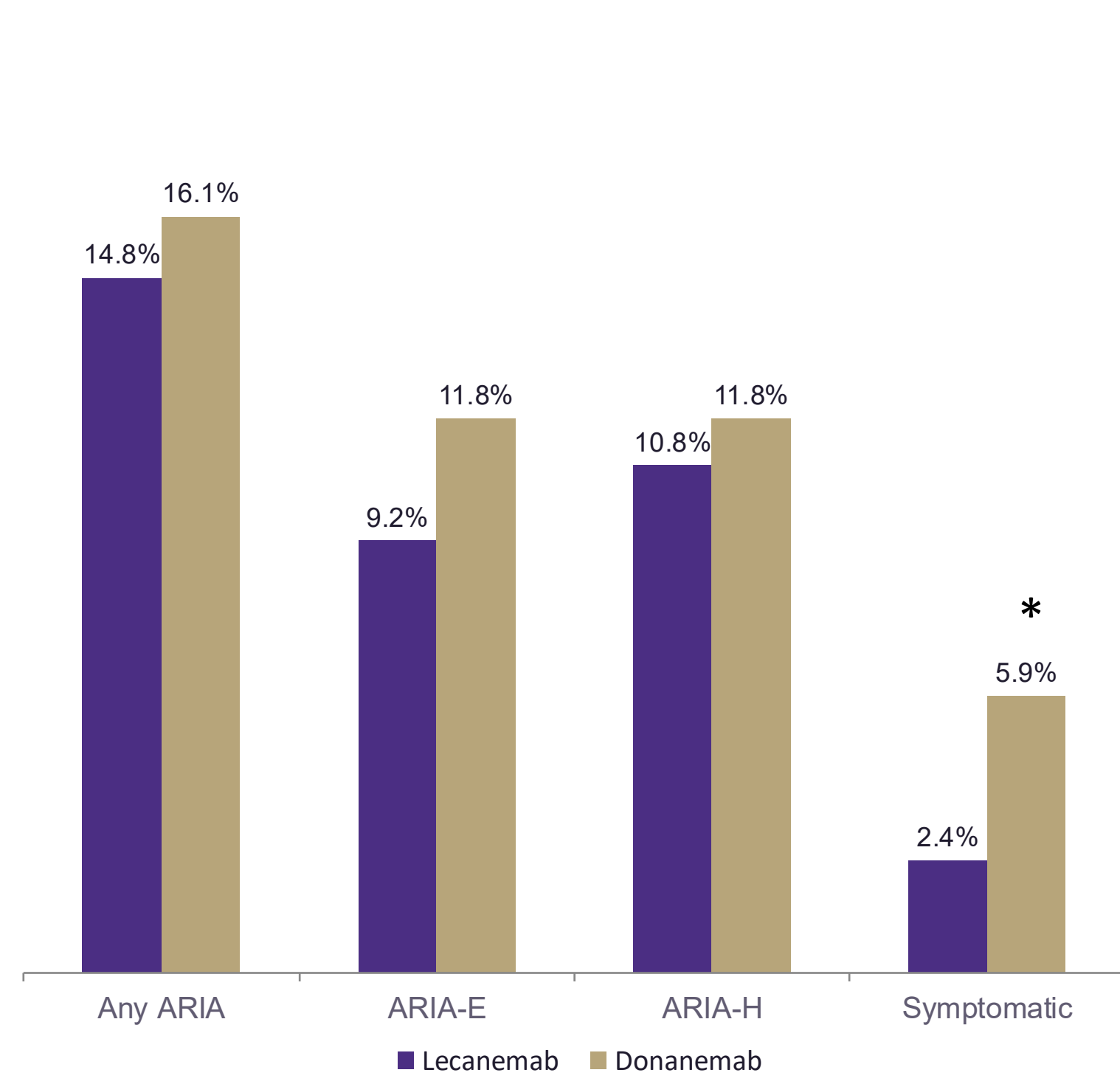
Table 1. Patient characteristics by site (≥6 mo)

	ANA (n=165)	KU (n=181)	UW (n=152)	All (n=498)
Drug				
Donanemab	16 (9.7%)	52 (28.7%)	39 (25.7%)	107 (21.5%)
Lecanemab	149 (90.3%)	129 (71.3%)	113 (74.3%)	391 (78.5%)
Initial diagnosis				
MCI	50 (30.3%)	158 (87.3%)	101 (66.4%)	309 (62%)
Mild dementia	115 (69.7%)	23 (12.7%)	51 (33.6%)	189 (38%)
ARIA				
ARIA (any)	19 (11.5%)	23 (12.7%)	44 (28.9%)	86 (17.3%)
Isolated ARIA-H	3 (1.8%)	5 (2.8%)	23 (15.1%)	31 (6.2%)
Isolated ARIA-E	13 (7.9%)	8 (4.4%)	3 (2%)	24 (4.8%)
Overall ARIA-H	6 (3.6%)	15 (8.3%)	41 (27%)	62 (12.4%)
Overall ARIA-E	16 (9.7%)	18 (9.9%)	21 (13.8%)	55 (11%)
ARIA-H/E	3 (1.8%)	10 (5.5%)	18 (11.8%)	31 (6.2%)
Symptomatic ARIA				
Symptomatic ARIA	3 (1.8%)	3 (1.7%)	9 (5.9%)	15 (3%)
Asymptomatic ARIA	16 (9.7%)	21 (11.6%)	35 (23%)	72 (14.5%)
APOE genotype				
E2/E3	3 (1.8%)	5 (2.8%)	6 (3.9%)	14 (2.8%)
E2/E4	3 (1.8%)	6 (3.3%)	3 (2%)	12 (2.4%)
E3/E3	40 (24.2%)	52 (28.7%)	36 (23.7%)	128 (25.7%)
E3/E4	98 (59.4%)	101 (55.8%)	88 (57.9%)	287 (57.6%)
E4/E4	21 (12.7%)	17 (9.4%)	19 (12.5%)	57 (11.4%)
APOE carrier status				
APOE e2 carrier	6 (3.6%)	11 (6.1%)	9 (5.9%)	26 (5.2%)
APOE e4 carrier	122 (73.9%)	124 (68.5%)	110 (72.4%)	356 (71.5%)
Discontinuation				
Discontinued treatment	8 (4.8%)	15 (8.3%)	35 (23%)	58 (11.6%)

Values are n (%) of each site cohort treated ≥6 mo. Symptomatic / asymptomatic shown as % of total treated; ARIA-H/E = combined ARIA-H and ARIA-E.

ARIA RATES BY DRUG

Figure 1. ARIA incidence (% of treated), unadjusted



Only symptomatic ARIA rates statistically differed (χ^2 test $p=0.062$).

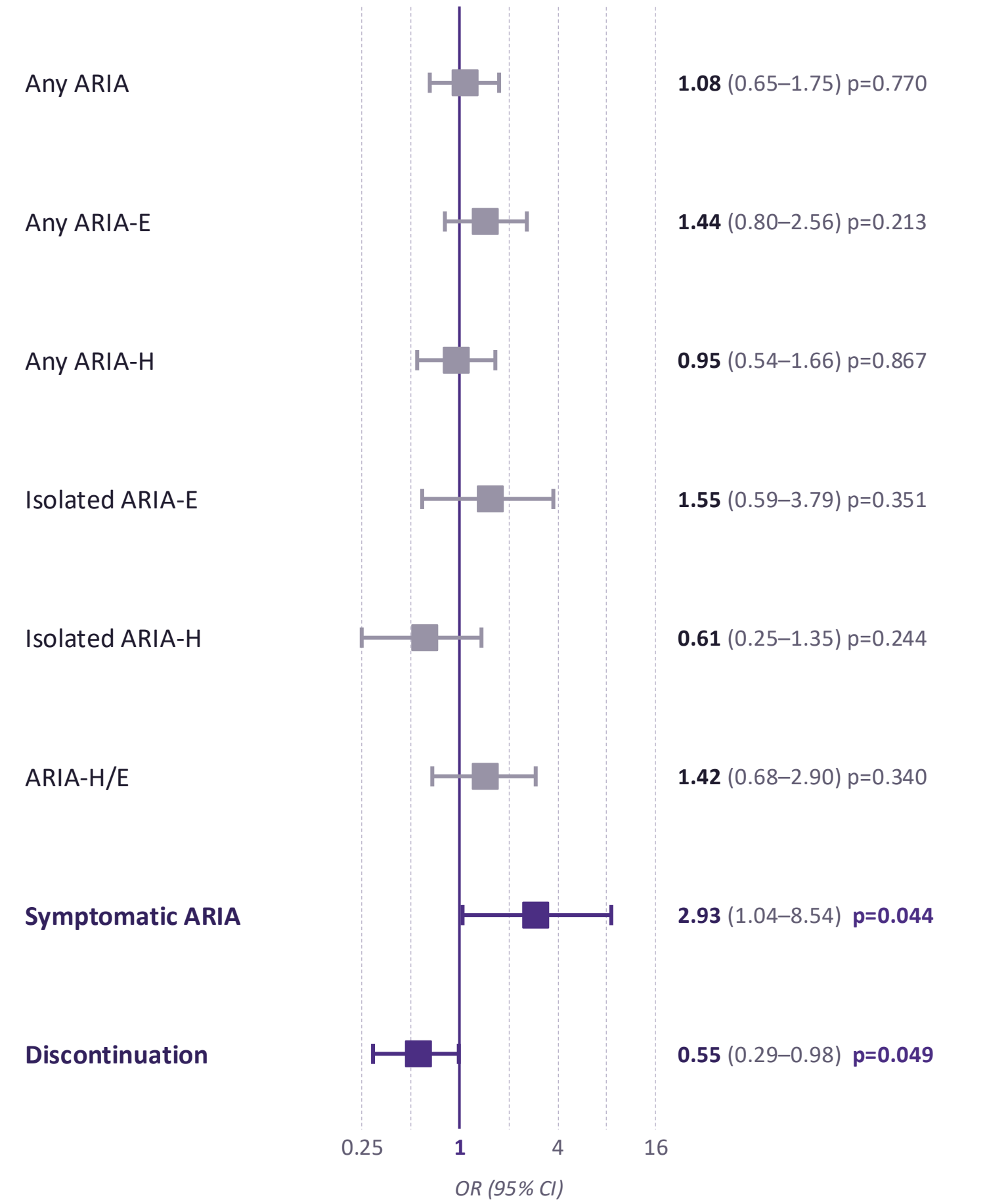
DISCLOSURES & FUNDING

MHR has received honoraria from Eisai, Lilly, Medscape, and Johnson and Johnson.
DW has received honoraria from Eisai and Lilly.

ARIA RISK: DRUG

Figure 2. Donanemab vs lecanemab — adjusted odds ratios

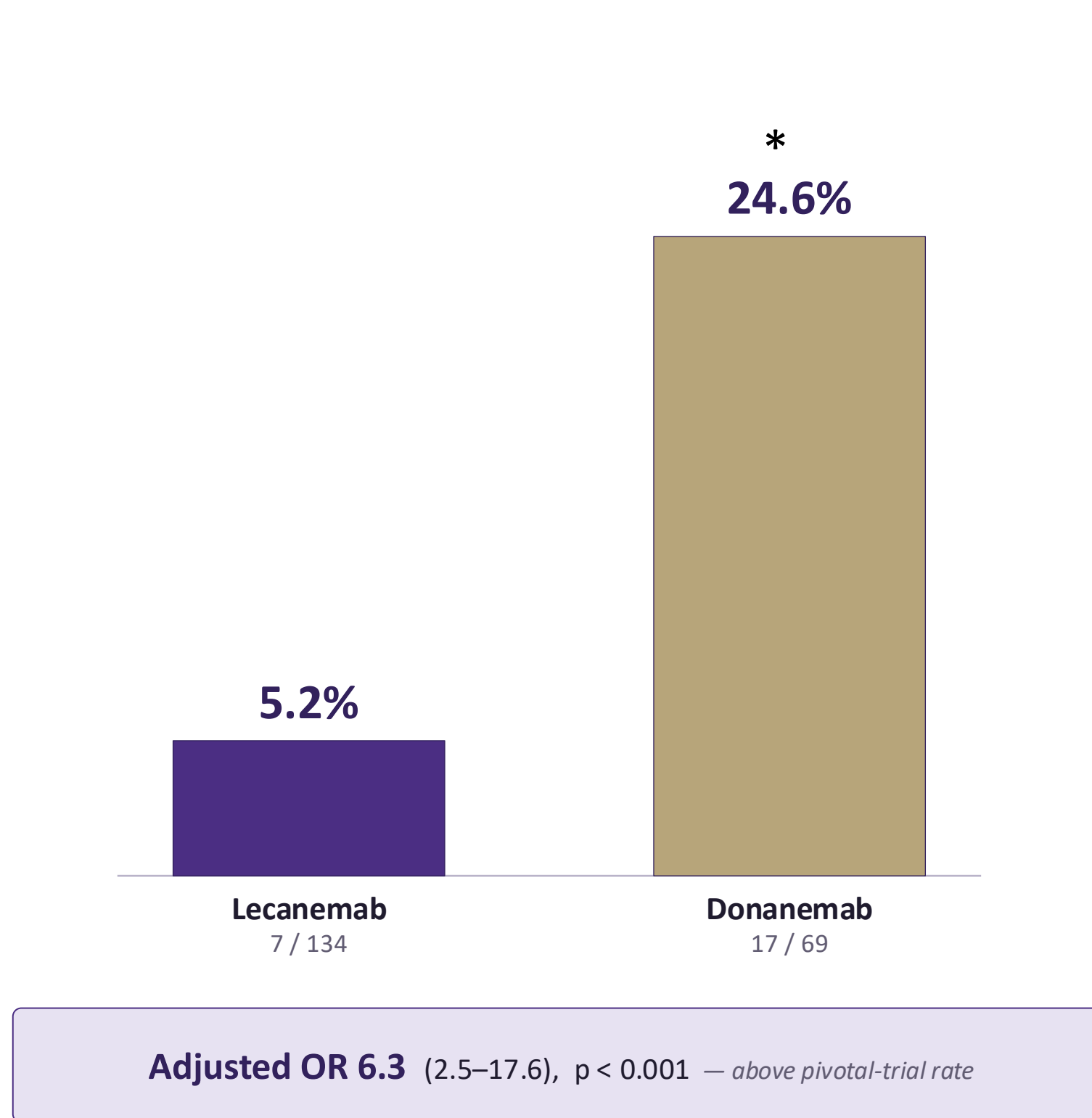
Multivariable logistic regression adj. APOE e4/e4 + site; reference = lecanemab.
OR > 1 favors higher odds with donanemab. ■ = $p < 0.05$. No statistical differences in ARIA rate.



Sensitivity analyses adjusting for diagnosis and e2-carriership and restricting cohort to those treated >6mo similar to primary analysis

INFUSION REACTIONS

Figure 3. Grade ≥2 IRRs — single site (n=203)



Adjusted OR 6.3 (2.5–17.6), $p < 0.001$ — above pivotal-trial rate

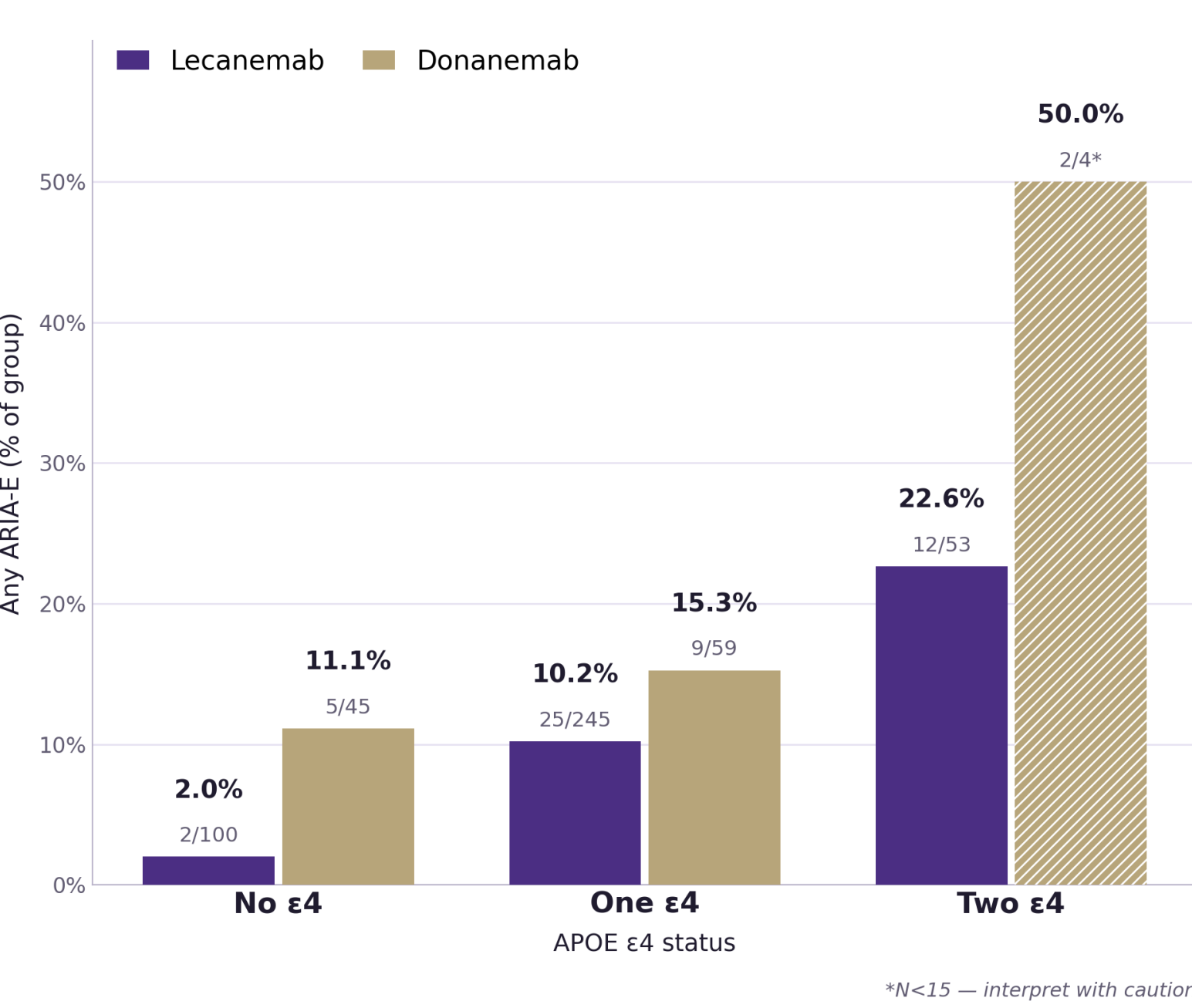
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ARIA-E: DRUG × APOE e4

Figure 4. ARIA-E rates based on APOE carrier status

Bars show % of each drug × e4 group with any ARIA-E (≥6 mo).



*N<15 — interpret with caution

Event/total shown on each bar. *Donanemab e4/e4 n=4 — interpret with caution.

CONCLUSIONS

- Both AATs were well-tolerated with ARIA incidence at ≥6 months (17.3%) comparable to pivotal trials.
- Overall ARIA rates did not differ significantly between lecanemab and donanemab ($p=0.77$).
- Donanemab showed higher symptomatic ARIA (OR 2.93, $p=0.044$).
- Lecanemab discontinuation rate was higher than donanemab; result impacted by duration of use and withdrawal for progression to moderate stage.
- APOE e4/e4 carriers had the highest ARIA risk (ARIA-E OR 2.78; $p=0.002$).
- Donanemab caused markedly more grade ≥2 IRRs than lecanemab (24.6% vs 5.2%; adj. OR 6.3, $p<0.001$) at UW.

LIMITATIONS & FUTURE INVESTIGATION

- Observational, non-randomized; groups differed at baseline (diagnosis, APOE, follow-up).
- Some risk covariates (i.e. baseline MRI) not included.
- IRRs were captured at a single site (n=203) only.
- Rolling enrollment → variable follow-up; crude rates underestimate cumulative risk.
- Further real-world studies required to understand long-term effects of ARIA events with AATs.

CONTACT

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