

Real-World Anti-Amyloid Therapy Is Associated With Lower All-Cause Mortality

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INTRODUCTION

Amyloid-targeting therapies (ATT) with monoclonal antibodies (lecanemab and donanemab) have demonstrated efficacy in slowing cognitive decline in early Alzheimer's disease (AD). Despite this, concerns regarding safety in routine clinical practice, including potential effects on mortality, have limited broader adoption. Real-world evidence addressing this concern remains scarce, and most available data derive from controlled trial settings that may not reflect the complexity of clinical practice populations.

METHODS

Retrospective, propensity score-matched cohort study using the TriNetX Global Collaborative Network. Patients with a diagnosis of Alzheimer's disease treated with ATT (lecanemab or donanemab) were matched 1:1 to untreated AD controls on demographic and clinical characteristics. Patients with prior conditions that could confound mortality ascertainment were excluded. The primary outcome was all-cause mortality. Survival analyses were conducted using unrestricted follow-up and restricted to one year; hazard ratios were calculated using Cox regression.

RESULTS

Among 1,078 matched pairs with balanced baseline characteristics, all-cause mortality during unrestricted follow-up was substantially lower in the ATT group (1.1%) compared with untreated controls (8.3%), corresponding to a markedly higher event-free survival in the ATT cohort (HR 0.17; 95% CI 0.09–0.31; Figure 1). In one-year restricted analyses, no deaths were observed among ATT-treated patients, precluding time-restricted hazard ratio estimation. Agent-specific mortality estimates for lecanemab and donanemab individually could not be calculated, as events in each subgroup fell below the minimum reportable threshold (n < 10).

CONCLUSIONS

In this large real-world cohort of AD patients, treatment with anti-amyloid monoclonal antibodies was not associated with excess mortality. On the contrary, ATT was associated with markedly lower all-cause mortality compared with matched untreated controls - a finding directionally consistent across analytic approaches. These results challenge prevailing safety concerns and support the use of anti-amyloid therapies in appropriately selected

patients in routine clinical practice. Further real-world studies should evaluate additional safety outcomes, including ARIA-related events, in larger and more diverse populations.

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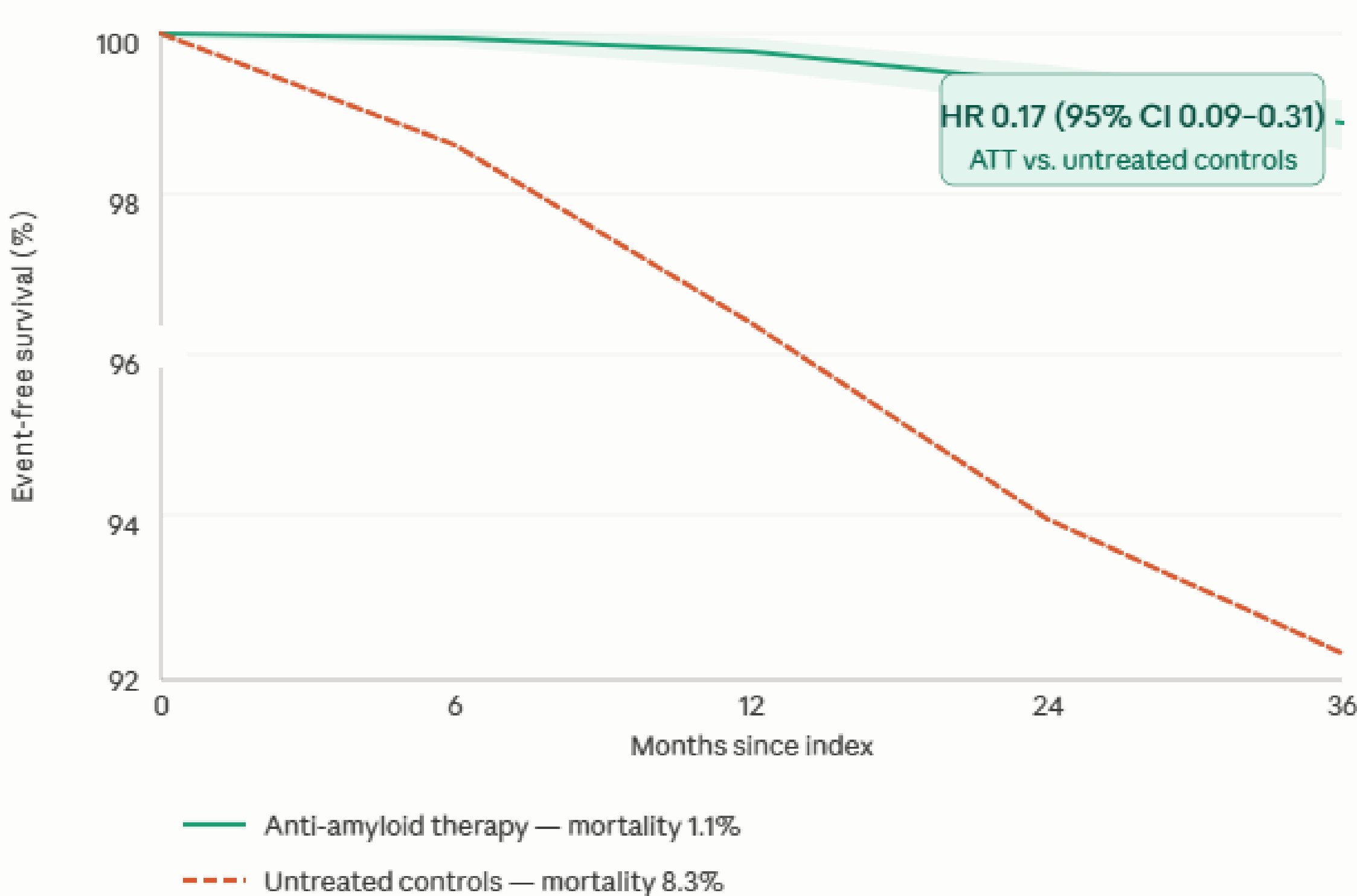


Figure 1. Illustrative Kaplan-Meier survival curves for all-cause mortality in propensity score-matched cohorts of anti-amyloid therapy-treated and untreated Alzheimer's disease patients. Curves are modeled from reported event rates; HR estimated by Cox regression.

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