Title

Eligibility Rates among Racially and Ethnically Diverse US Participants in Phase 2 and Phase 3 Placebo-Controlled, Double-Blind, Randomized Trials of Lecanemab and Elenbecestat in Early Alzheimer Disease

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Eligibility rates among racially and ethnically diverse US participants in Phase 2 and Phase 3 placebo-controlled, double-blind, randomized trials of lecanemab and elenbecestat in early Alzheimer's disease

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Abstract

Objectives: Many factors contribute to inadequate diversity in Alzheimer's disease (AD) clinical trials. We evaluated eligibility rates among racial and ethnic groups at US sites in large global multisite trials in early AD.

Methods: Using screening data from four randomized, double-blind, placebo-controlled clinical trials in early AD, we assessed rates of eligibility among racial and ethnic groups controlling for other demographic covariates. Each trial incorporated PET and/or CSF to evaluate brain amyloid pathology, as well as typical eligibility criteria used in early AD trials.

Results: Across the trials, 10,804 US participants were screened: 193 (2%) were of Hispanic ethnicity and Black race, 2,624 (25%) were of Hispanic ethnicity and White race, 118 (1%) were of non-Hispanic ethnicity (NH) and Asian race, 696 (7%) were of NH ethnicity and Black race, and 7,017 (65%) were of NH ethnicity and White race. Data from 156 participants who

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JG, SD, RR and RS contributed to the conception and design of the study; CF, KE, RR, SD, KT, RH, MK, MG, MI, and LK contributed to the acquisition and analysis of data; JG, CF, KE, and RR contributed to drafting the text or preparing the figures.

Potential Conflicts of Interest:

JDG, CF, KE, RS, DMH, PA and RR report grant funding from Eisai.

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did not fit into these categories were excluded. Accounting for age, sex, and trial and using NH White participants as a reference group, we observed higher probabilities of ineligibility for amyloid biomarker criteria among Hispanic Black (OR=3.20, 95%CI: 2.11, 4.88), Hispanic White (OR=4.15, 95%CI: 3.58, 4.83), NH Asian (OR=2.35, 95%CI: 1.23, 4.55), and NH Black (OR=3.75, 95%CI: 2.80, 5.06) participants.

Conclusion: Differential eligibility may contribute to underrepresentation of some minoritized racial and ethnic groups in early AD trials. Amyloid biomarker eligibility is a requirement to confirm the diagnosis of AD and for treatment with amyloid lowering drugs and differed among racial and ethnic groups.

Introduction

Alzheimer's disease (AD) is an active area of treatment development.[1] Risk for AD may be highest among people of non-White race or Hispanic ethnicity.[2] Yet, AD trials rarely recruit representative samples.[3] Increasing diversity in AD clinical trials is a scientific, public health, and ethical imperative. Clinicians need to understand how AD drugs work in diverse populations, underserved communities need access to clinical trials and may be more willing to consider treatments for which trials were more inclusive,[4] and social justice demands addressing health and healthcare disparities through research.[5]

Several factors contribute to underrepresentation among distinct racial and ethnic groups in AD trials. These include internal and external barriers to enrollment,[6] but also potential differential exclusion based on eligibility criteria.[3,7] Modern AD trials frequently incorporate biomarker eligibility criteria to ensure AD as a cause of cognitive impairment, to maximize detection of treatment benefit if it exists, and to minimize risk of harm due to inappropriate treatment. FDA guidance emphasizes the need to consider risk of differential exclusion among underrepresented groups, especially in later stage trials, to ensure generalizability of trial results.[8,9] We assessed the diversity of enrollment in four recent late-stage AD trials conducted by a single sponsor, testing the hypothesis that racial and ethnic groups differed in eligibility based on specific enrollment criteria.

Methods

Data source:

We evaluated enrollment in four double-blind, placebo-controlled randomized trials in early AD that incorporated highly similar enrollment criteria and tested an oral β-secretase inhibitor (NCT02956486 [elenbecestat Study 301] and NCT03036280 [elenbecestat Study 302]) or a monoclonal antibody against protofibrillar Aβ (NCT01767311 [lecanemab Study 201][10] and NCT03887455 [lecanemab Study 301 (Clarity AD)][11]).

Participants.

The four trial protocols incorporated generally consistent eligibility criteria. Participants were required to have Mild Cognitive Impairment (MCI) or mild AD dementia, based on standard diagnostic criteria. The studies had a minimum age requirement of 50 years and a maximum age of 85 or 90 years. Participants in the elenbecestat studies were required

to have a global Clinical Dementia Rating Scale (CDR) score of 0.5. Participants in the lecanemab studies were permitted to have CDR 0.5 or 1.0. In each study, participants were required to demonstrate a positive biomarker for brain amyloid pathology, through either amyloid positron emission tomography (PET) or cerebrospinal fluid (CSF) assessment or both. Participants across the studies were excluded if they had a major psychiatric diagnosis, recent transient ischemic attack or stroke, or another neurological disorder. Contraindications to magnetic resonance imaging (MRI) or findings on MRI that could contribute to cognitive impairment or suggested a non-AD cause of impairment were also exclusionary.

The elenbecestat studies screened 2192 and 2246 US participants to enroll planned sample sizes of 850 participants each. The lecanemab trials screened 2728 and 3638 US participants to enroll planned sample sizes of 800 and 1766 participants, respectively.

Participants self-reported their race and ethnicity, selecting from categorical options based on the US Office of Management and Budget Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity. We assigned participants to mutually exclusive racial and ethnic groups incorporating both types of self-reported information. We limited analyses to groups that included a minimum size of n=100 but assessed unique groups to the greatest extent possible with adequate precision. This included participants who self-reported being Hispanic ethnicity and Black race (Hispanic Black), Hispanic ethnicity and White race (Hispanic White), non-Hispanic ethnicity and Asian race (NH Asian), NH ethnicity and Black race (NH Black), and NH ethnicity and White race (NH White). We present data for racial and ethnic groups alphabetically.[12] There were 156 participants who did not fit into the specified racial and ethnic categories (13 American Indian or Alaskan Native, [14 Native Hawaiian or other Pacific Islander, 102 classified as other race, 26 with missing race and or ethnicity). Due to the small number of participants in these categories, these participants were excluded from the analyses.

Analyses.

Sponsor analysis data sets were shared with academic partners who independently conducted all analyses of the scientific hypotheses under study. To enhance precision and account for differences in data collection schedule between studies, several operational assumptions were incorporated. If a participant was randomized, we assumed that all eligibility assessments had been performed and deemed eligible. If a participant was ineligible due to a specific criterion (e.g., amyloid biomarker), we assumed that test was performed and that prior tests required by protocol had been performed and deemed eligible (e.g., all participants undergoing amyloid biomarker testing underwent and were eligible based on MRI).

Participant characteristics at baseline were summarized with frequencies and percentages for categorical variables and with means and standard deviations for continuous data.

In an effort to address causality, we identified four categories of ineligibility (our outcomes of interest) based on the full enrollment criteria: (1) overall ineligibility for any reason, (2)

ineligibility based on cognitive or clinical criteria, (3) ineligibility based on MRI findings, and (4) ineligibility based on amyloid biomarker testing.

We assessed each of the four outcomes of interest by fitting a logistic regression model. Ethnic and racial category was the independent variable of interest adjusting for age, sex and study. Since the main scientific objective of this study was to compare typically underrepresented groups to those typically overrepresented in AD trials, we used NH White participants as a reference group. We reported Odds Ratios (OR) obtained from the logistic regression analyses for the dependent variable of interest with respect to the reference group for each model. In exploratory analyses (due to high rates of data missingness), we ran logistic regression models for the eligibility outcomes that also included apolipoprotein E (APOE) genotype, coded as carriers vs. non-carriers of the ε4 allele. All analyses were conducted using the statistical software R (version 4.3.0).[38]

Ethics.

Each trial was approved by the relevant Institutional Review Board at individual sites or overseeing the study conduct centrally. Participants consented to study activities as well as secondary use of their data for studies such as this one. The current analyses are not considered human subjects research and therefore required no further approvals.

Results

Participants.

Table 1 describes the sample analyzed, reported as mutually exclusive racial and ethnic groups. Among 10,648 US participants screened and included in the analysis, 193 (2%) were Hispanic Black, 2,624 (25%) were Hispanic White, 118 (1%) were NH Asian, 696 (7%) were NH Black, and 7,017 (65%) were NH White. Among screened participants, NH Asian and NH White participants had higher education levels and were more frequently male sex, compared to the remaining groups. NH White and NH Black participants were more often carriers of the APOE ε4 allele. The groups were otherwise well balanced. Of the participants included in the analysis, a total of 2,444 were randomized, including 34 (1%) who were Hispanic Black, 412 (17%) who were Hispanic White, 17 (<1%) who were NH Asian, 63 (3%) who were NH Black, and 1918 (78%) who were NH White.

Table 2 describes the sample separated by trial and demonstrates the suitability of combining the datasets. The trials were generally similar in the composition and eligibility rates, though the elenbecestat trials included a higher proportion of MCI participants than the lecanemab trials. The lecanemab trials enrolled a higher proportion of Hispanic White participants. Table 3 includes characteristics of those deemed ineligible compared to those randomized.

Rates and reasons for ineligibility.

Overall, 77% of those screened were deemed ineligible. Among the criteria that were assessed, cognitive or clinical criteria were the most frequent reasons for ineligibility (n=3677, 34.5%). Few participants (n=387, 6.9%) were deemed ineligible based on MRI

criteria. Amyloid biomarker testing resulted in the highest proportion ineligible; among the 4675 participants undergoing amyloid biomarker testing, 2012 (43.0%) were ineligible.

Among screened participants, 82% of Hispanic Black participants, 84% of Hispanic White participants, 86% of NH Asian participants, 91% of NH Black participants, and 73% of NH White participants were ineligible. Accounting for covariates and using NH White participants as a reference group, we observed higher odds of ineligibility among all other racial and ethnic groups (Hispanic Black OR=1.6, 95% CI 1.1, 2.4; Hispanic White OR=1.8, 95% CI 1.6, 2.0; NH Asian OR=2.1, 95% CI 1.3, 3.7; NH Black OR=3.2, 95 CI% 2.5, 4.2).

When examining the specific reasons for ineligibility, we found that, compared to NH White participants, NH Asian participants were more likely to be ineligible due to clinical and cognitive screening assessments (OR=1.61, 95%CI: 1.11, 2.33; p=0.012), while NH Black participants were no different (OR=1.12, 95%CI: 0.95, 1.32; p=0.161) and Hispanic Black (OR=0.27, 95%CI: 0.18, 0.39; p<0.001) and Hispanic White (OR=0.40, 95%CI: 0.36, 0.45; p<0.001) participants were less likely to be ineligible. No differences were observed in eligibility rates based on MRI criteria. Hispanic Black (OR=3.20, 95%CI: 2.11, 4.88; p<0.001), Hispanic White (OR=4.15, 95%CI: 3.58, 4.83; p<0.001), NH Asian (OR=2.35, 95%CI: 1.23, 4.55; p=0.01), and NH Black (OR=3.75, 95%CI: 2.80, 5.06; p<0.001) participants were all more likely than NH White participants to be ineligible based on amyloid biomarker criteria. In exploratory models that included APOE, the probability of ineligibility based on amyloid biomarker criteria was attenuated but remained significant for each group except for NH Asian participants (Hispanic Black n=142, OR=2.7, 95% CI 1.7, 4.2; Hispanic White n=1768, OR=3.0, 95% CI 2.5, 3.5; NH Asian n=48, OR=2.0, 95% CI 0.9, 3.9; NH Black n=293, OR=2.7, 95 CI% 1.7, 4.2).

Discussion

In this study, we assessed an important potential contributor to underrepresentation of some racial and ethnic groups in AD trials: trial eligibility. To do so, we used data from four late phase trials with a single sponsor that incorporated similar eligibility criteria and enrolled a diverse pool of participants, compared to previous AD trials.[3,13] We found that Hispanic Black, Hispanic White, NH Asian, and NH Black participants were significantly more likely than NH White participants to be deemed ineligible for the trial in which they screened. Furthermore, amyloid biomarker eligibility was the major driver of this difference. Across the studies, 43% of participants who underwent amyloid biomarker testing were deemed to have inadequately high brain amyloid levels, including 56% of Hispanic Black participants, 64% of Hispanic White participants, 55% of NH Asian participants, and 67% of NH Black participants. Compared to NH White participants (32% ineligibility for amyloid biomarker testing), each of these differences were significant in logistic regression models that accounted for covariates (OR 2.35–4.15).

We observed few differences at study entry among the participant groups, including relatively similar representation of MCI compared to mild AD dementia. This contrasts observations in recent biomarker studies in which Hispanic, NH Asian, and NH Black groups were relatively overrepresented among participants with dementia (compared to

MCI),[14] perhaps due to barriers to timely diagnosis in these communities.[15] In the included trials, only NH Asian participants were more often deemed ineligible due to cognitive and clinical criteria. Although we did not perform adjusted analyses examining individual cognitive or clinical criteria, we note that for two of the four trials a greater proportion of NH Asian participants were ineligible due to failure to meet adequate memory impairment criteria (at least 1 SD below age-adjusted means for objective tests of memory), compared to NH White participants; however, in one trial a greater proportion of NH Asian participants were ineligible for scoring too low on MMSE (data not shown). NH Asian participants, in particular, may have faced challenges related to performing cognitive tests in English that would not have been experienced if they had the opportunity to undertake these assessments in their primary language. Unfortunately, data were not available related to preferred spoken language among participants in these trials to examine whether this or other unique aspects of the trial participants were associated with these findings. Hispanic Black and Hispanic White participants were less likely than NH White participants to be ineligible due to clinical or cognitive criteria.

The observed differential rates of amyloid biomarker eligibility among racial and ethnic groups fit with some,[7,14] but not all,[16,17] recent studies examining racial differences in amyloid PET. Studies incorporating CSF protein levels as outcomes have not typically demonstrated differences among racial groups in amyloid, though some have observed differences for phosphorylated and total tau.[16,18,19] Amyloid PET is a sensitive and specific assay for fibrillar amyloid pathology,[20] suggesting that differential utility of this biomarker among racial and ethnic groups may be less likely, though autopsy confirmation studies of antemortem PET imaging in diverse cohorts are limited. Instead, the current observations suggest that cognitively impaired participants from underrepresented racial and ethnic groups in these trials were less likely, on average, to have AD as a cause of their cognitive impairment. It may also be possible that lower levels of amyloid pathology (below the thresholds used for eligibility in these studies) were sufficient to result in cognitive impairment in these groups. This hypothesis may indicate that cognitive impairment could result from total brain pathological burden, rather than the specific pathologies present,[21] since some groups (e.g., NH Blacks in one study[22]) may be more likely to have mixed pathologies. Recruitment bias also warrants consideration, if underrepresented participants differed from NH White participants in their recruitment sources[7] and were therefore more likely to demonstrate reduced AD pathology or more mixed pathologies compared to typical clinical research cohorts.[23]

One key potential neuropathological substrate that could contribute to cognitive impairment and differ among racial and ethnic groups is vascular injury. Autopsy studies find differential rates of vascular injury, particularly among Hispanic and NH Black individuals,[22,24,25] and recent evidence suggests that vascular pathology may be a key contributor to cognitive decline, perhaps particularly among those with elevated brain amyloid.[26] We did not observe differences in eligibility among the groups for exclusionary MRI findings, which the protocols defined as the presence of macrohemorrhage or superficial siderosis in each trial, more than 4 microhemorrhages in the lecanemab trials, and a Wahlund age-related white matter change score of ≥3 in the elenbecestat trials. We cannot, however, rule out that the frequency of more subtle vascular brain injury or exclusion prior to screening due

to history of cerebrovascular events differed between the groups. We also did not include vascular risk factors (e.g., hypertension, diabetes) in our analyses.

Race and ethnicity are social, not biological, constructs. Recent studies, however, demonstrate potential differences in AD genetic risk among racial groups, such as NH Blacks compared to NH Whites,[27,28] and differences in genetic associations with AD biomarker outcomes.[29] The strongest genetic risk factor for AD is APOE ε4. Here, NH Whites demonstrated the highest proportion of ε4 carriers. Rates of missingness related to APOE were high across the included trials due to the screening process (i.e., APOE testing occurred after confirmation of elevated amyloid biomarker). This limits conclusions that can be drawn from analyses of APOE data. In an exploratory model for the outcome of overall ineligibility, however, inclusion of carrier status as a covariate had little effect on the observed results (data not shown). In models for the outcome of amyloid eligibility that had less missingness, the difference between NH Asians and NH Whites was no longer significant, but the estimate was largely unchanged and non-significance was presumed to be due to reduced sample sizes. Differences among the remaining racial and ethnic groups, compared to NH Whites, remained significant.

Overall, these results have important implications to future AD trials. Eligibility criteria are key to ensuring trial integrity, participant safety, and internal validity to the extent that they ensure the presence of the investigational treatment target. Though ineligibility rates were higher among specific racial and ethnic groups, randomized participants were confirmed to have AD as the likely cause of their cognitive impairment, ensuring the integrity of assessments of potential effect modification, compared to trials without biomarker confirmation.[30,31] The results reaffirm the need for greater emphasis on recruitment of diverse participants, given that underrepresented groups are more likely to be ineligible for randomization. Continued efforts to be trustworthy and gain trust, and to identify, test, and invest in recruitment interventions demonstrating evidence of efficacy remain urgently needed.[32,33] Moreover, substantial research remains needed to more fully understand the current results and instruct future trial protocols, including epidemiological studies with biomarker confirmation of AD to clarify causes of cognitive impairment across populations.

The implications to practice are equally critical. Lecanemab, which was tested in two of the four included trials, was recently approved by the FDA for treatment of early AD. Aducanumab, another anti-amyloid antibody, was approved under the accelerated approval pathway. Appropriate use criteria for these agents restrict treatment to those with biomarker evidence of AD.[34,35] The current results, as with others,[14] suggest that patients of Hispanic ethnicity and Black or Asian race may be less likely to qualify for these treatments due to lower rates of biomarker confirmed AD. Community-based cohort studies will be needed to confirm the current observations, but registries proposed to address coverage needs for disease-modifying AD treatments may also be positioned to collect key data about patient eligibility for treatment.[36] Ultimately, a greater therapeutic armamentarium, including treatments for non-amyloid targets or treatments agnostic to underlying etiology, will be needed to ensure equitable and optimal care for all patients with cognitive impairment.

This study had several key strengths that included the combining of data across four modern AD trials that incorporated biomarker criteria; a sample size that enabled precise estimates of differential eligibility, including the opportunity to assess specific racial and ethnic groups rarely examined (e.g., Hispanic Black participants; though we also provide traditional groupings treating race and ethnicity separately [Table 4]); and the ability to examine differential contributors to eligibility (e.g., MRI compared to amyloid criteria).

This study also had limitations. Although we increased statistical precision by combining data across trials, they were independent studies with differences in the time and locations of conduct, as well as minor differences between study protocols, including eligibility criteria. Our analyses captured major categories of eligibility, but not all reasons for exclusion. Close inspection of the data reveals that some participants were deemed ineligible for other reasons. While our sample sizes for specific racial and ethnic groupings are a strength, they are still relatively small for some groups and generalizability may be limited by this and recruitment bias, particularly given that data are from interventional trials. A small number of participants (n=156) were not included because of small sample sizes or incomplete or insufficient information to classify these individuals into distinct subcategories based on race and ethnicity. Ideally, we would have been able to include these participants and classify individuals into more granular sub-categories to investigate even more specific groups (e.g., Caribbean Hispanics or Chinese Asian Americans). It is unclear how systematic screening approaches could have affected these results. That is, the exclusion of participants due to cognitive and clinical criteria could have biased the MRI and amyloid biomarker assessments. Finally, we lacked data related to socioeconomic status or other social determinants of health, which may have mediated, moderated, or contributed to these observations.[37]

In conclusion, differential eligibility may contribute to underrepresentation of some racial and ethnic groups in early AD trials. These results suggest that observed differences in eligibility resulted primarily from differences in the likelihood that amyloid was a contributing cause of cognitive impairment among racial and ethnic groups who entered screening.

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Data availability:

Data from these analyses will not be made available.

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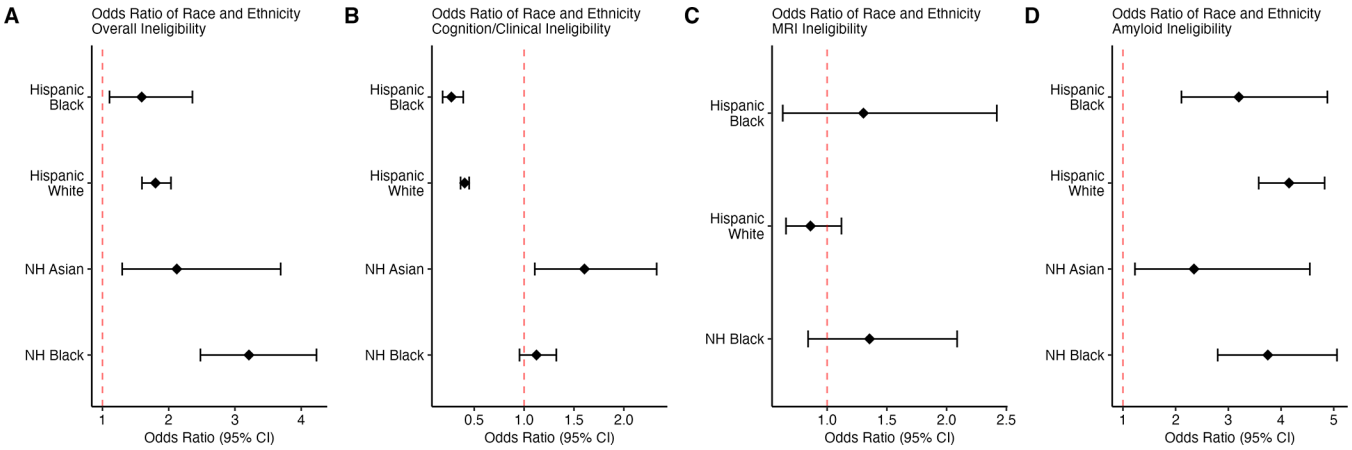

Figure 1.

Odds ratios (OR) for logistic regression models for the outcomes of overall ineligibility (A), ineligibility due to clinical/cognitive criteria (B), ineligibility due to MRI criteria (C), and ineligibility due to amyloid biomarker criteria (D). OR are presented with 95% confidence intervals for each independent racial and ethnic group assessed in this study. No NH Asian participants were ineligible due to MRI criteria.

Table 1.

Characteristics of the sample at screening, stratified by racial and ethnic group.

Characteristic	Hispanic Black	Hispanic White	NH Asian	NH Black	NH White	Total
N screened	193	2624	118	696	7017	10648
Eligible, N (%)	34 (17.6)	412 (15.7)	17 (14.4)	63 (9.1)	1918 (27.3)	2444 (23.0)
Study						
Lecanemab Study 201, n (%)	14 (7.3)	309 (11.8)	27 (22.9)	236 (33.9)	2122 (30.2)	2708 (25.4)
Lecanemab Clarity-AD, n (%)	83 (43.0)	917 (34.9)	38 (32.2)	140 (20.1)	2409 (34.3)	3587 (33.7)
Elenbecestat Study 301, n (%)	47 (24.4)	649 (24.7)	19 (16.1)	139 (20.0)	1295 (18.5)	2149 (20.2)
Elenbecestat Study 302, n (%)	49 (25.4)	749 (28.5)	34 (28.8)	181 (26.0)	1191 (17.0)	2204 (20.7)
Female sex, N (%)	128 (66.3)	1638 (62.4)	58 (49.2)	453 (65.1)	3516 (50.1)	5793 (54.4)
Age, mean (SD)	69.0 (8.1)	69.0 (8.2)	70.5 (9.0)	66.5 (8.4)	71.8 (8.4)	70.7 (8.5)
Education, mean (SD) *	11.3 (3.7)	11.7 (3.5)	16.1 (3.3)	14.0 (2.9)	15.0 (3.0)	14.0 (3.5)
APOE carrier, N (%) *	47 (33.1)	439 (24.8)	16 (33.3)	149 (50.9)	1931 (53.0)	2582 (43.8)
CDR-SB, mean (SD) *	3.1 (1.2)	3.0 (1.3)	3.0 (1.9)	2.7 (1.6)	2.8 (1.6)	2.9 (1.5)
MMSE, mean (SD) *	25.0 (2.6)	25.3 (2.8)	25.1 (3.9)	25.2 (3.2)	25.9 (3.2)	25.7 (3.1)
ADAS-cog, mean (SD) *	23.1 (6.05)	22.3 (6.9)	19.3 (8.1)	19.2 (8.3)	21.0 (7.6)	21.2 (7.5)
Clinical Diagnosis *						
MCI, N (%)	125 (75.8)	1599 (79.7)	43 (74.1)	280 (78.2)	3407 (73.0)	5454 (75.2)
Mild AD, N (%)	40 (24.2)	408 (20.3)	15 (25.9)	78 (21.8)	1259 (27.0)	1800 (24.8)
Clinical/cognitive assessment, n eligible /n screened	159/193	2007/2624	58/118	400/696	4347/7017	6971/10648
MRI assessment, n eligible /n screened	120/130	1454/1537	44/44	261/284	3340/3611	5205/5606
Amyloid biomarker assessment, n eligible /n screened	44/101	463/1275	18/40	44/101	75/229	2063/3030

* Sample sizes differ due to missing data resulting from varying study requirements or stages of screening at which these variables were collected

Table 2.

Characteristics of the sample at screening, stratified by trial

Characteristic	Lecanemab Study 201	Lecanemab Clarity-AD	Elenbecestat Study 301	Elenbecestat Study 302	Total
N screened	2708	3587	2149	2204	10648
Eligible, N (%)	684 (25.3)	945 (26.3)	438 (20.4)	377 (17.1)	2444 (23.0)
Female sex, N (%)	1422 (52.5)	1945 (54.2)	1158 (53.9)	1268 (57.5)	5793 (54.4)
Age, mean (SD)	70.6 (9.1)	71.5 (8.3)	70.4 (8.1)	69.7 (8.4)	70.7 (8.5)
Education, mean (SD) *	14.6 (2.9)	NA	13.8 (4.0)	13.8 (3.4)	14.0 (3.5)
APOE carrier, N (%) *	715 (49.1)	910 (46.1)	509 (41.2)	448 (36.5)	2582 (43.8)
CDR-SB, mean (SD) *	2.7 (1.4)	3.3 (1.6)	2.6 (1.2)	2.5 (1.4)	2.9 (1.5)
MMSE, mean (SD) *	26.2 (2.4)	25.1 (3.3)	26.0 (3.0)	25.9 (3.3)	25.7 (3.1)
ADAS-cog, mean (SD) *	19.3 (7.9)	23.2 (7.0)	21.0 (6.7)	20.7 (7.0)	21.2 (7.5)
Clinical diagnosis *					
- MCI, n (%)	1227 (70.0)	2050 (66.4)	1047 (88.8)	1130 (91.5)	5454 (75.2)
- Mild AD, n (%)	526 (30.0)	1037 (33.6)	132 (11.2)	105 (8.5)	1800 (24.8)
Race and Ethnicity					
Hispanic Black, N (%)	14 (0.5)	83 (2.3)	47 (2.2)	49 (2.2)	193 (1.8)
Hispanic White, N (%)	309 (11.4)	917 (25.6)	649 (30.2)	749 (34.0)	2624 (24.6)
NH Asian, N (%)	27 (1.0)	38 (1.1)	19 (0.9)	34 (1.5)	118 (1.1)
NH Black, N (%)	236 (8.7)	140 (3.9)	139 (6.5)	181 (8.2)	696 (6.5)
NH White, N (%)	2122 (78.4)	2409 (67.2)	1295 (60.3)	1191 (54.0)	7017 (65.9)

* Sample sizes differ due to missing data resulting from varying study requirements or stages of screening at which these variables were collected

Table 3.

Characteristics of the sample at screening, stratified by Participant Eligibility Status.

	Randomized (N=2444)	Ineligible (N=8204)	Total (N=10648)
Study			
Lecanemab Study 201, n (%)	684 (28.0)	2024 (24.7)	2708 (25.4)
Lecanemab Clarity-AD, n (%)	945 (38.7)	2642 (32.2)	3587 (33.7)
Elenbecestat Study 301, n (%)	438 (17.9)	1711 (20.9)	2149 (20.2)
Elenbecestat Study 302, n (%)	377 (15.4)	1827 (22.3)	2204 (20.7)
Female sex, n (%)	1223 (50.0)	4570 (55.7)	5793 (54.4)
Age, mean (SD)	72.3 (7.7)	70.2 (8.7)	70.7 (8.5)
Education, mean yrs (SD) *	14.6 (3.4)	13.8 (3.5)	14.0 (3.5)
APOE ε4, n (%) *	1582 (64.9)	1000 (28.9)	2582 (43.8)
CDR-SB, mean (SD) *	2.9 (1.3)	2.9 (1.6)	2.9 (1.5)
MMSE, mean (SD) *	26.0 (2.2)	25.6 (3.4)	25.7 (3.1)
ADAS-cog, mean (SD) *	22.3 (7.2)	19.4 (7.7)	21.2 (7.5)
Clinical diagnosis *			
- MCI, n (%)	1744 (71.5)	3710 (77.1)	5454 (75.2)
- Mild AD, n (%)	695 (28.5)	1105 (22.9)	1800 (24.8)
Race and Ethnicity			
Hispanic Black, N (%)	34 (1.4)	159 (1.9)	193 (1.8)
Hispanic White, N (%)	412 (16.9)	2212 (27.0)	2624 (24.6)
NH Asian, N (%)	17 (0.7)	101 (1.2)	118 (1.1)
NH Black, N (%)	63 (2.6)	633 (7.7)	696 (6.5)
NH White, N (%)	1918 (78.5)	5099 (62.2)	7017 (65.9)

* Sample sizes differ due to missing data resulting from varying study requirements or stages of screening at which these variables were collected

Table 4.

Characteristics of the sample at screening, stratified by trial (Including "Other" Race and Ethnicity)

Characteristic	Lecanemab Study 201	Lecanemab Clarity-AD	Elenbecestat Study 301	Elenbecestat Study 302	Total
N screened	2728	3638	2192	2246	10804
Eligible, N (%)	686 (25.1)	947 (26.0)	444 (20.3)	381 (17.0)	2458 (22.8)
Female sex, N (%)	1434 (52.6)	1978 (54.4)	1186 (54.1)	1292 (57.5)	5890 (54.5)
Age, mean (SD)	70.6 (9.1)	71.4 (8.3)	70.4 (8.2)	69.7 (8.4)	70.7 (8.5)
Education, mean (SD) *	14.6 (2.9)	NA	13.8 (4.0)	13.8 (3.4)	14.0 (3.5)
APOE carrier, N (%) *	719 (49.1)	917 (46.2)	515 (41.2)	449 (36.1)	2600 (43.7)
CDR-SB, mean (SD) *	2.7 (1.4)	3.3 (1.6)	2.6 (1.2)	2.5 (1.4)	2.9 (1.5)
MMSE, mean (SD) *	26.2 (2.4)	25.1 (3.3)	26.0 (3.0)	25.9 (3.3)	25.7 (3.1)
ADAS-cog, mean (SD) *	19.3 (7.9)	23.2 (7.0)	21.1 (6.7)	20.7 (7.0)	21.2 (7.5)
Clinical diagnosis *					
- MCI, n (%)	1235 (70.1)	2071 (66.4)	1060 (88.9)	1146 (91.5)	5512 (75.2)
- Mild AD, n (%)	528 (29.9)	1049 (33.6)	133 (11.1)	106 (8.5)	1816 (24.8)
Race					
American Indian/Alaska Native, N (%)	1 (<0.1)	3 (0.1)	3 (0.1)	6 (0.3)	13 (0.1)
Asian, N (%)	28 (1.0)	38 (1.0)	19 (0.9)	34 (1.5)	119 (1.1)
Black, N (%)	250 (9.2)	223 (6.1)	186 (8.5)	230 (10.2)	889 (8.2)
Other, N (%)	12 (0.4)	34 (0.9)	29 (1.3)	27 (1.2)	102 (0.9)
Native Hawaiian/Pacific Islander, N (%)	1 (<0.1)	6 (0.2)	3 (0.1)	4 (0.2)	14 (0.1)
White, N (%)	2431 (89.3)	3326 (91.6)	1948 (89.0)	1944 (86.6)	9649 (89.5)
Hispanic ethnicity, N (%)	329 (12.1)	1022 (28.1)	715 (32.7)	817 (36.5)	2883 (26.7)

* Sample sizes differ due to missing data resulting from varying study requirements or stages of screening at which these variables were collected