Diversity in Phase 2 and Phase 3 Placebo-Controlled, Double-Blind, Lecanemab and Elenbecestat Early Alzheimer's Disease Studies

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Introduction

- Increasing diversity in clinical trials is a scientific, public health, and ethical imperative.
- Clinicians need to understand how a drug works in representative disease populations, diverse communities need access to clinical trials, and social justice demands addressing health and healthcare disparities.
- Several factors contribute to underrepresentation among racial and ethnic groups in Alzheimer's disease (AD) clinical trials, including barriers to enrollment but also potential differential exclusion based on eligibility criteria.

Methods

- We evaluated enrollment in four double blind placebo-controlled clinical trials in early AD that incorporated highly similar enrollment criteria (NCT03887455, NCT01767311, NCT02956486, NCT03036280).
- We assessed the impact of eligibility criteria. Racial and ethnic information were self-reported separately by participants but here are used as mutually exclusive categories.
- Each trial incorporated PET or CSF to evaluate brain amyloid pathology, as well as typical inclusion and exclusion criteria used in early AD trials.
- We used logistic regression to estimate the likelihood (Odds Ratio [OR]) of participants from specific racial and ethnic groups meeting eligibility criteria (using non-Hispanic White participants as a reference group), controlling for clinical and demographic covariates.

Table. Demographic characteristics of screened participants across trials

	Black (n=889)	Hispanic (N=2689)	Asian (N=119)	NH White (N=7017)	Other (N=90)	Total (N=10,804)
Study						
NCT03887455, n (%)	250 (28)	314 (12)	28 (23)	2122 (30)	14 (16)	2728 (25)
NCT01767311, n (%)	223 (25)	939 (35)	38 (32)	2409 (34)	29 (32)	3638 (34)
NCT02956486, n (%)	186 (21)	668 (25)	19 (16)	1295 (18)	24 (27)	2192 (20)
NCT03036280, n (%)	230 (26)	768 (29)	34 (29)	1191 (17)	23 (26)	2246 (21)
Female sex, n (%)	581 (65)	1682 (63)	58 (49)	3516 (50)	53 (60)	5890 (54)
Age, mean (SD)	67.1 (8.4)	69.0 (8.2)	70.5 (9.0)	71.8 (8.4)	69.9 (9.4)	70.6 (8.5)
Education, mean yrs (SD)	13.5 (3.2)	11.8 (3.5)	16.0 (3.3)	15.0 (3.0)	15.7 (3.8)	14.0 (3.5)
APOE ε4, n (%)	196 (45)	448 (25)	16 (33)	1931 (53)	9 (39)	2600 (44)
Clinical diagnosis						
- MCI, n (%)	405 (77)	1626 (80)	44 (75)	3407 (73)	30 (81)	5512 (75)
- Dementia, n (%)	118 (23)	417 (20)	15 (25)	1250 (27)	7 (19)	1816 (25)

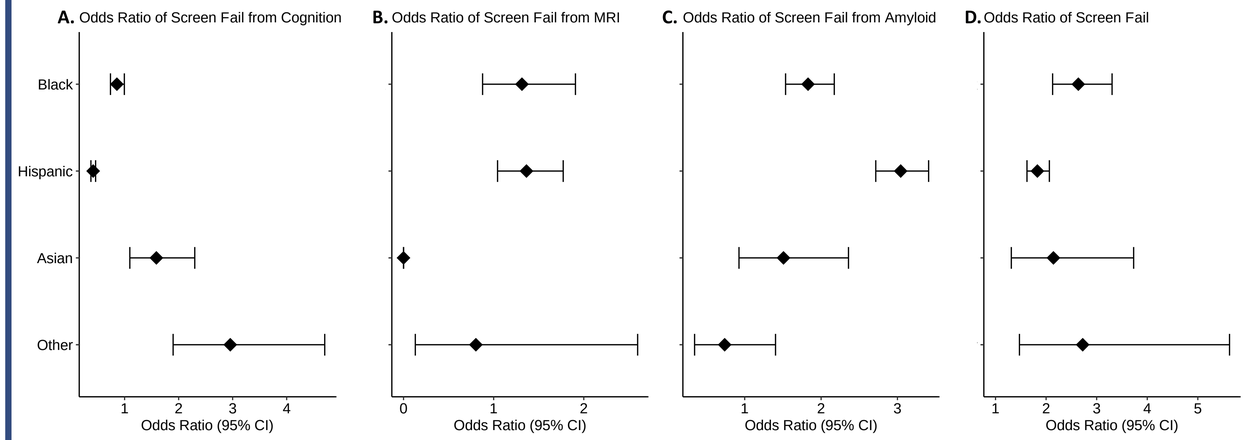

Figure. Odds Ratios of screen failure based on cognitive/clinical criteria (A), MRI criteria (B), amyloid biomarker criteria (C), and overall (D), by race and ethnicity. Reference Group: Non-Hispanic White. Odds ratios are adjusted for age, sex, and study.

Results

- Across the trials, 10,804 US participants were screened: 889 (8%) were of Black race, 119 (<1%) were of Asian race, and 2,883 (27%) were of Hispanic ethnicity.
- 2,458 participants were randomized, including 97 (4%) of Black race, 17 (<1%) of Asian race, and 450 (18%) of Hispanic ethnicity.
- The distribution of age and disease stage (MCI or mild AD dementia) among screened participants were similar across the racial and ethnic groups (Table).
- Females were more highly represented for Black and Hispanic participants (Table)
- Overall, 23% of those screened were randomized: 27% of non-Hispanic White participants compared to 11% of Black race participants, 14% of Asian race participants, and 16% of Hispanic ethnicity participants.
- Across trials, underrepresented group participants were more likely to be screen failed, overall (Figure, D).
- Among those assessed, Asians were less likely to qualify based on cognitive/clinical assessments (Figure, A).
- Among those assessed, Blacks were less likely to qualify based on MRI criteria (Figure, B)
- Among those assessed, Hispanics and Blacks were less likely to qualify by amyloid biomarker criteria (Figure, C)

Discussion and conclusions

- Early AD clinical trials have high rates of screen failure and disparities in eligibility may exacerbate underrepresentation of racial and ethnic minorities in AD trials.
- Efforts are needed to evaluate eligibility criteria for opportunities to create more equitable inclusion, though caution toward safety is an important consideration

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