

KEY FINDINGS & CONCLUSIONS

- Overall, flying during lecanemab therapy was NOT associated with a higher incidence of ARIA (flyers 17.6% [6/34] vs non-flyers 32.0% [16/50]; Fisher's p = 0.206).
- Total number of flights (9.0 vs 4.2; p = 0.30), average number of infusions prior to ARIA onset (6.2 vs 7.2; p = 0.69) and treatment duration (15.3 vs 13.8 months; p = 0.37) did not differ between the group of patients who flew and those who did not.
- However, among patients who flew, those who developed ARIA (n = 6) had flown for the first time significantly earlier than patients who flew and did not develop ARIA (n = 28) — 3.3 vs 18.1 infusions before first flight (p < 0.001).
- The risk of ARIA fell by 39% with each extra infusion received before the first flight.
- Air travel was not associated with an increased risk of ARIA in patients treated with lecanemab. However, a potential signal of increased ARIA risk during the earliest phase of treatment was observed. Pending confirmation in larger cohorts, clinicians may consider advising patients to defer non-essential air travel during the first 3–4 months of treatment (approximately the first 6–8 infusions).**

BACKGROUND

- ARIA (ARIA-E oedema; ARIA-H microhaemorrhage / siderosis) is the major imaging complication of anti-amyloid antibodies — thought to be driven by antibody-mediated disruption of vascular amyloid, blood–brain-barrier (BBB) breakdown and vascular inflammation, APOE ε4 carriage, baseline microhaemorrhages and CAA burden raise risk.
- ARIA incidence is highest in the first months of therapy, when vascular amyloid and permeability transiently increase.
- Current risk mitigation (MRI screening, APOE genotyping, clinical surveillance) offers no guidance on the potential impact of environmental stressors such as high altitudes or commercial air travel.
- Commercial cabins cause only mild hypoxia (≈1,500–2,440 m), yet preclinical work shows mild hypoxia can transiently alter cerebral blood flow and BBB permeability which could potentially increase early-treatment vulnerability.

OBJECTIVE

Determine whether the timing and frequency of commercial air travel are associated with ARIA incidence in lecanemab-treated early Alzheimer's disease.

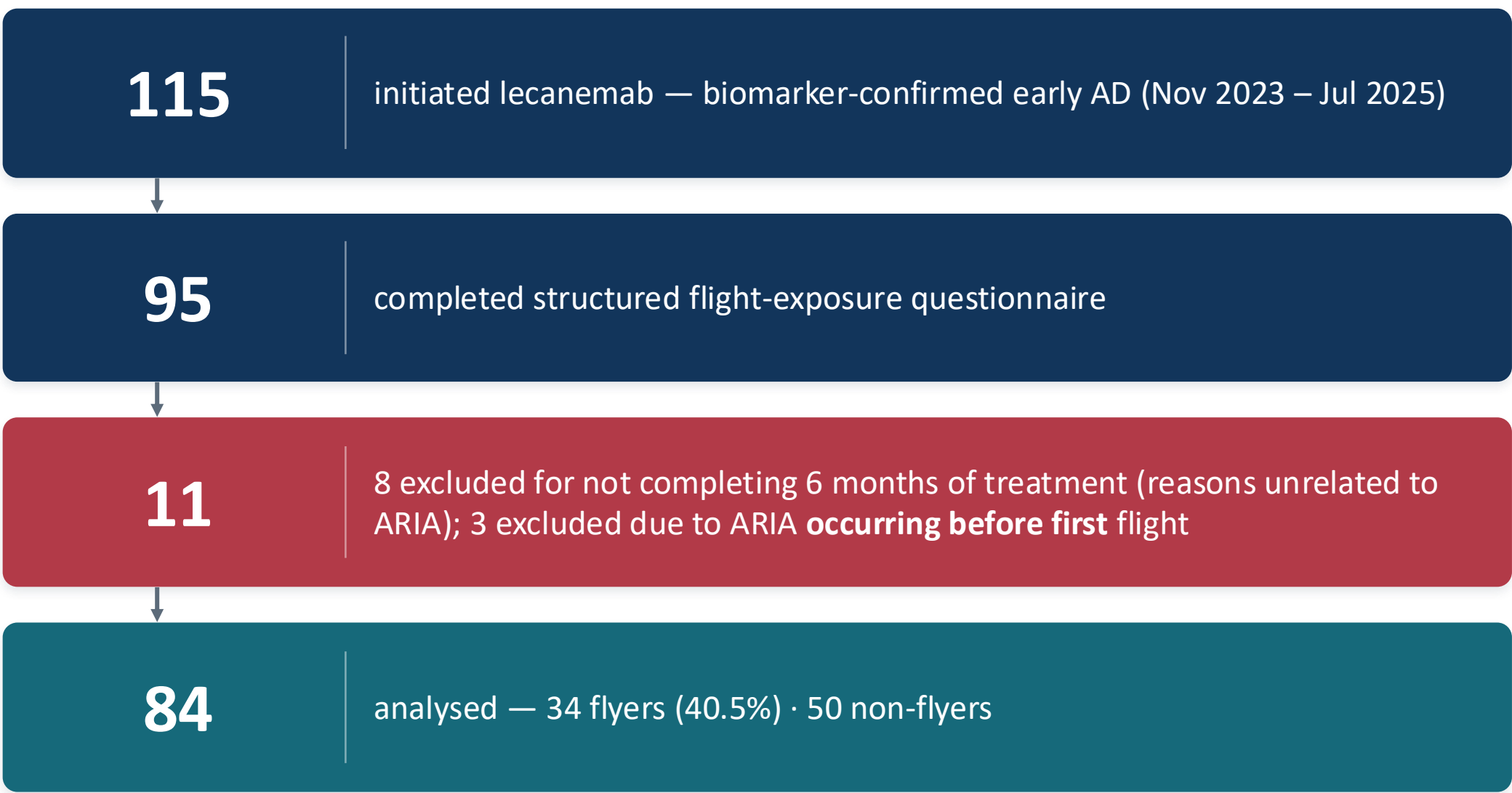
DOUBLE-HIT HYPOTHESIS

Antibody-mediated vascular instability during early therapy, combined with **mild cabin hypoxia** (↓ cerebral blood flow, ↑ BBB permeability), may together lower the threshold for ARIA. Aviation likely acts as a **conditional stressor** — **not an independent cause**.

METHODS

- Design** — single-centre retrospective cohort at the Cognitive Neurology Unit, TASMCM (Nov 2023 – Jul 2025) of biomarker-confirmed early AD (MCI / mild dementia) treated with lecanemab. APOE4 homozygotes were not included due to treatment ineligibility under European clinical guidelines.
- Flight exposure** — structured patient / caregiver questionnaire to record the number of infusions before first flight, total flights, and infusions before ARIA onset.
- Imaging & outcomes** — clinical MRI ARIA surveillance
- Statistics** — χ^2 for incidence; t-tests (Welch); binary logistic regression for ARIA predictors (infusions before first flight + covariates). SPSS v29, α = 0.05.

COHORT FLOW



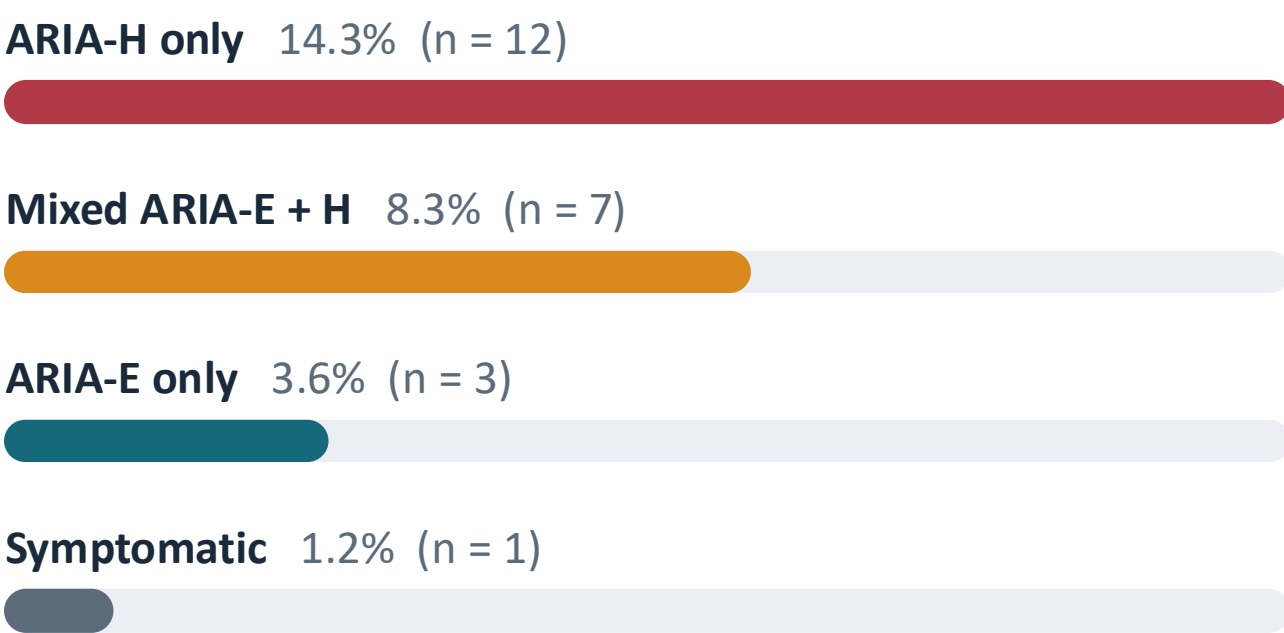
COHORT CHARACTERISTICS

Baseline (N = 84)	
Age at first infusion, years	71.5 ± 8.2 (45–84)
Female	51.2% (n = 43)
APOE ε4 heterozygote	54.8% (n = 46)
Hypertension (treated)	44.0% (n = 37)
Hyperlipidaemia / Type 2 diabetes	53.6% (45) / 19.0% (16)
Baseline aspirin use	36.9% (n = 31)
Treatment duration, months	14.4 ± 7.1

Values are mean ± SD or %. Flyers, n = 34; non-flyers, n = 50.

ARIA CHARACTERISTICS

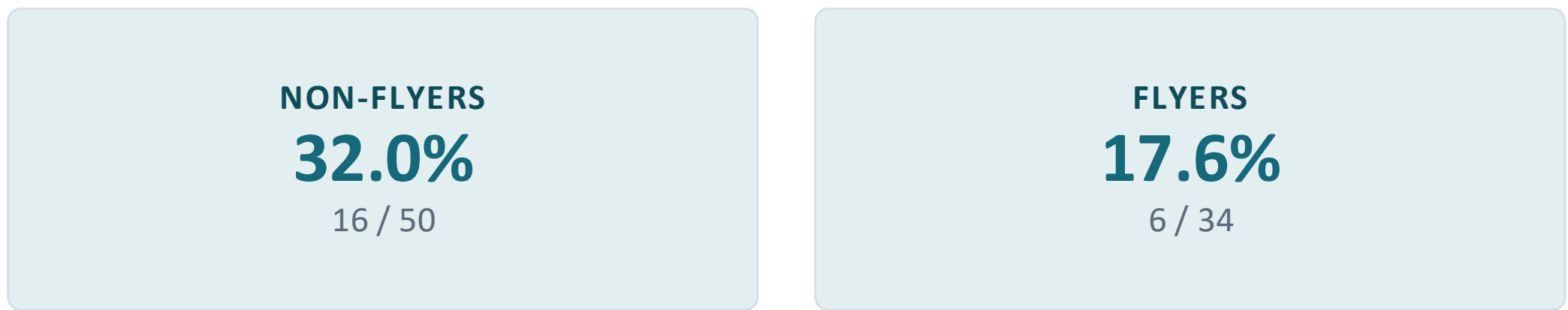
26.2% developed ARIA (22 / 84)



FLIGHT EXPOSURE & ARIA

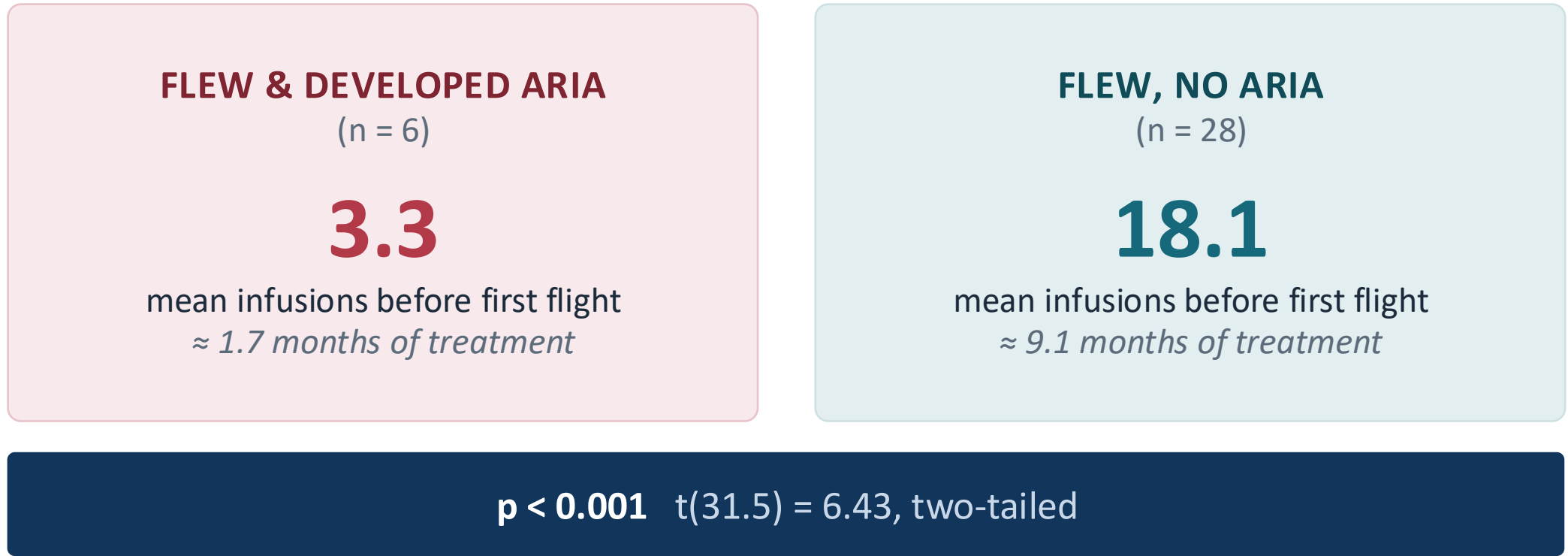
40.5% flew during treatment (n = 34)

Overall flight exposure NOT associated with ARIA · Fisher's p = 0.206 (ns)



TIMING COMPARISON

Among the 34 flyers, those who developed ARIA had flown far earlier in treatment.



Trend persisted adjusting for APOE (OR 0.55, p = 0.072); age (p = 0.168), sex (p = 1.00), hyperlipidemia (p = 0.878), T2DM (p = 0.515) and baseline microbleeds (p = 0.284) did not differ between ARIA and non-ARIA flyers.

EARLY FLIGHT RAISES ARIA PROBABILITY

