

Early Clinical Outcomes and Amyloid-Related Imaging Abnormalities in Lecanemab-Treated Patients at an Academic Health System

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In a real-world clinical setting at an academic health system, lecanemab-treated patients generally experienced a cognitive and functional decline, as expected from the phase 3 trial. Infusion-related reaction rates were higher than observed in the phase 3 trial. ARIA-E rates were generally similar to what was reported in the clinical trial, but the ARIA-H rates were generally higher.

INTRODUCTION	RESULTS	RESULTS	RESULTS	CONCLUSIONS																																																																																																																																																																										
Lecanemab is an anti-amyloid therapy for early symptomatic Alzheimer’s disease, with side effect of Infusion-related reactions (IRR) and amyloid-related imaging abnormalities (ARIA).¹ ¹van Dyck et al., NEJM, 2023	<table><tr><th colspan="2">Table 1. Baseline demographic and clinical characteristics of patients.</th></tr><tr><th>Characteristic</th><th>N = 399</th></tr><tr><td>Age, mean (SD), years</td><td>72.0 (7.9)</td></tr><tr><td>Biological sex, n (%)</td><td></td></tr><tr><td>Female</td><td>227 (57%)</td></tr><tr><td>Male</td><td>172 (43%)</td></tr><tr><td>Race, n (%)</td><td></td></tr><tr><td>Asian</td><td>7 (1.8%)</td></tr><tr><td>Black</td><td>5 (1.3%)</td></tr><tr><td>Native Hawaiian or Other Pacific Islander</td><td>1 (0.3%)</td></tr><tr><td>White</td><td>372 (93%)</td></tr><tr><td>Other/Unavailable/Declined</td><td>14 (3.5%)</td></tr><tr><td>Ethnicity, n (%)</td><td></td></tr><tr><td>Hispanic</td><td>8 (2.0%)</td></tr><tr><td>Not Hispanic</td><td>366 (92%)</td></tr><tr><td>Unavailable/Declined</td><td>25 (6.3%)</td></tr><tr><td>Baseline diagnosis, n (%)</td><td></td></tr><tr><td>Mild cognitive impairment</td><td>252 (63%)</td></tr><tr><td>Mild dementia</td><td>147 (37%)</td></tr><tr><td>APOE ε4 carriership, n (%)</td><td></td></tr><tr><td>No</td><td>149 (37%)</td></tr><tr><td>Yes</td><td>250 (63%)</td></tr><tr><td>Duration of follow-up, median (IQR), months</td><td>14.3 (8.6, 19.0)</td></tr><tr><td>Time difference between baseline assessment and first infusion, median (IQR), months</td><td>2.1 (1.4, 3.1)</td></tr><tr><td>Max treatment time, median (IQR), months</td><td>12.2 (6.4, 15.5)</td></tr><tr><td>MMSE, mean (SD)</td><td>25.1 (3.1)</td></tr><tr><td>FAQ, mean (SD)</td><td>8.9 (6.1)</td></tr></table>	Table 1. Baseline demographic and clinical characteristics of patients.		Characteristic	N = 399	Age, mean (SD), years	72.0 (7.9)	Biological sex, n (%)		Female	227 (57%)	Male	172 (43%)	Race, n (%)		Asian	7 (1.8%)	Black	5 (1.3%)	Native Hawaiian or Other Pacific Islander	1 (0.3%)	White	372 (93%)	Other/Unavailable/Declined	14 (3.5%)	Ethnicity, n (%)		Hispanic	8 (2.0%)	Not Hispanic	366 (92%)	Unavailable/Declined	25 (6.3%)	Baseline diagnosis, n (%)		Mild cognitive impairment	252 (63%)	Mild dementia	147 (37%)	APOE ε4 carriership, n (%)		No	149 (37%)	Yes	250 (63%)	Duration of follow-up, median (IQR), months	14.3 (8.6, 19.0)	Time difference between baseline assessment and first infusion, median (IQR), months	2.1 (1.4, 3.1)	Max treatment time, median (IQR), months	12.2 (6.4, 15.5)	MMSE, mean (SD)	25.1 (3.1)	FAQ, mean (SD)	8.9 (6.1)	Figure 1. Cognitive and Functional Trajectories of Lecanemab-Treated Participants. The overall group trajectory is indicated with a gray line and shaded 95% confidence interval. The x-axis indicates the follow-up time in months. The y-axis is the estimated (A) MMSE, (B) FAQ, or (C) QDRS score based on the linear mixed-effects models.	<table><tr><th colspan="2">Table 2. Infusion-Related Reactions.</th></tr><tr><td>All</td><td>204 (51 %)</td></tr><tr><td>Grade 1</td><td>103 (26 %)</td></tr><tr><td>Grade 2</td><td>101 (25 %)</td></tr></table> <table><tr><th colspan="6">Table 3. ARIA Rates.</th></tr><tr><th></th><th>Total Treated</th><th>Any ARIA</th><th>Any ARIA-E</th><th>Any ARIA-H</th><th>Symptomatic ARIA</th></tr><tr><td>Total</td><td>399</td><td>129 (32.2%)</td><td>58 (14.5%)</td><td>113 (28.3%)</td><td>29 (7.3%)</td></tr><tr><td>Mild</td><td></td><td></td><td>35 (8.8%)</td><td>90 (22.6%)</td><td>28 (7.0%)</td></tr><tr><td>Moderate</td><td></td><td></td><td>23 (5.8%)</td><td>10 (2.5%)</td><td>1 (0.3%)</td></tr><tr><td>Severe</td><td></td><td></td><td>0 (0%)</td><td>13 (3.3%)</td><td>0 (0%)</td></tr><tr><td>0 APOE ε4 Alleles</td><td>149</td><td>38 (25.5%)</td><td>19 (12.8%)</td><td>32 (21.5%)</td><td>7 (4.7%)</td></tr><tr><td>Mild</td><td></td><td></td><td>12 (8.1%)</td><td>27 (18.1%)</td><td>6 (4.0%)</td></tr><tr><td>Moderate</td><td></td><td></td><td>7 (4.7%)</td><td>2 (1.3%)</td><td>1 (0.7%)</td></tr><tr><td>Severe</td><td></td><td></td><td>0 (0%)</td><td>3 (2.0%)</td><td>0 (0%)</td></tr><tr><td>1 APOE ε4 Allele</td><td>211</td><td>76 (36.0%)</td><td>29 (13.7%)</td><td>69 (32.7%)</td><td>18 (8.5%)</td></tr><tr><td>Mild</td><td></td><td></td><td>17 (8.1%)</td><td>56 (26.5%)</td><td>18 (8.5%)</td></tr><tr><td>Moderate</td><td></td><td></td><td>12 (5.7%)</td><td>5 (2.7%)</td><td>0 (0%)</td></tr><tr><td>Severe</td><td></td><td></td><td>0 (0%)</td><td>8 (3.8%)</td><td>0 (0%)</td></tr><tr><td>2 APOE ε4 Alleles</td><td>39</td><td>15 (39%)</td><td>10 (26%)</td><td>12 (31%)</td><td>4 (10%)</td></tr><tr><td>Mild</td><td></td><td></td><td>6 (15%)</td><td>7 (18%)</td><td>4 (10%)</td></tr><tr><td>Moderate</td><td></td><td></td><td>4 (10%)</td><td>3 (8%)</td><td>0 (0%)</td></tr><tr><td>Severe</td><td></td><td></td><td>0 (0%)</td><td>2 (5%)</td><td>0 (0%)</td></tr></table>	Table 2. 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Total Treated	Any ARIA	Any ARIA-E	Any ARIA-H	Symptomatic ARIA	Total	399	129 (32.2%)	58 (14.5%)	113 (28.3%)	29 (7.3%)	Mild			35 (8.8%)	90 (22.6%)	28 (7.0%)	Moderate			23 (5.8%)	10 (2.5%)	1 (0.3%)	Severe			0 (0%)	13 (3.3%)	0 (0%)	0 APOE ε4 Alleles	149	38 (25.5%)	19 (12.8%)	32 (21.5%)	7 (4.7%)	Mild			12 (8.1%)	27 (18.1%)	6 (4.0%)	Moderate			7 (4.7%)	2 (1.3%)	1 (0.7%)	Severe			0 (0%)	3 (2.0%)	0 (0%)	1 APOE ε4 Allele	211	76 (36.0%)	29 (13.7%)	69 (32.7%)	18 (8.5%)	Mild			17 (8.1%)	56 (26.5%)	18 (8.5%)	Moderate			12 (5.7%)	5 (2.7%)	0 (0%)	Severe			0 (0%)	8 (3.8%)	0 (0%)	2 APOE ε4 Alleles	39	15 (39%)	10 (26%)	12 (31%)	4 (10%)	Mild			6 (15%)	7 (18%)	4 (10%)	Moderate			4 (10%)	3 (8%)	0 (0%)	Severe			0 (0%)	2 (5%)	0 (0%)	- The majority of lecanemab-treated patients experience a cognitive and functional decline on treatment, but clinical effectiveness cannot be inferred from these data - IRR were generally mild, though the rates were generally higher than expected, possibly due to increased vigilance - ARIA-E rates were generally as expected - ARIA-H rates were generally higher, possibly due to use of more sensitive SWI sequences for monitoring
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- Design: IRB-approved retrospective cohort study - Participants: Lecanemab-treated patients with at least 6 months of follow-up (September 2023-February 2026) - Data collection: Artificial-intelligence-assisted extraction of electronic health record data - Primary outcomes: MMSE, FAQ, and QDRS trajectories modeled using linear mixed-effects models - Secondary outcomes: IRR and ARIA rates				- Comparison of lecanemab-treated patients with historical controls as an estimation of clinical effectiveness in a real-world setting - Evaluation of donanemab outcomes - Correlation of imaging outcomes and cognitive outcomes																																																																																																																																																																										