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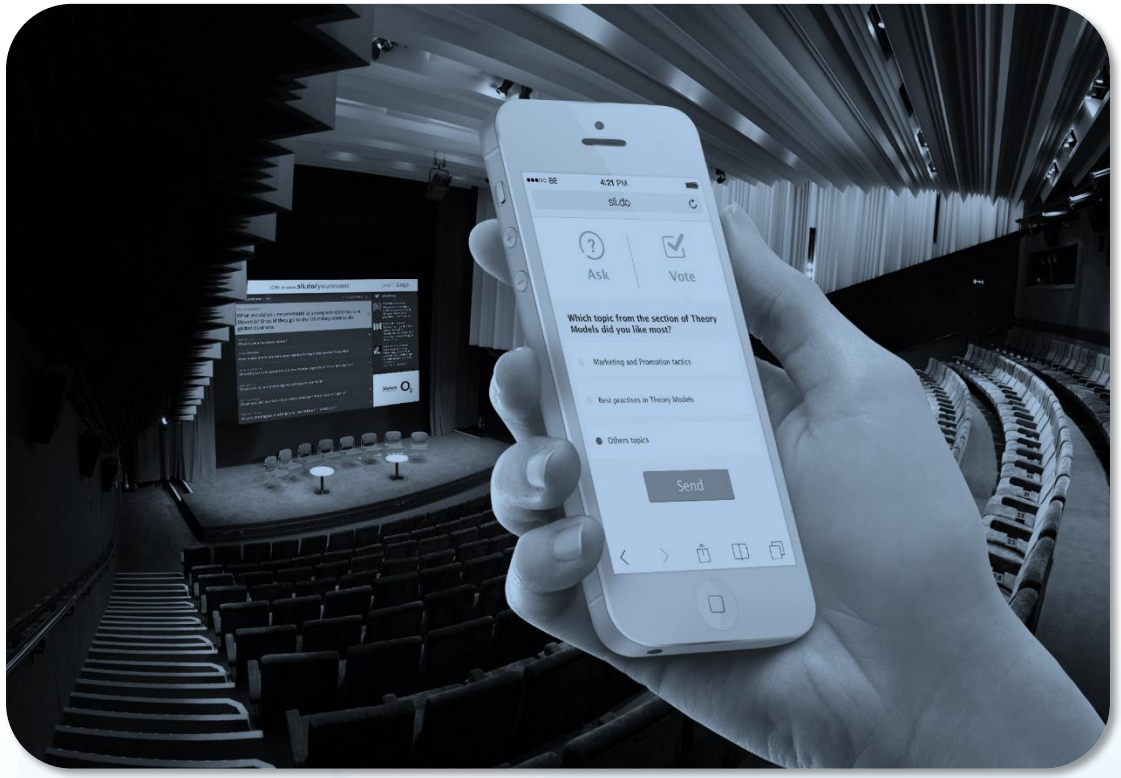

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Introduction

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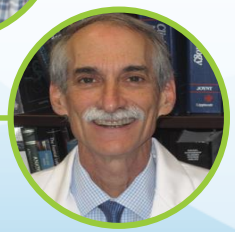

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Disclosures

- PA has received grants from Lilly, Janssen, NIH, FNIH and the Alzheimer's Association, and has received consulting fees from Biogen, Merck, Roche, Proclara, Eisai, Lundbeck and ImmunoBrain Checkpoint. He also co-chairs the Investigator Steering Committee for the aducanumab Phase 3 program
- SC has received grants from AbbVie, AgeneBio, Avid, Axovant, Biogen, Centre for Aging and Brain Health Innovation (CABHI), Canada China Health Institute (CCHI), Eisai, Eli Lilly, Genentech, Janssen, Lundbeck, Merck, Novartis, Regenera, Roche, TauRx Therapeutics Ltd, and vTv Therapeutics; SC has received honoraria for serving on the Biogen Aducanumab Steering Committee, Eli Lilly Lanabecestat Executive Steering Committee, EUCAN Alzheimer's Advisory Board, ProMIS Neuroscience Scientific Advisory Board, and Zaloplex Scientific Advisory Board; SC has received consultancy fees from Alector, CogState, Mediti Pharma, and Regenera
- RP has served as a consultant or on the DSMB for Roche, Merck, Biogen, Eisai, and Genentech and as an educational presenter for GE Healthcare
- SS was a site PI for the PRIME and ENGAGE studies and he co-chairs the Investigator Steering Committee for the aducanumab Phase 3 program. He is also the Project Arm Leader for gantenerumab in the DIAN-TU study; SS receives research support and consultation fees from Biogen, Lilly, Eisai, Genentech, Roche, Novartis and Avid
- SBH, CvH, YT, SC, KKM, TC, SW, JL, LS, LN, RR, GD, KH, IN, YZ, CM, and AS are employees of Biogen

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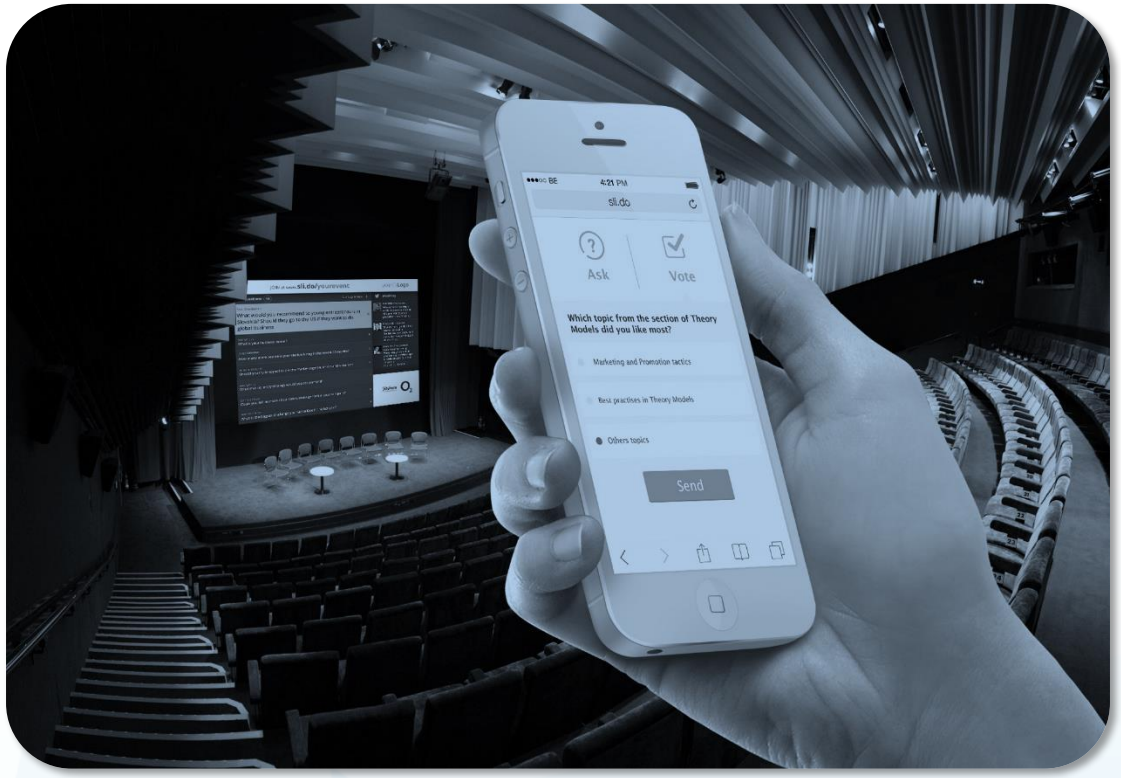

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EMERGE and ENGAGE Topline Results: Two Phase 3 Studies to Evaluate Aducanumab in Patients With Early Alzheimer's Disease

Samantha Budd Haeberlein,[1] Christian von Hehn,[1] Ying Tian,[1] Spyros Chalkias,[1] Kumar Kandadi Muralidharan,[1] Tianle Chen,[1] Shuang Wu,[1] Jie Li,[1] LeAnne Skordos,[1] Laura Nisenbaum,[1] Raj Rajagovindan,[1] Gersham Dent,[1] Katie Harrison,[1] Ivan Nestorov,[1] Ying Zhu,[1] Craig Mallinckrodt,[1] Alfred Sandrock[1]

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CTAD 2019, San Diego, CA, USA

December 5, 2019

Forward-looking statements

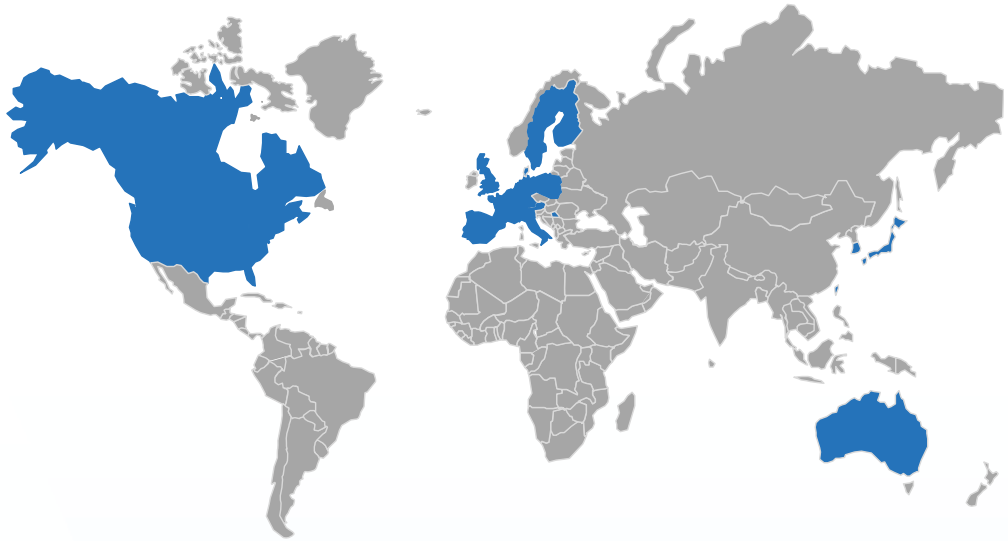
- This presentation contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to additional results from the Phase 3 clinical studies of aducanumab; the potential clinical effects of aducanumab; the potential benefits, safety, and efficacy of aducanumab; potential regulatory discussions, submissions, and approvals and the timing thereof; clinical development programs, clinical trials, data readouts, and presentations related to aducanumab; the enrollment of any future clinical studies of aducanumab; the treatment of Alzheimer's disease; the potential of Biogen's commercial business and pipeline programs, including aducanumab; the anticipated benefits and potential of Biogen's collaboration arrangements with Eisai Co, Ltd; and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will," "would," and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later-stage or larger-scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.
- These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including actual timing and content of submissions to and decisions made by the regulatory authorities regarding aducanumab; regulatory submissions may take longer or be more difficult to complete than expected; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen's drug candidates, including aducanumab; actual timing and enrollment of future studies of aducanumab; the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; risks of unexpected costs or delays; the risks of other unexpected hurdles; uncertainty of success in the development and potential commercialization of aducanumab; failure to protect and enforce Biogen's data, intellectual property, and other proprietary rights and uncertainties relating to intellectual property claims and challenges; risks relating to the potential launch of aducanumab, including preparedness of healthcare providers to treat patients, the ability to obtain and maintain adequate reimbursement for aducanumab, and other unexpected difficulties or hurdles; product liability claims; third-party collaboration risks; and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments, or otherwise.

Legal disclaimer

- Aducanumab is an investigational compound and is not yet approved
- Biogen licensed the worldwide rights to aducanumab from Neurimmune Holding AG in 2007 and is responsible for its development and commercialization
- As of October 22, 2017, Biogen and Eisai are collaborating on the development and commercialization of aducanumab globally

Aducanumab Phase 3 studies EMERGE and ENGAGE

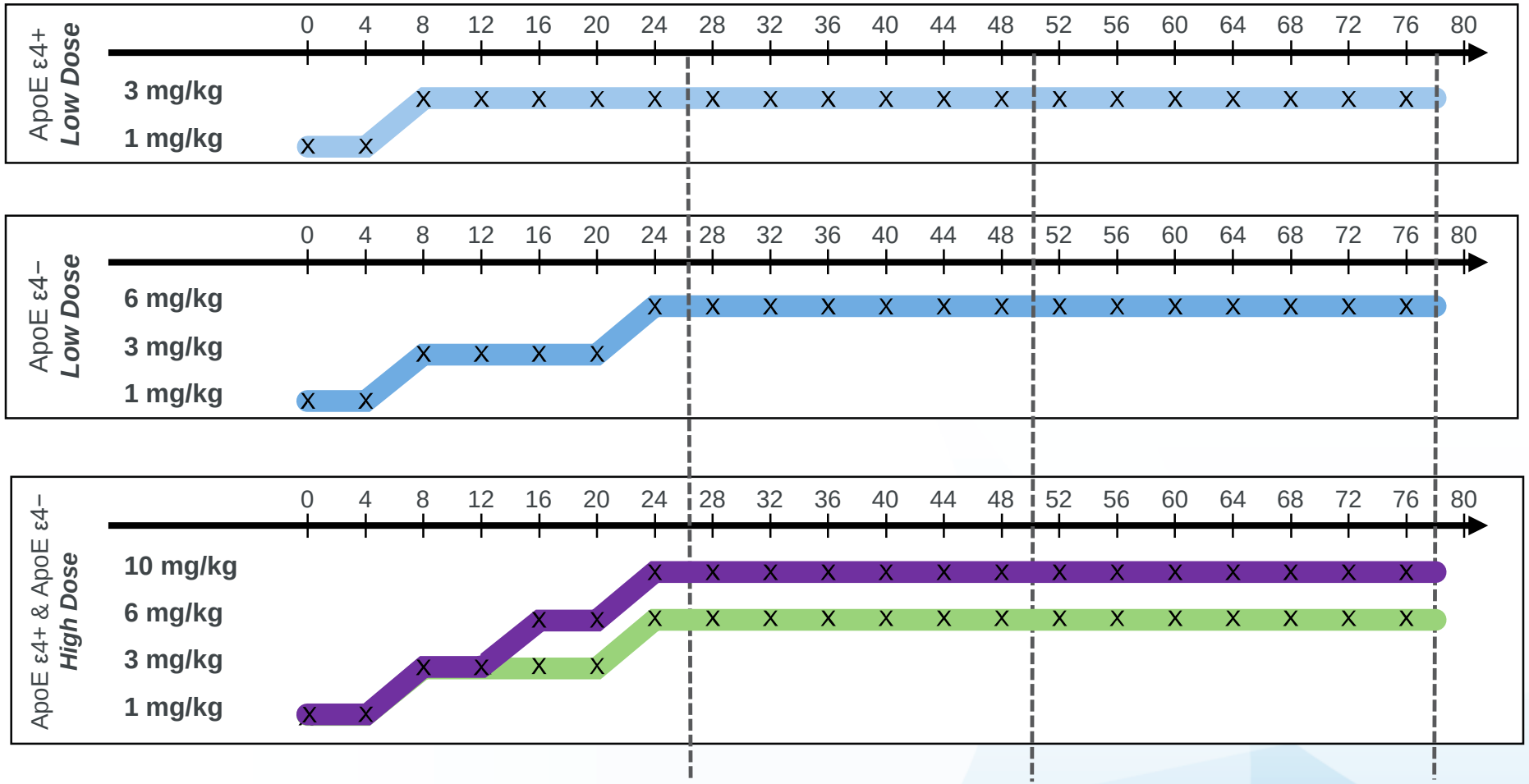
Studies	Two 18-month, randomized, double-blind, placebo-controlled, Phase 3 studies
Geography/ sample size	3285 patients at 348 sites in 20 countries
Population	▪ Early Alzheimer's disease (MCI due to Alzheimer's disease + mild Alzheimer's disease dementia) • MMSE 24-30, CDR-G 0.5, RBANS ≤ 85, with confirmed amyloid pathology
Doses	▪ Two dosing regimens (low and high) and placebo; randomized 1:1:1
Primary endpoint	▪ CDR-SB at 18 months
Other endpoints	▪ Secondary: MMSE, ADAS-Cog 13, ADCS-ADL-MCI ▪ Sub-studies: amyloid PET, tau PET, CSF disease-related biomarkers



Countries with active sites included:
Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Italy, Japan, the Netherlands, Poland, Portugal, South Korea, Spain, Sweden, Switzerland, Taiwan, United Kingdom, United States

1. ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT02477800. Accessed November 2019; ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT02484547. Accessed November 2019; Data on file.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; PET, positron-emission tomography; RBANS, Repeatable Battery for Assessment of Neuropsychological Status.

EMERGE and ENGAGE: Dose regimen



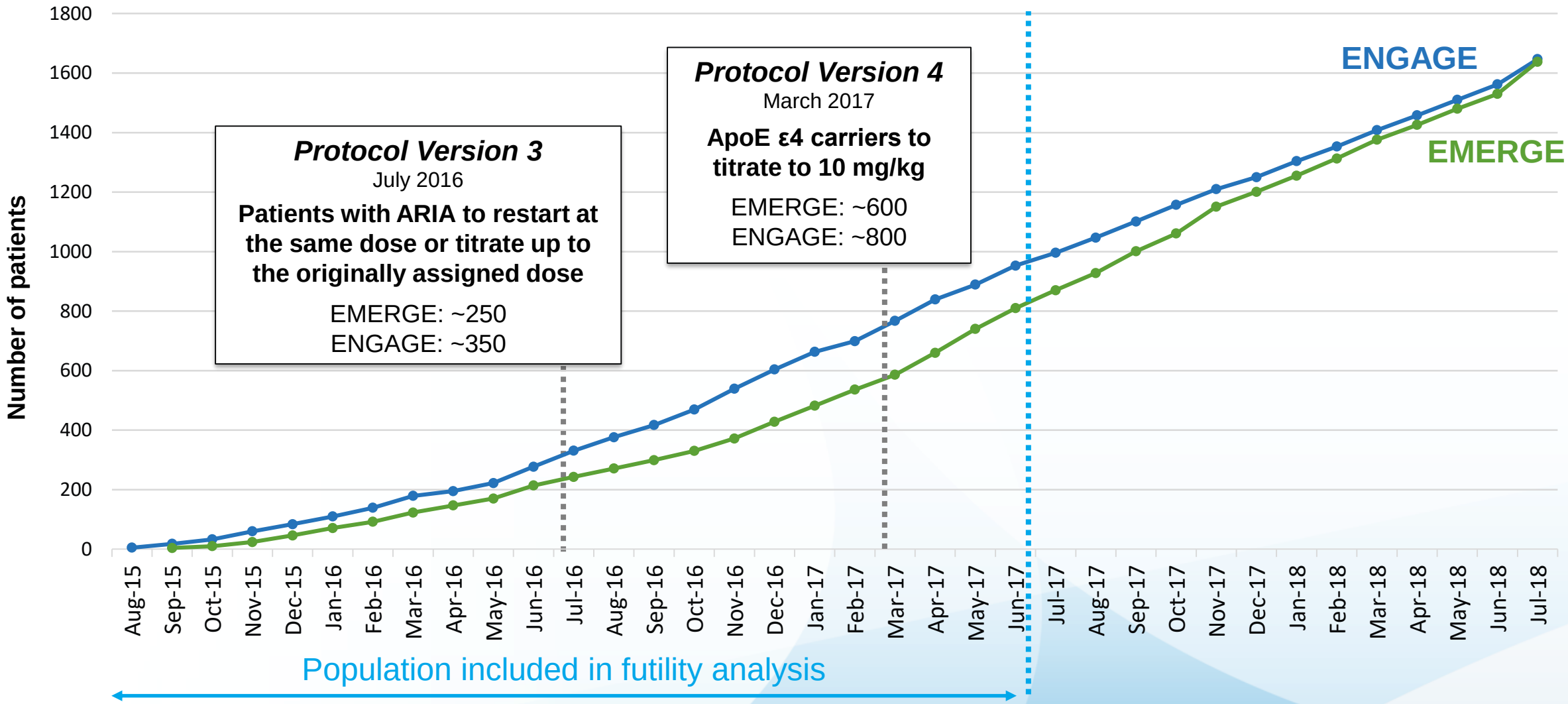
- Low dose titrated to 3 or 6 mg/kg
- Maintained throughout study

- High dose titrated to 6 or 10 mg/kg for Protocol Versions 1-3
- High dose titrated to 10 mg/kg for Protocol Version 4 and higher

Expected # of 10 mg/kg in high dose group ***by Week 26*: 1 dose** ***by Week 50*: 7 doses** ***by Week 78*: 14 doses**

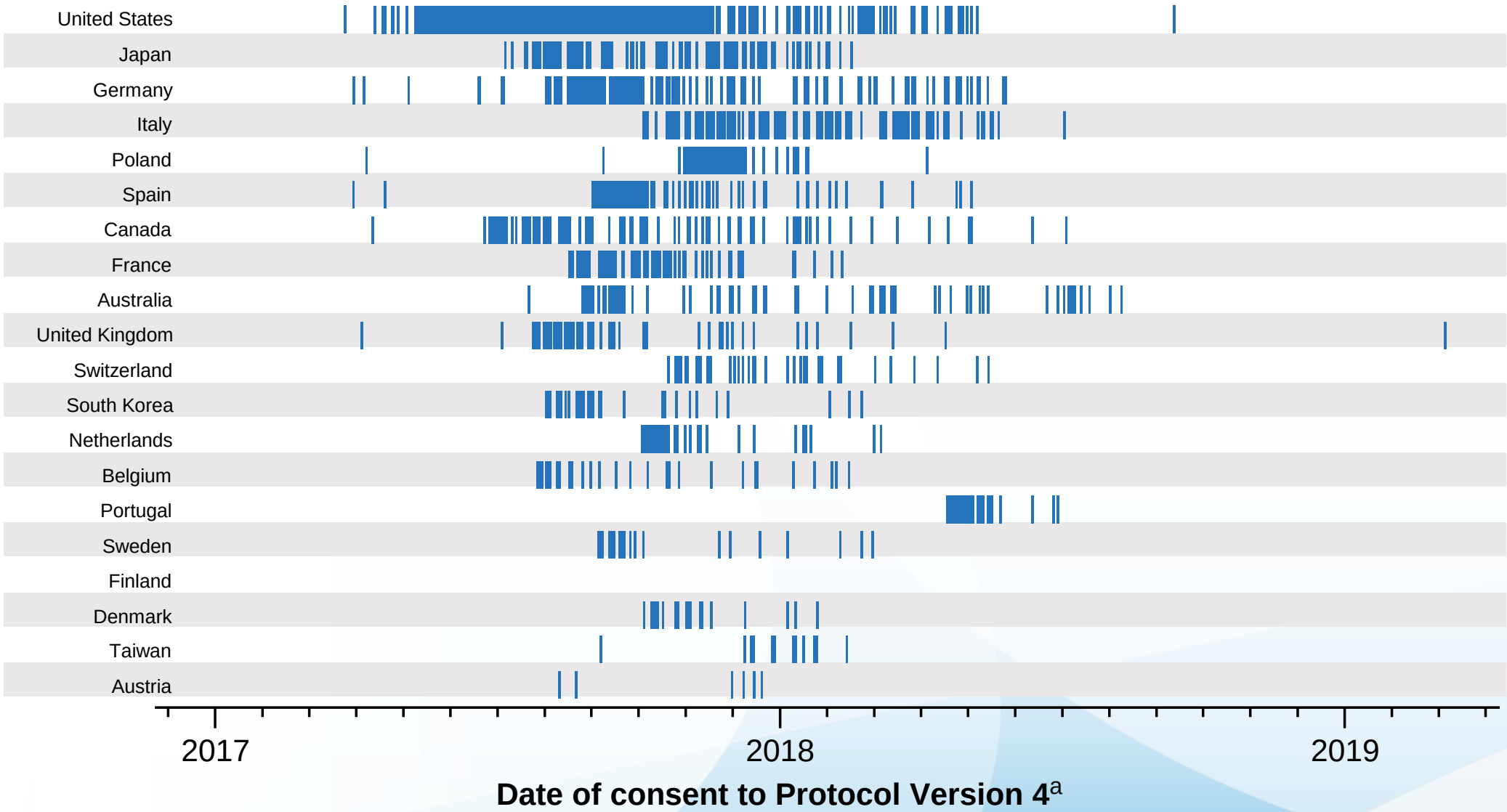
ApoE, apolipoprotein E.

Enrollment and timing of key protocol amendments



ApoE, apolipoprotein E; ARIA, amyloid-related imaging abnormalities.

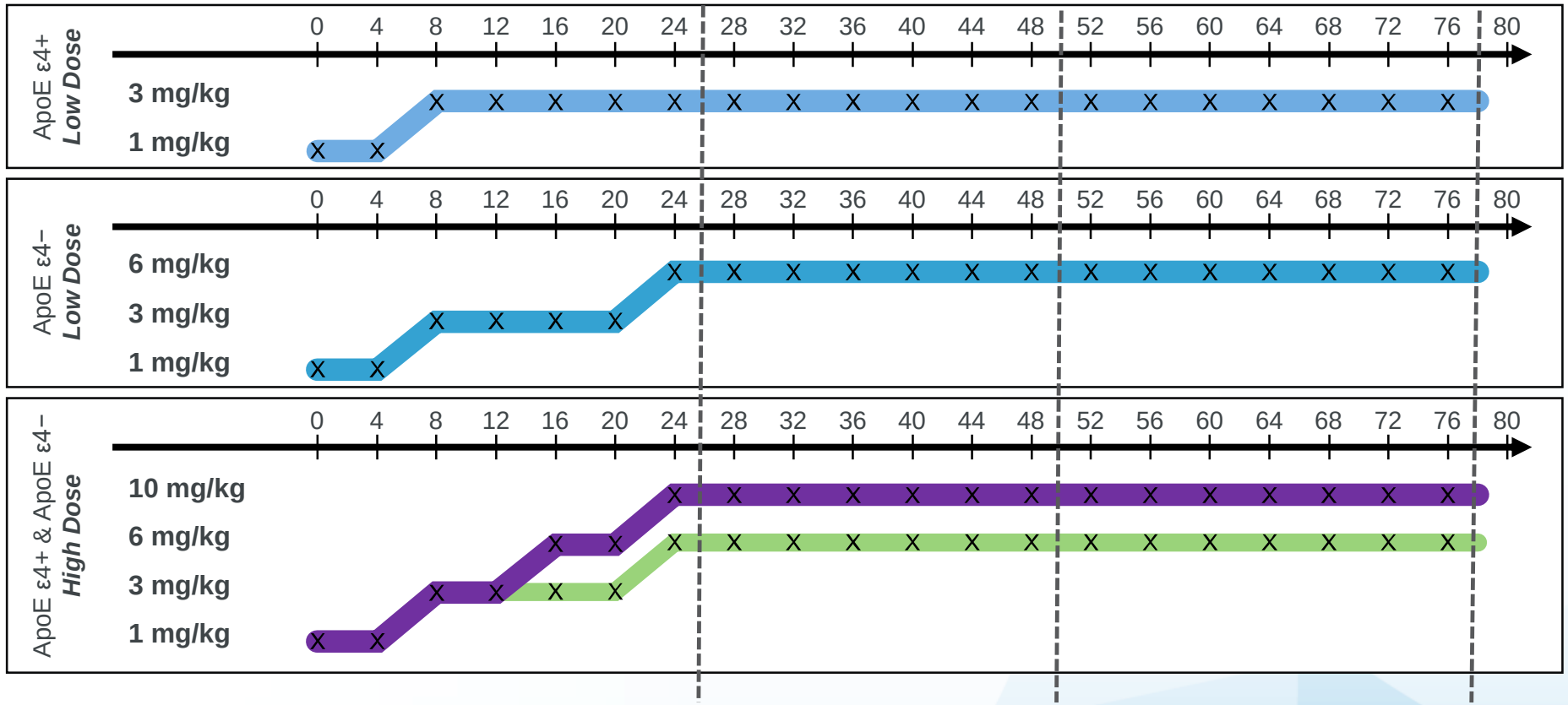
Individual patient consent timing to Protocol Version 4



[a]Some patients never consented to Protocol Version 4.

EMERGE and ENGAGE: Dose regimen

Early enrolled patients in the high dose arm received a lower dose



Median cumulative dose at Week 78

56 mg/kg

98 mg/kg

116 mg/kg (pre-PV4)

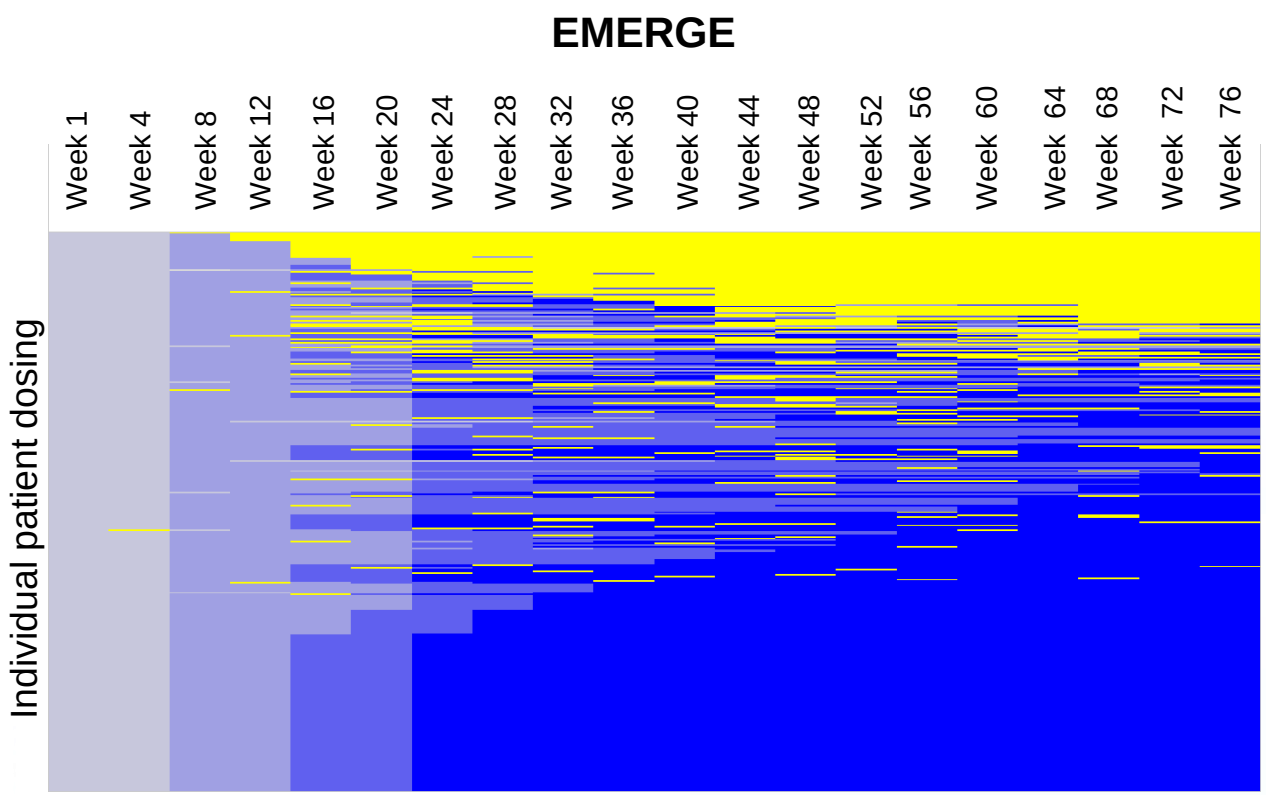
153 mg/kg (post-PV4)

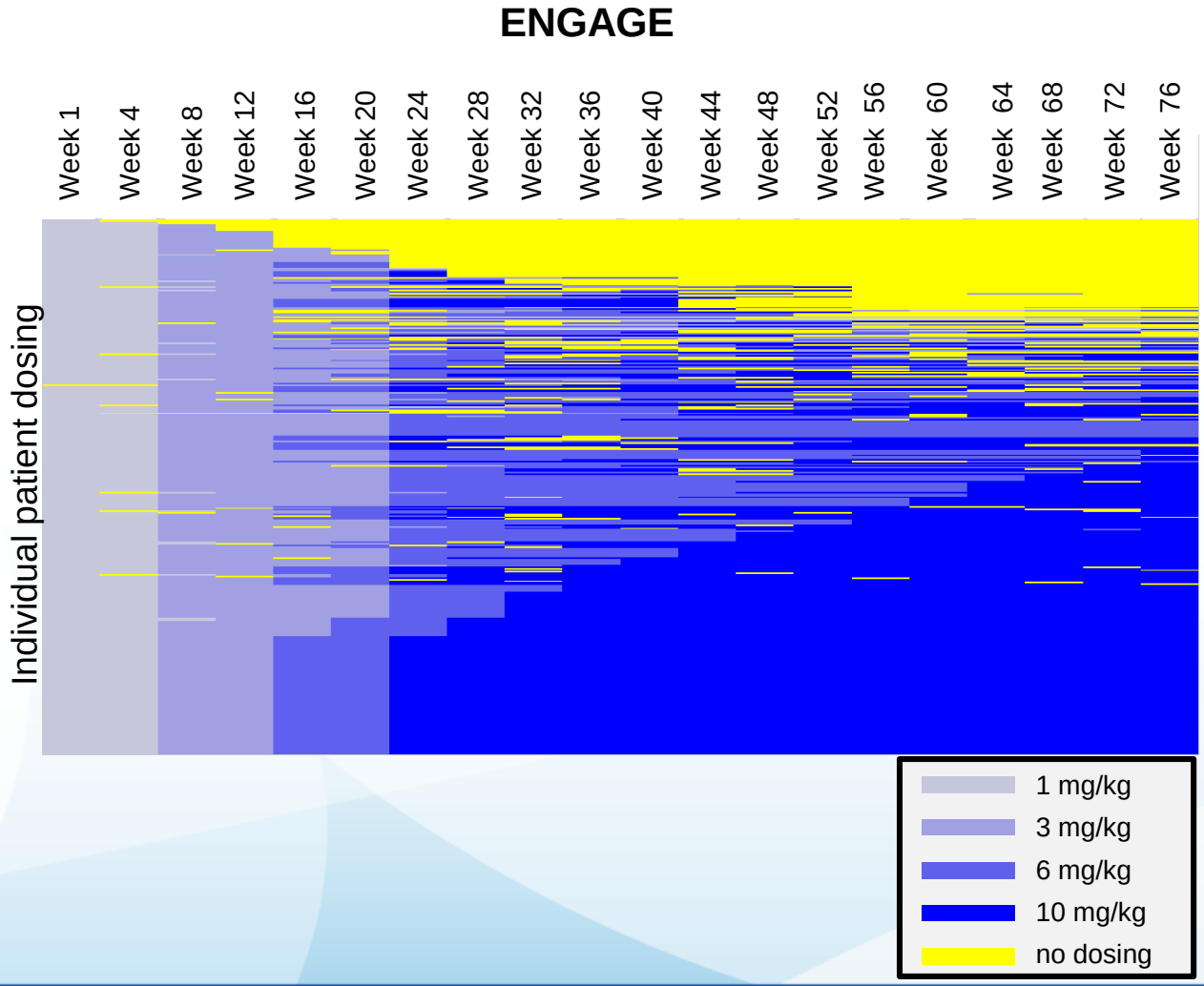
Expected # of 10 mg/kg in high dose group *by Week 26*: 1 dose *by Week 50*: 7 doses *by Week 78*: 14 doses

ApoE, apolipoprotein E; PV4, Protocol Version 4.

High dose regimen: Individual-level dosing

29% of patients in EMERGE and 22% of patients in ENGAGE received the full possible 14 doses of 10 mg/kg doses





OTC population.
OTC, opportunity to complete.

EMERGE and ENGAGE Topline Results

EMERGE and ENGAGE: Data sets

Data set	Population	EMERGE n (%)	ENGAGE n (%)
Futility	**Opportunity to complete (OTC)** Patients who have had the opportunity to complete Week 78 visit by December 26, 2018	803 (49%)	945 (57%)
Larger data set[a]	**Opportunity to complete (OTC)** Patients who have had the opportunity to complete Week 78 visit by March 20, 2019	982 (60%)	1084 (66%)
	Intent to treat (ITT) All patient data (data after March 20 are censored for efficacy analyses) *Data cleaning was ongoing for a small amount of data*	1638 (100%)	1647 (100%)
Final data set	**Intent to treat (ITT)** All patient data (data after March 20 are censored for efficacy analyses)	1638 (100%)	1647 (100%)
Sub-studies	**Amyloid PET**	485 (30%)	582 (35%)
	CSF	68 (4%)	57 (3%)
	Tau PET	6 (<1%)	30 (2%)

[a]Unless otherwise specified, all of the results presented in this presentation are based on the larger dataset.
CSF, cerebrospinal fluid; ITT, intent to treat; OTC, opportunity to complete; PET, positron emission tomography.

EMERGE and ENGAGE

Futility analysis

EMERGE and ENGAGE: Prespecified futility analysis

- **Conditional power**: probability that primary efficacy endpoint analysis would be statistically significant at final analysis
- **Prespecified criteria**: both dose arms of both studies having less than 20% conditional power to meet the primary endpoint at final analysis
- **Prespecified methodology**: given identical study design, conditional power would be calculated using pooled data from both studies to predict the future behavior of the remaining patients
    - Pooling was believed to be a more powerful statistical methodology
- Using this methodology, the futility criteria were met
- At the time of futility analysis, EMERGE was trending positive, whereas ENGAGE was not

Phase 3 Topline Results

EMERGE

EMERGE: Baseline demographics

	EMERGE		
	Placebo (n=548)	**Low dose (n=543)**	**High dose (n=547)**
Age in years, mean ± SD	70.8±7.40	70.6±7.45	70.6±7.47
Female, n (%)	290 (52.9)	269 (49.5)	284 (51.9)
Race, n (%)			
Asian	47 (8.6)	38 (7.0)	41 (7.5)
White	415 (75.7)	418 (77.0)	405 (74.0)
Education years, mean ± SD	14.5±3.82	14.5±3.63	14.6±3.74
Alzheimer's disease medications used, n (%)	279 (50.9)	277 (51.0)	277 (50.6)
ApoE ε4, n (%)			
Carriers	367 (67.0)	362 (66.7)	365 (66.7)
Non-carriers	178 (32.5)	178 (32.8)	181 (33.1)
Clinical stage, n (%)			
MCI due to Alzheimer's disease	446 (81.4)	452 (83.2)	438 (80.1)
Mild Alzheimer's disease	102 (18.6)	91 (16.8)	109 (19.9)
Amyloid PET SUVR, mean composite ± SD (n) *PET sub-study population only*	1.37±0.175 (157)	1.39±0.181 (157)	1.38±0.183 (171)

ITT population.
ApoE, apolipoprotein E; ITT, intent to treat; MCI, mild cognitive impairment; PET, positron-emission tomography; SD, standard deviation; SUVR, standardized uptake value ratio.

EMERGE: Baseline disease characteristics

	EMERGE		
	Placebo (n=548)	Low dose (n=543)	High dose (n=547)
RBANS delayed memory score, mean ± SD	60.5±14.23	60.0±14.02	60.7±14.15
MMSE score, mean ± SD	26.4±1.78	26.3±1.72	26.3±1.68
CDR global score, n (%)			
0.5	544 (99.3)	543 (100)	546 (99.8)
1	3 (0.5)	0	1 (0.2)
CDR-SB score, mean ± SD	2.47±0.999	2.46±1.011	2.51±1.053
ADAS-Cog 13 score, mean ± SD	21.9±6.73	22.5±6.76	22.2±7.08
ADCS-ADL-MCI score, mean ± SD	42.6±5.73	42.8±5.48	42.5±5.82

ITT population.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; RBANS, Repeatable Battery for Assessment of Neuropsychological Status.

EMERGE: Patient disposition

Randomized	EMERGE (N=1643)		
Dosed	n=1638		
	Placebo n=548	Low dose n=543	High dose n=547
Discontinued treatment[a], n (%)	**82 (15.0)**	**108 (19.9)**	**131 (23.9)**
Adverse event	16 (2.9)	41 (7.6)	46 (8.4)
Consent withdrawn	6 (1.1)	22 (4.1)	18 (3.3)
Death	5 (0.9)	0	5 (0.9)
Study visit burden	2 (0.4)	7 (1.3)	5 (0.9)
Site terminated by sponsor	21 (3.8)	10 (1.8)	14 (2.6)
Other	23 (4.2)	23 (4.2)	28 (5.1)
Withdrew from study[a], n (%)	**39 (7.1)**	**54 (9.9)**	**66 (12.1)**
Adverse event	10 (1.8)	11 (2.0)	18 (3.3)
Consent withdrawn	8 (1.5)	28 (5.2)	22 (4.0)
Death	5 (0.9)	0	6 (1.1)
Study visit burden	2 (0.4)	7 (1.3)	5 (0.9)
Site terminated by sponsor	0	0	1 (0.2)
Other	3 (0.5)	4 (0.7)	3 (0.5)
Completed placebo-controlled period, n (%)	**275 (50.2)**	**274 (50.5)**	**285 (52.1)**

ITT population. [a]Some categories with less than 1% patients are not displayed, including lost to follow-up, disease progression, pregnancy, investigator decision, relocation, change of treatment, withdrawal by parent/guardian, protocol amendment, site terminated by investigator and loss of capacity.
ITT, intent to treat.

EMERGE: Primary and secondary endpoints from larger data set at Week 78

	Placebo decline (n=548)	Difference vs. placebo (%)[a] p-value[b]	
		Low dose (n=543)	High dose (n=547)
CDR-SB	1.74	**-0.25** (-14%) 0.1171	**-0.40** (-23%) 0.0101
MMSE	-3.3	**-0.1** (3%) 0.6900	**0.5** (-15%) 0.0620
ADAS-Cog 13	5.171	**-0.747** (-14%) 0.1672	**-1.395** (-27%) 0.0098
ADCS-ADL-MCI	-4.3	**0.7** (-16%) 0.1556	**1.7** (-40%) 0.0009

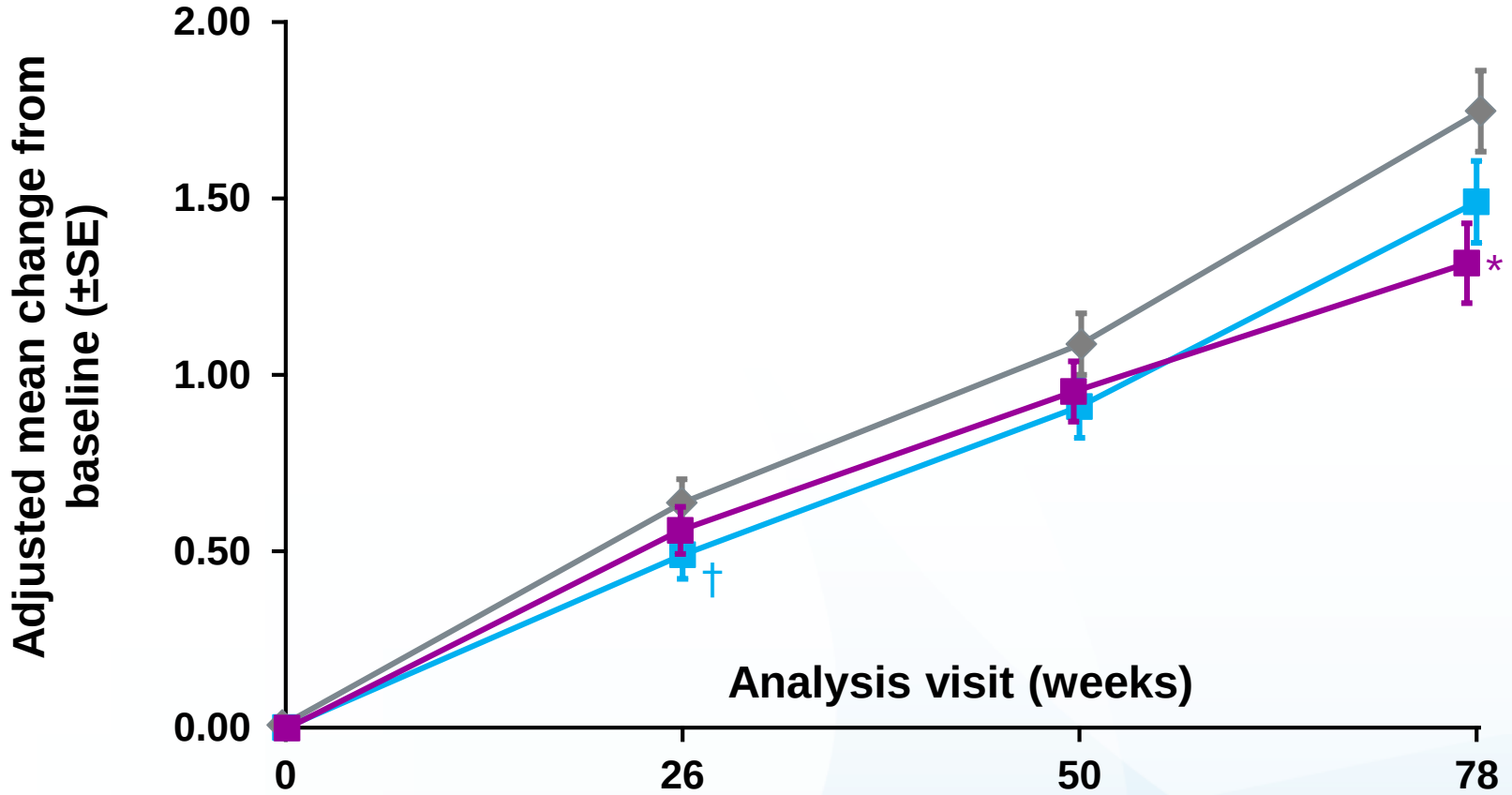
ITT population. [a]Difference vs placebo at Week 78. Negative percentage means less progression in the treated arm. [b]Nominal.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

EMERGE: Primary and secondary endpoints from final data set at Week 78

	Placebo decline (n=548)	Difference vs. placebo (%)[a] p-value	
		Low dose (n=543)	High dose (n=547)
CDR-SB	1.74	**-0.26** (-15%) 0.0901	**-0.39** (-22%) 0.0120
MMSE	-3.3	**-0.1** (3%) 0.7578	**0.6** (-18%) 0.0493
ADAS-Cog 13	5.162	**-0.701** (-14%) 0.1962	**-1.400** (-27%) 0.0097
ADCS-ADL-MCI	-4.3	**0.7** (-16%) 0.1515	**1.7** (-40%) 0.0006

ITT population. [a]Difference vs placebo at Week 78. Negative percentage means less progression in the treated arm.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

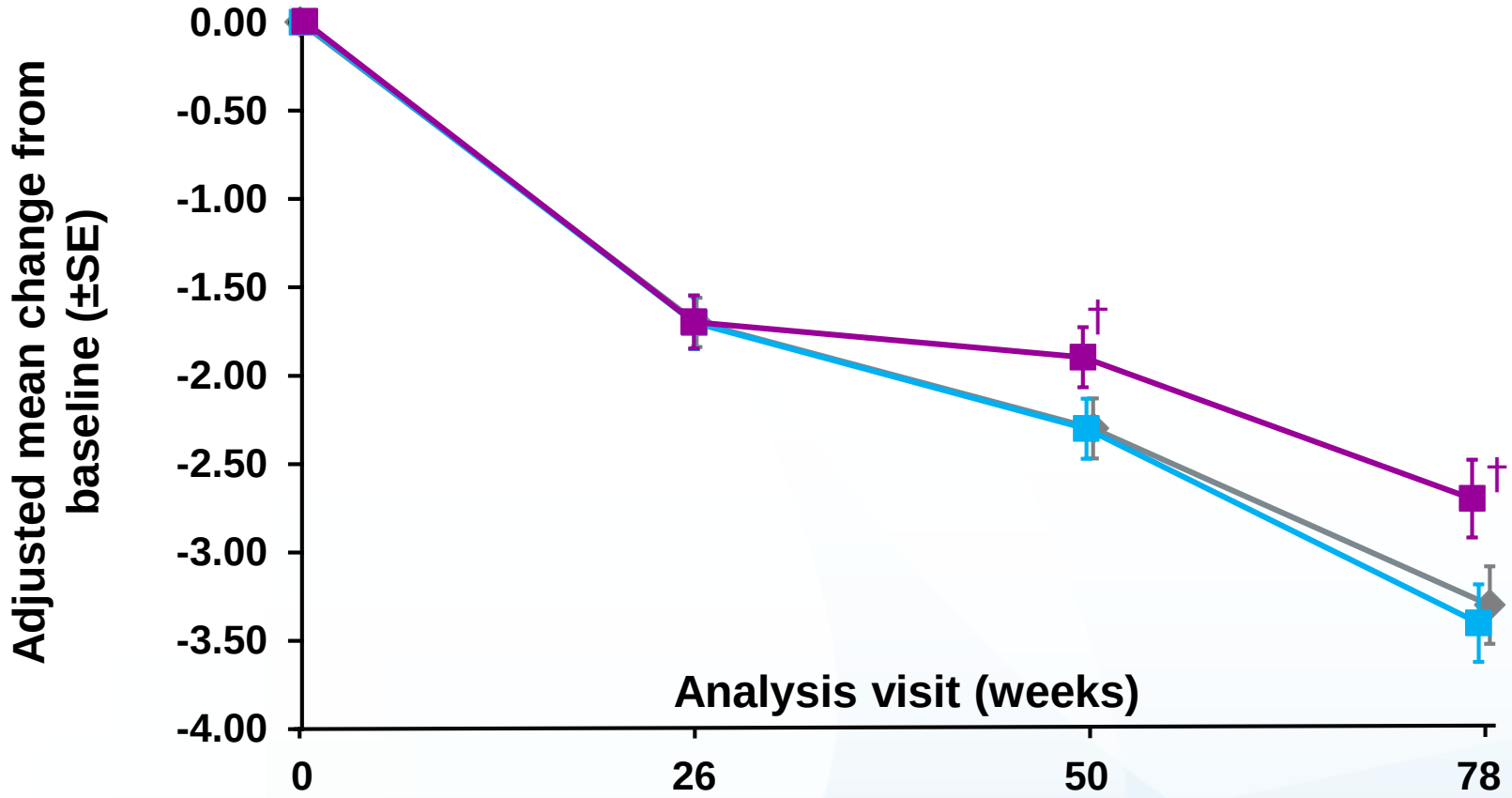
EMERGE: Longitudinal change from baseline in CDR-SB



Placebo	n=547	531	429	288
Low dose aducanumab	n=543	512	420	289
High dose aducanumab	n=547	513	431	299

ITT population. *p <0.05, †p<0.1 and ≥0.05 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in CDR-SB as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline CDR-SB, baseline CDR-SB by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

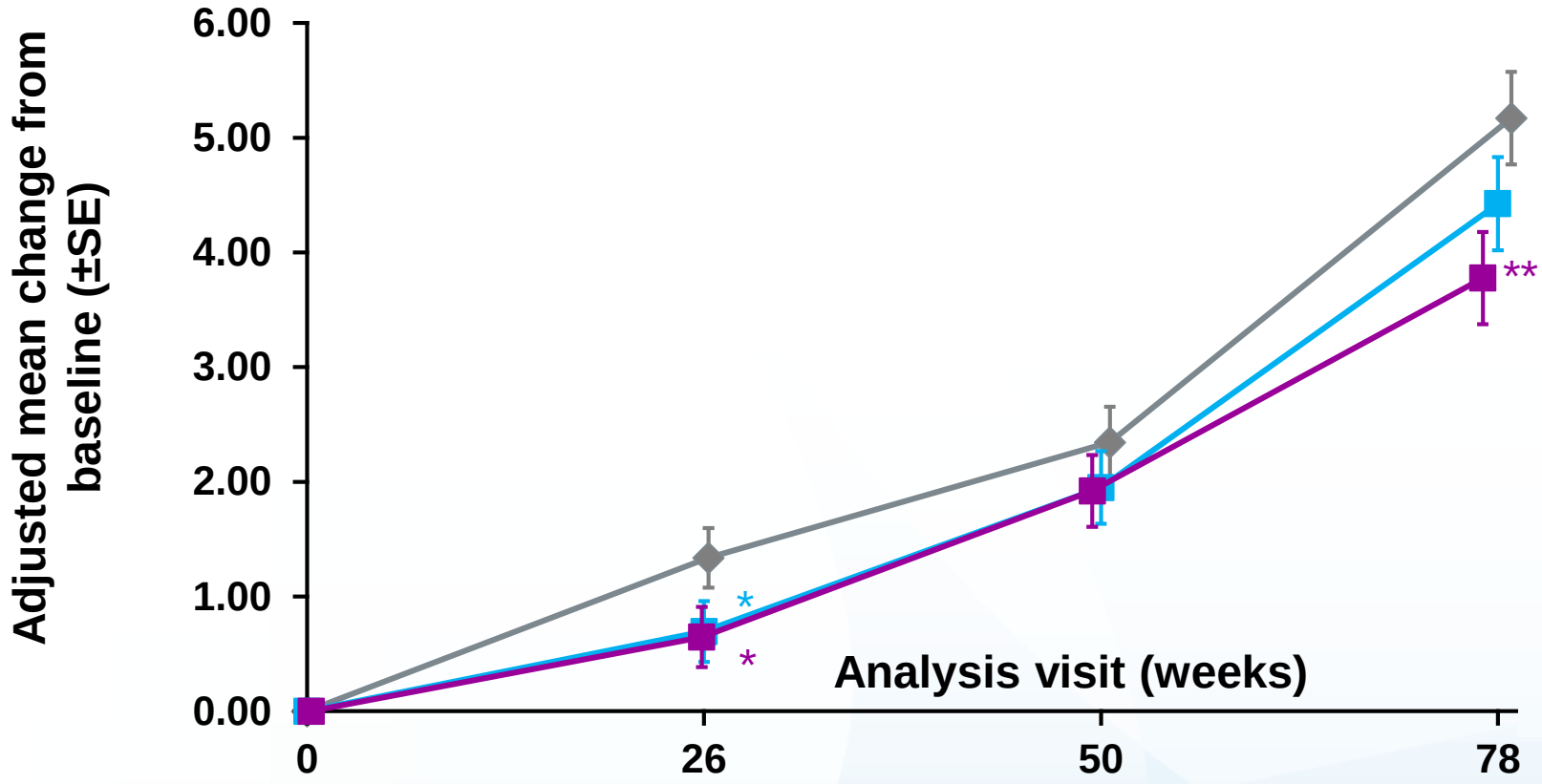
EMERGE: Longitudinal change from baseline in MMSE



Placebo	n=548	531	434	288
Low dose aducanumab	n=543	516	423	293
High dose aducanumab	n=547	521	433	298

ITT population. †p<0.1 and ≥0.05 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in MMSE as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline MMSE, baseline MMSE by visit interaction, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status.
ApoE, apolipoprotein E; ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

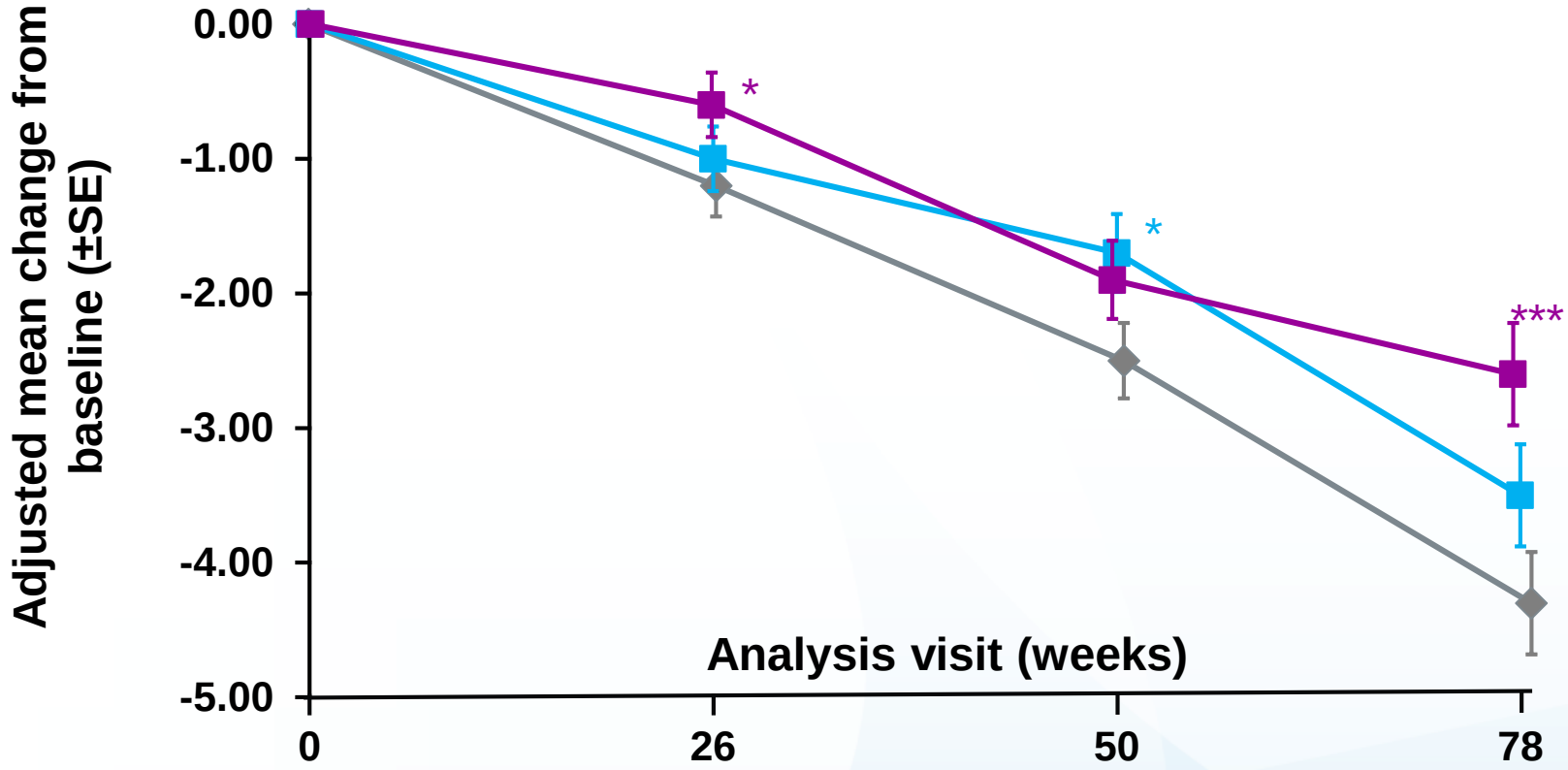
EMERGE: Longitudinal change from baseline in ADAS-Cog 13



Placebo	n=545	528	431	287
Low dose aducanumab	n=542	514	420	290
High dose aducanumab	n=545	518	430	292

ITT population. *p<0.05, **p<0.01 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in ADAS-Cog 13 as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADAS-Cog 13, baseline ADAS-Cog 13 by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

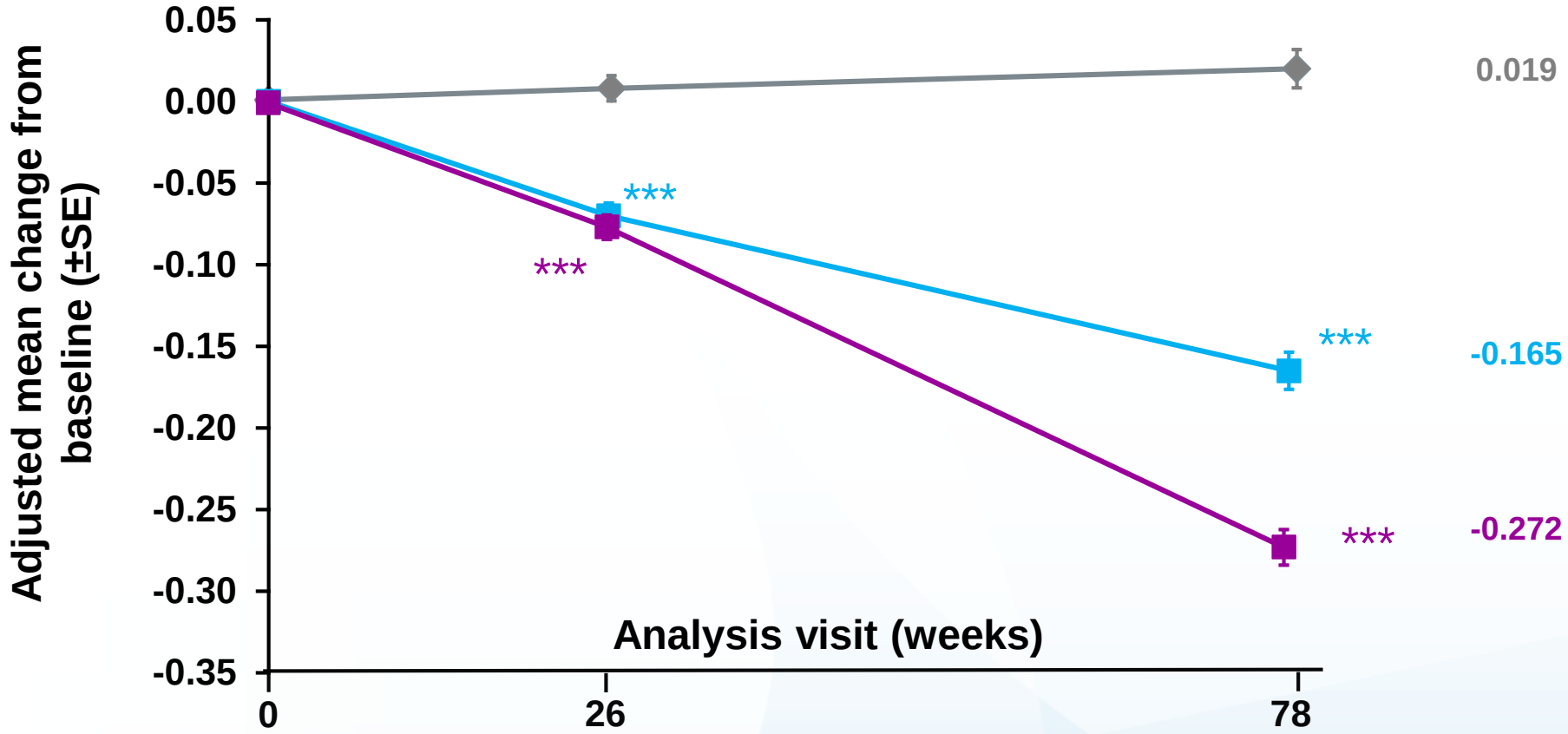
EMERGE: Longitudinal change from baseline in ADCS-ADL-MCI



Placebo	n=545	528	430	283
Low dose aducanumab	n=540	509	416	286
High dose aducanumab	n=544	513	428	293

ITT population. *p<0.05, ***p<0.001 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in ADCS-ADL-MCI as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADCS-ADL-MCI, baseline ADCS-ADL-MCI by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

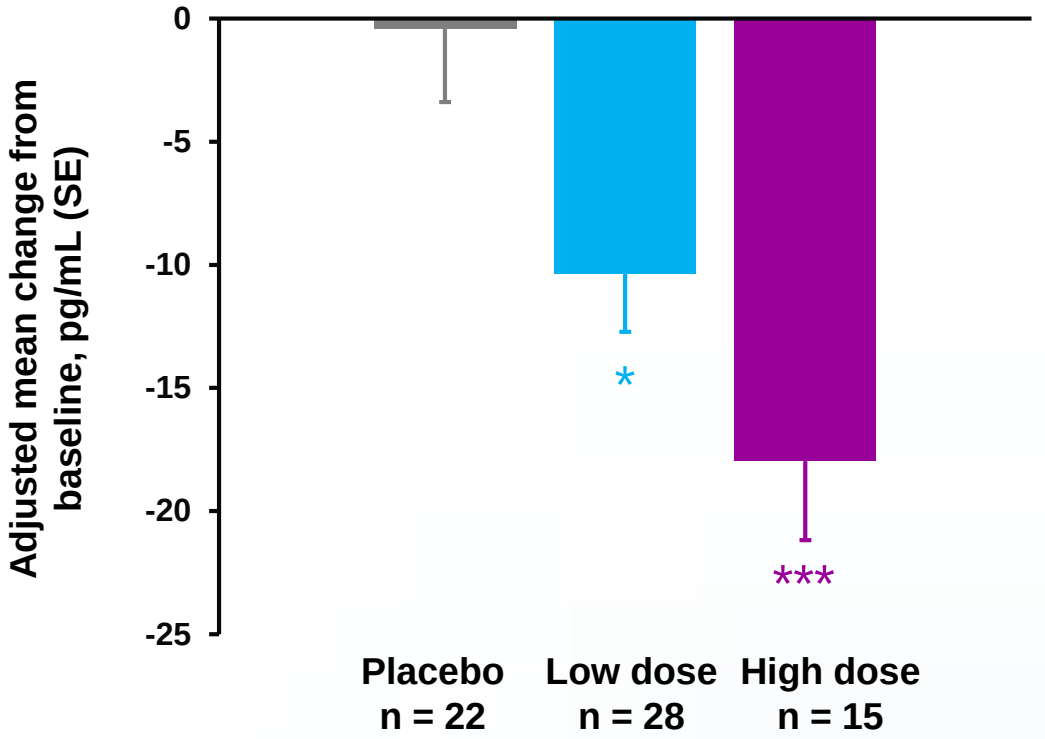
EMERGE: Longitudinal change from baseline in amyloid PET SUVR



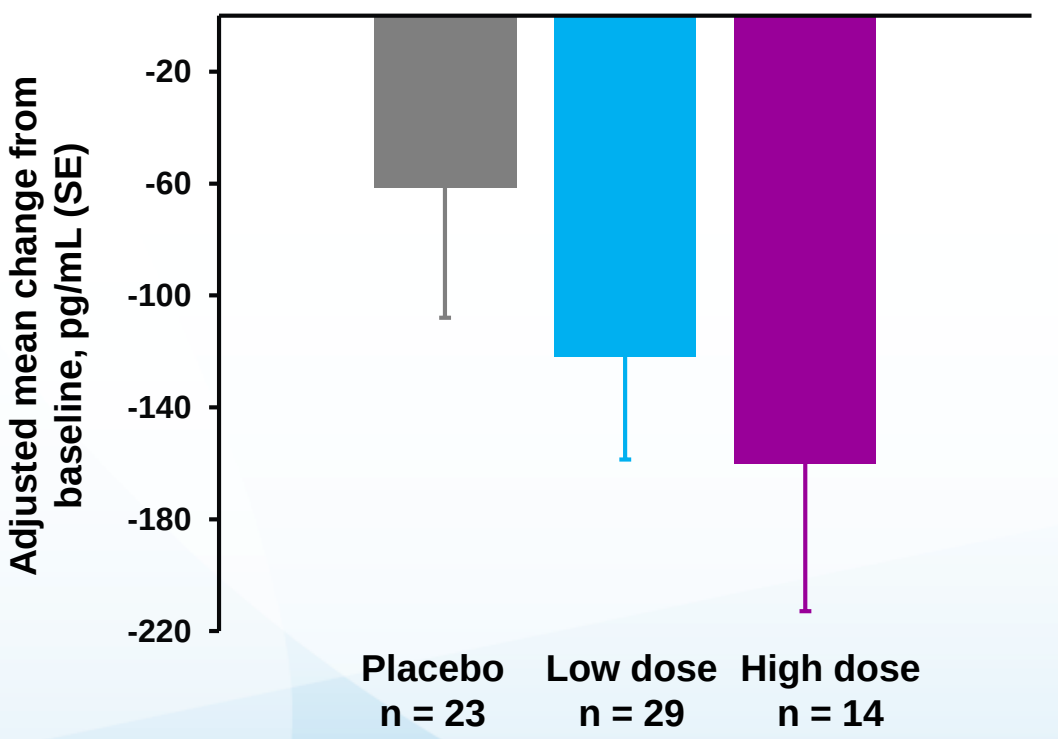
[18]F-florbetapir amyloid PET analysis population. ***p<0.0001 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in MMSE as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline SUVR, baseline SUVR by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; PET, positron emission tomography; SE, standard error; SUVR, standardized uptake value ratio.

EMERGE: CSF biomarkers of tau pathology and neurodegeneration

CSF p-tau



CSF total tau



CSF modified analysis population (patients with both baseline and post-baseline CSF assessments). *p<0.05, ***p<0.001 compared with placebo (nominal). Values were based on an ANCOVA model at Week 78, fitted with change from baseline as the dependent variable, and with categorical treatment, baseline biomarker value, baseline age, and laboratory ApoE ε4 status (carrier and non-carrier) as the independent variables.
ANCOVA, analysis of covariance; ApoE, apolipoprotein; CSF, cerebrospinal fluid; SE, standard error.

Phase 3 Topline Results

ENGAGE

ENGAGE: Baseline demographics

	ENGAGE		
	Placebo (n=545)	**Low dose (n=547)**	**High dose (n=555)**
Age in years, mean ± SD	69.8±7.72	70.4±6.96	70.0±7.65
Female, n (%)	287 (52.7)	284 (51.9)	292 (52.6)
Race, n (%)			
Asian	55 (10.1)	55 (10.1)	65 (11.7)
White	413 (75.8)	412 (75.3)	413 (74.4)
Education years, mean ± SD	14.7±3.66	14.6±3.77	14.6±3.72
Alzheimer's disease medications used, n (%)	293 (53.8)	307 (56.1)	307 (55.3)
ApoE ε4, n (%)			
Carriers	376 (69.0)	391 (71.5)	378 (68.1)
Non-carriers	167 (30.6)	156 (28.5)	176 (31.7)
Clinical stage, n (%)			
MCI due to Alzheimer's disease	443 (81.3)	440 (80.4)	442 (79.6)
Mild Alzheimer's disease	102 (18.7)	107 (19.6)	113 (20.4)
Amyloid PET SUVR, mean composite ± SD (n) *PET sub-study population only*	1.38±0.198 (203)	1.39±0.186 (198)	1.41±0.177 (181)

ITT population.

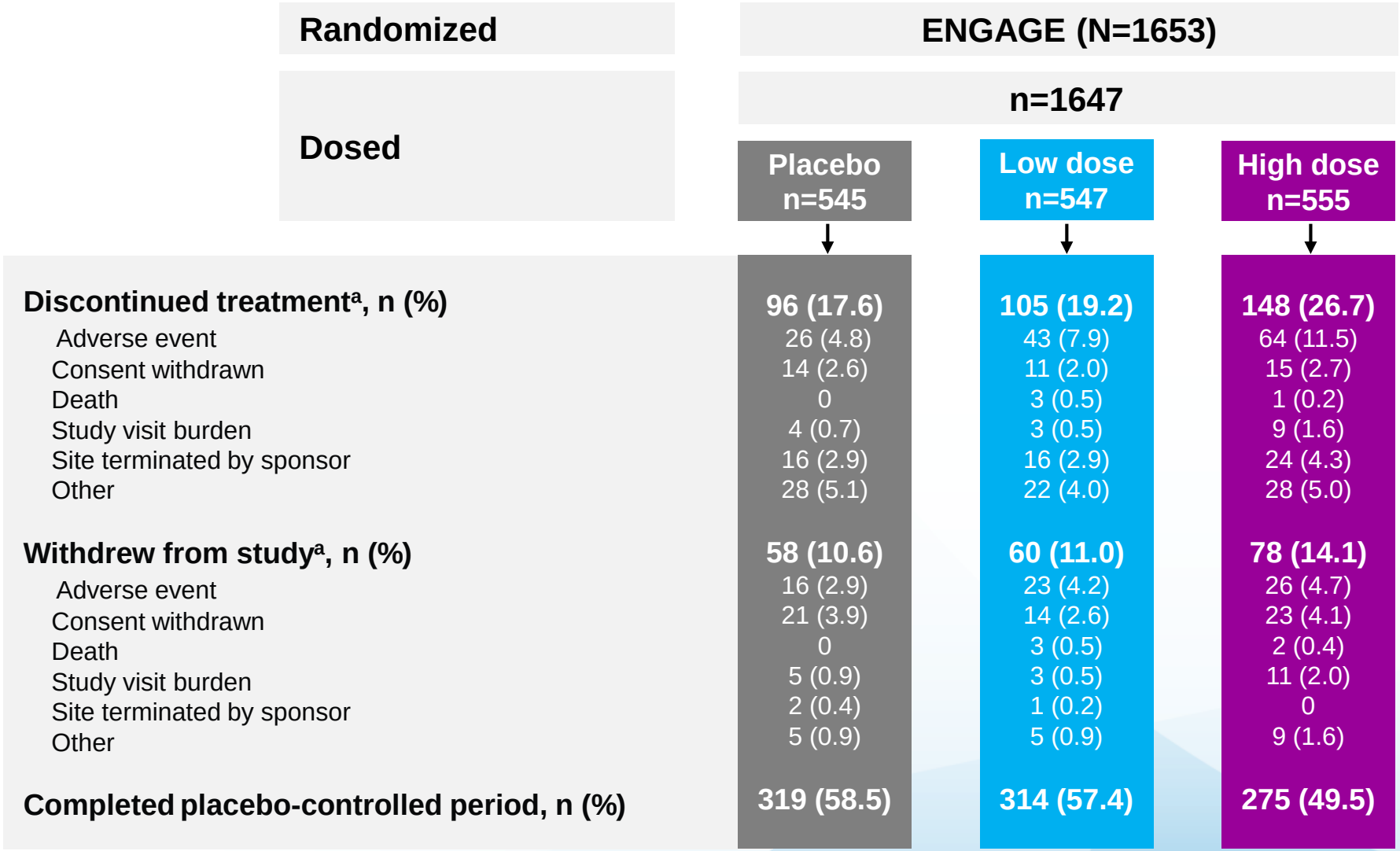
ApoE, apolipoprotein E; MCI, mild cognitive impairment; ITT, intent to treat; PET, positron-emission tomography; SD, standard deviation; SUVR, standardized uptake value ratio.

ENGAGE: Baseline disease characteristics

	ENGAGE		
	Placebo (n=545)	Low dose (n=547)	High dose (n=555)
RBANS delayed memory score, mean ± SD	60.0±13.65	59.5±14.16	60.6±14.09
MMSE score, mean ± SD	26.4±1.73	26.4±1.78	26.4±1.77
CDR global score, n (%)			
0.5	544 (99.8)	546 (99.8)	554 (99.8)
1	1 (0.2)	1 (0.2)	0
CDR-SB score, mean ± SD	2.40±1.012	2.43±1.014	2.40±1.009
ADAS-Cog 13 score, mean ± SD	22.5±6.56	22.5±6.30	22.4±6.54
ADCS-ADL-MCI score, mean ± SD	43.0±5.55	42.9±5.73	42.9±5.70

ITT population.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; RBANS, Repeatable Battery for Assessment of Neuropsychological Status.

ENGAGE: Patient disposition



ITT population. [a]Some categories with less than 1% patients are not displayed, including lost to follow-up, disease progression, pregnancy, investigator decision, relocation, change of treatment, withdrawal by parent/guardian, protocol amendment, site terminated by investigator and loss of capacity.
ITT, intent to treat.

ENGAGE: Primary and secondary endpoints from larger data set at Week 78

	Placebo decline (n=545)	Difference vs. placebo (%)[a] p-value[b]	
		Low dose (n=547)	High dose (n=555)
CDR-SB	1.55	**-0.18** (-12%) 0.2362	**0.03** (2%) 0.8252
MMSE	-3.5	**0.2** (-6%) 0.4875	**-0.1** (3%) 0.7961
ADAS-Cog 13	5.171	**-0.590** (-11%) 0.2475	**-0.605** (-12%) 0.2446
ADCS-ADL-MCI	-3.8	**0.7** (-18%) 0.1345	**0.7** (-18%) 0.1520

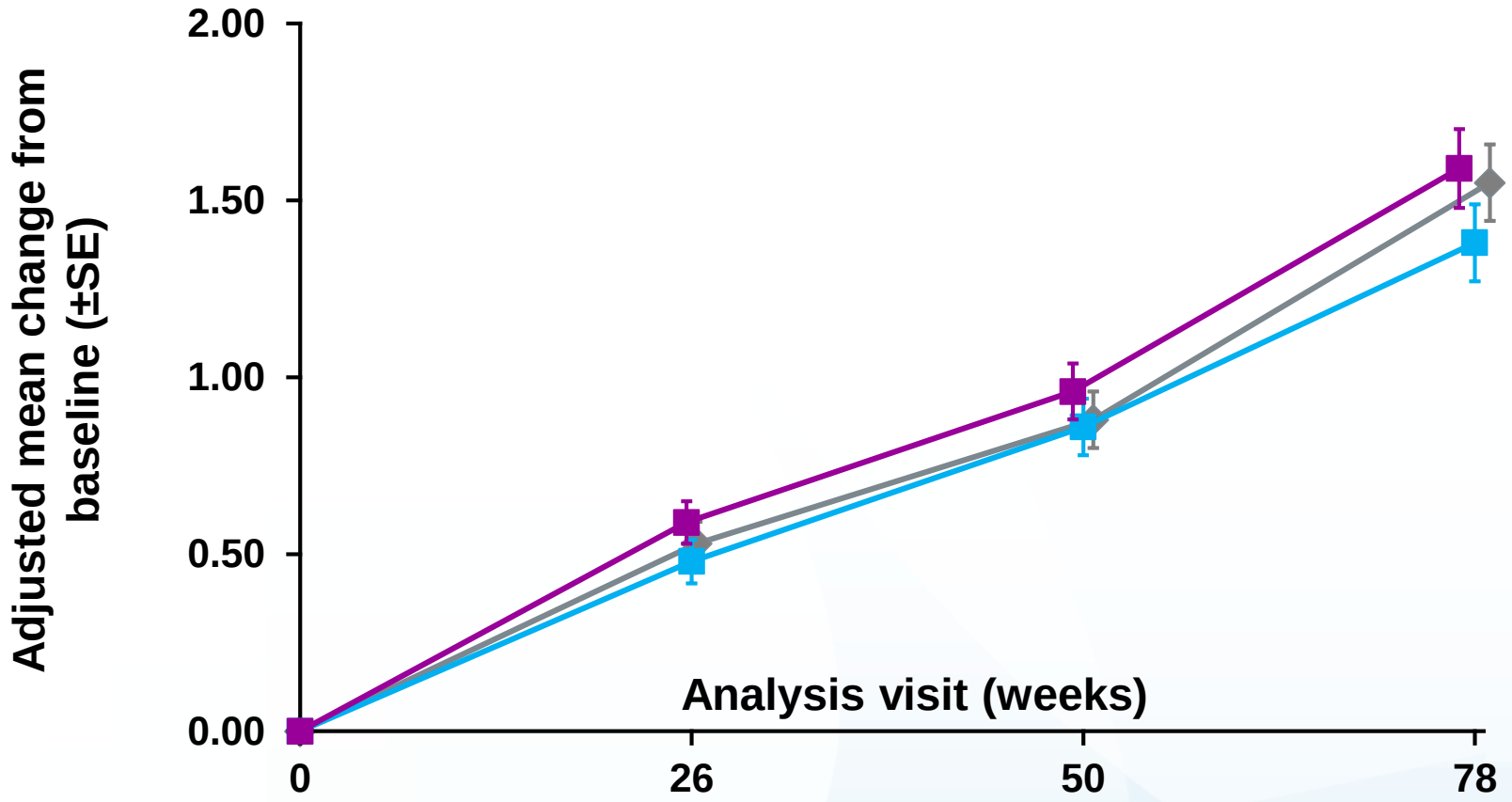
ITT population. [a]Difference vs placebo at Week 78. Negative percentage means less progression in the treated arm. [b]Nominal.
Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

ENGAGE: Primary and secondary endpoints from final data set at Week 78

	Placebo decline (n=545)	Difference vs. placebo (%)[a] p-value[b]	
		Low dose (n=547)	High dose (n=555)
CDR-SB	1.56	**-0.18** (-12%) 0.2250	**0.03** (2%) 0.8330
MMSE	-3.5	**0.2** (-6%) 0.4795	**-0.1** (3%) 0.8106
ADAS-Cog 13	5.140	**-0.583** (-11%) 0.2536	**-0.588** (-11%) 0.2578
ADCS-ADL-MCI	-3.8	**0.7** (-18%) 0.1225	**0.7** (-18%) 0.1506

ITT population. [a]Difference vs placebo at Week 78. Negative percentage means less progression in the treated arm. [b]Nominal for MMSE, ADAS-Cog 13, and ADCS-ADL-MCI.
ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination.

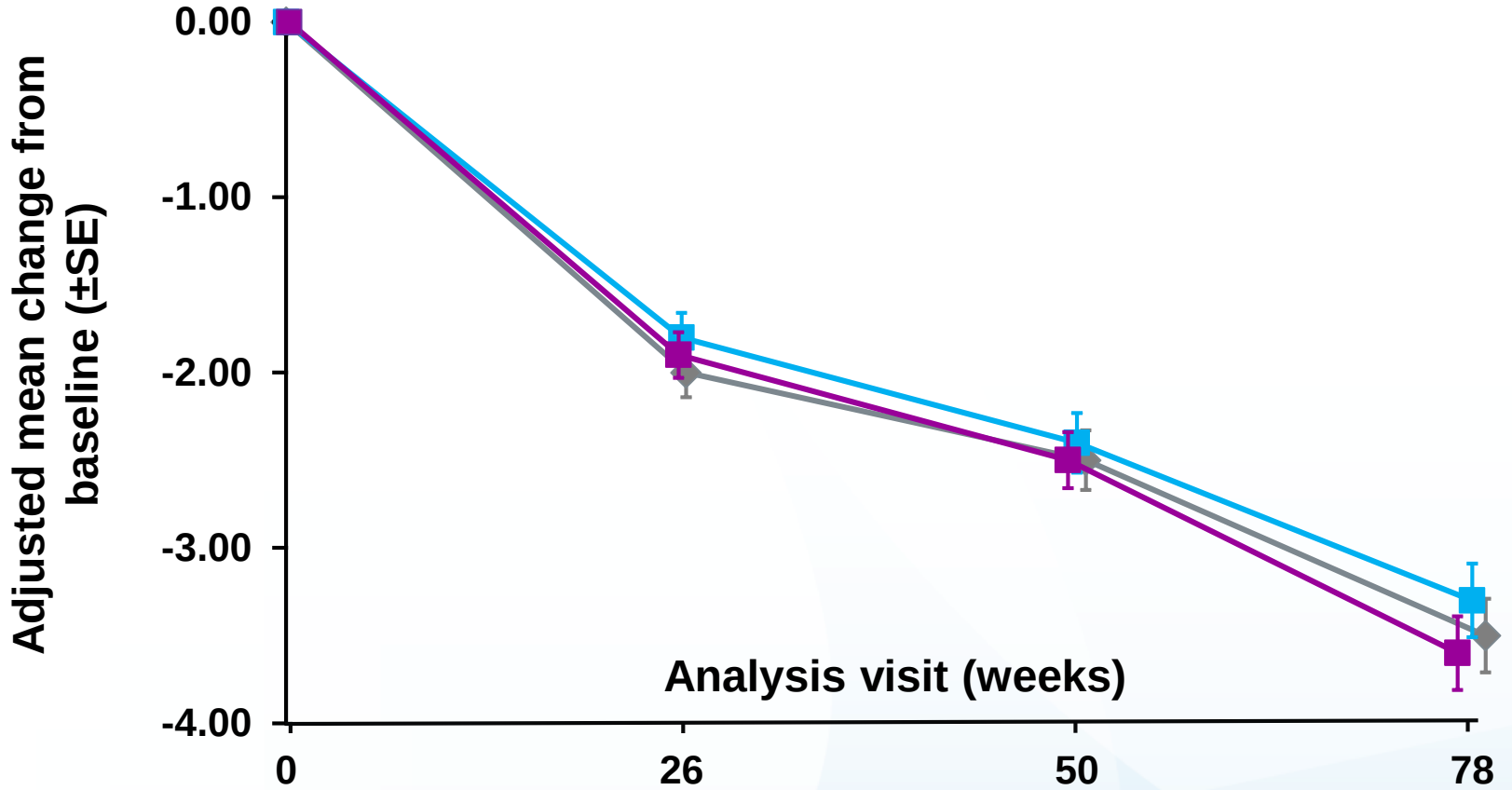
ENGAGE: Longitudinal change from baseline in CDR-SB



Placebo	n=545	522	455	333
Low dose aducanumab	n=547	529	454	331
High dose aducanumab	n=554	532	448	293

ITT population. Values at each time point were based on an MMRM model, with change from baseline in CDR-SB as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline CDR-SB, baseline CDR-SB by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status.
ApoE, apolipoprotein E; CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

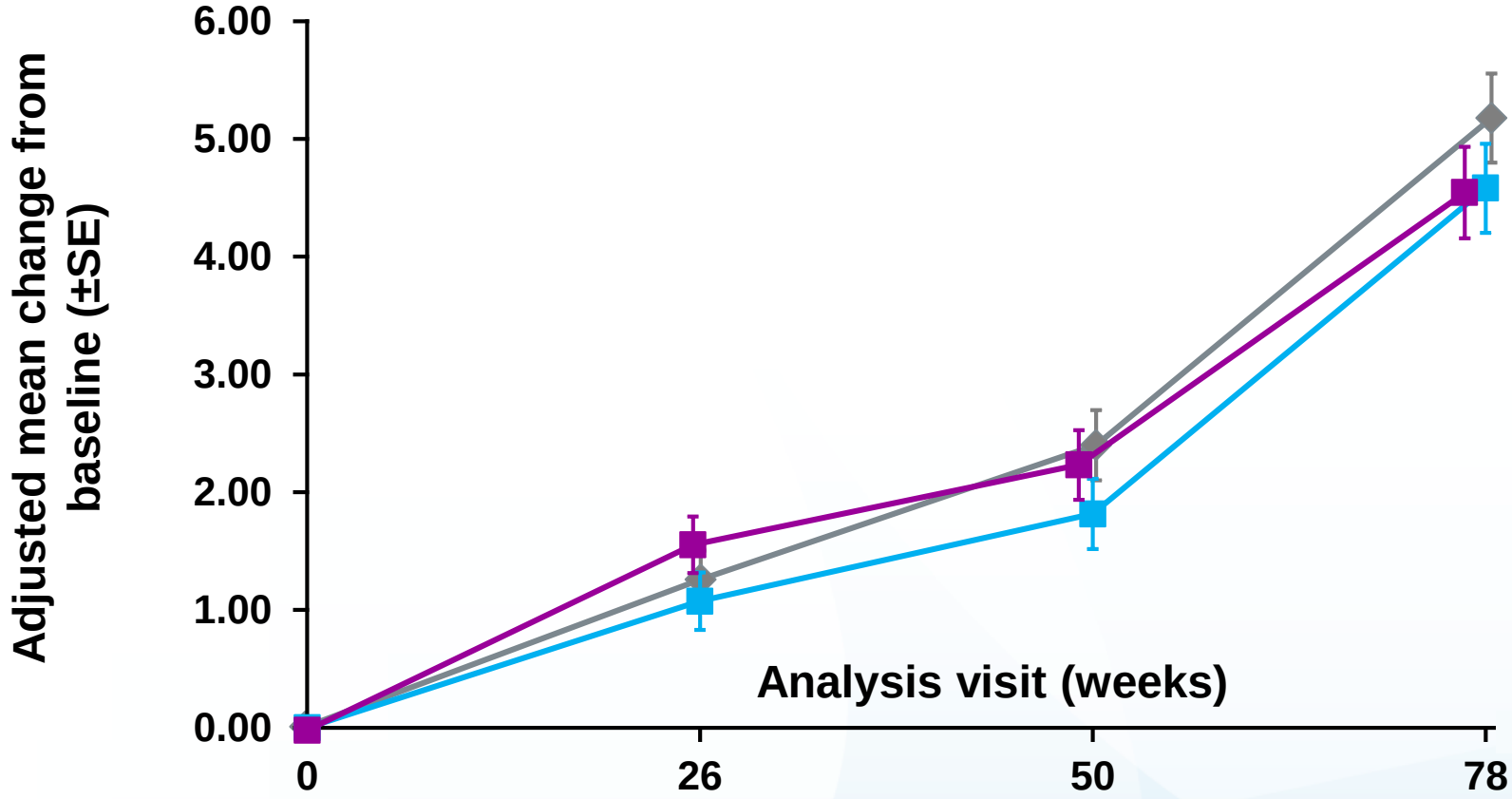
ENGAGE: Longitudinal change from baseline in MMSE



Placebo	n=545	525	457	332
Low dose aducanumab	n=547	532	457	334
High dose aducanumab	n=555	537	454	296

ITT population. Values at each time point were based on an MMRM model, with change from baseline in MMSE as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline MMSE, baseline MMSE by visit interaction, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status.
ApoE, apolipoprotein E; ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

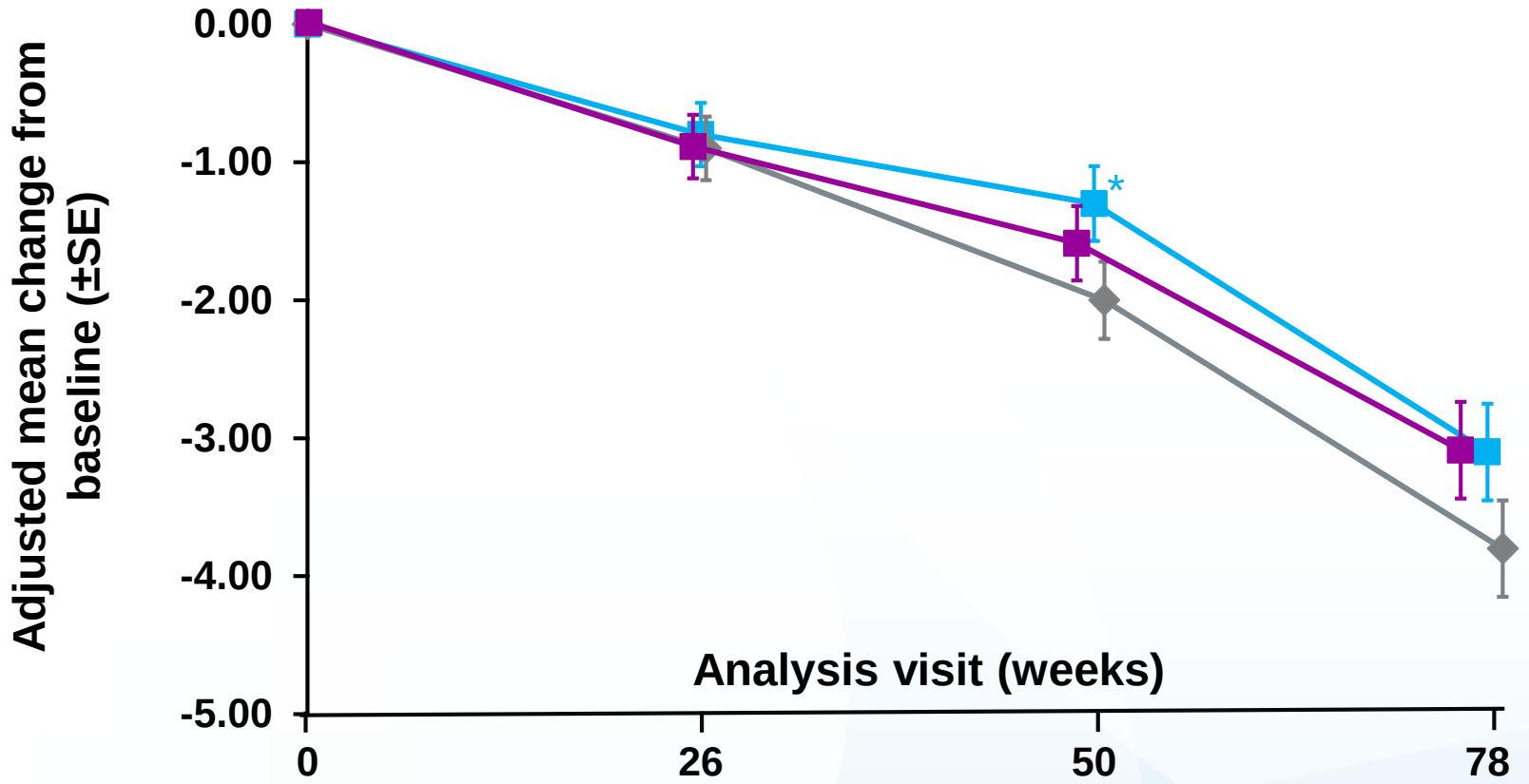
ENGAGE: Longitudinal change from baseline in ADAS-Cog 13



Placebo	n=542	521	454	331
Low dose aducanumab	n=547	531	457	333
High dose aducanumab	n=553	533	453	293

ITT population. Values at each time point were based on an MMRM model, with change from baseline in ADAS-Cog 13 as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADAS-Cog 13, baseline ADAS-Cog 13 by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; ADAS-Cog 13, Alzheimer's Disease Assessment Scale–Cognitive Subscale (13-item); ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

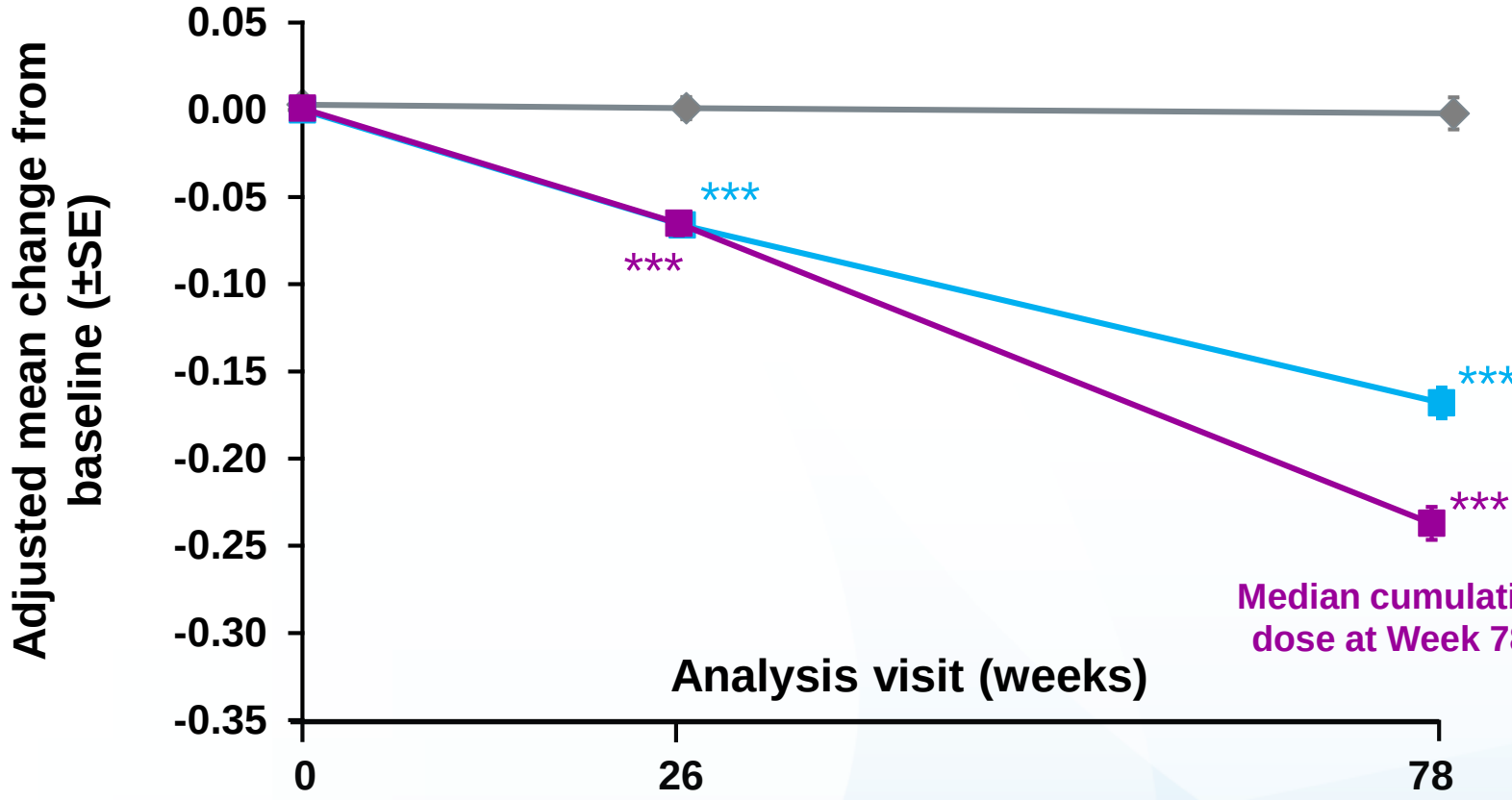
ENGAGE: Longitudinal change from baseline in ADCS-ADL-MCI



Placebo	n=541	517	451	331
Low dose aducanumab	n=546	530	455	330
High dose aducanumab	n=553	532	450	298

ITT population. *p <0.05 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in ADCS-ADL-MCI as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADCS-ADL-MCI, baseline ADCS-ADL-MCI by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; ADCS-ADL-MCI, Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory (mild cognitive impairment version); ITT, intent to treat; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; SE, standard error.

ENGAGE: Longitudinal change from baseline in amyloid PET SUVR



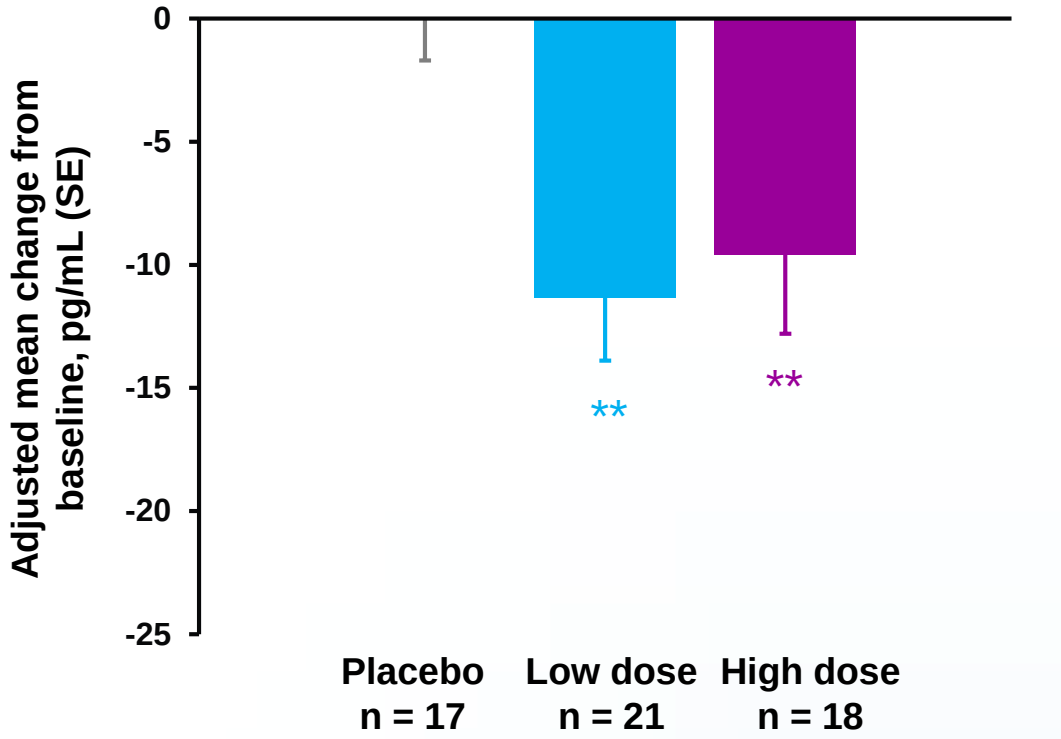
	ENGAGE	EMERGE
Placebo	-0.005	0.019
Low dose aducanumab	-0.168	-0.165
High dose aducanumab	-0.238	-0.272
Median cumulative dose at Week 78[a]	126 mg/kg	140 mg/kg

Placebo	n=203	164	104
Low dose aducanumab	n=198	166	116
High dose aducanumab	n=181	149	97

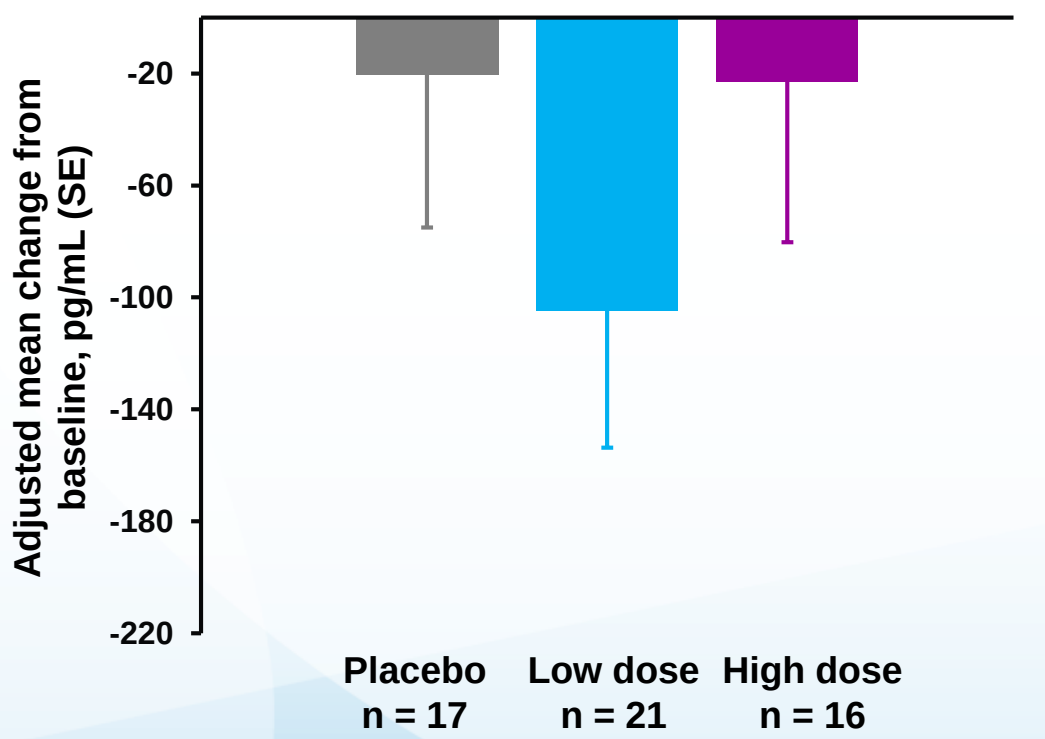
[a]Calculated from patients with Week 78 PET assessment.[18]F-florbetapir amyloid PET analysis population. ***p <0.0001 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in MMSE as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline SUVR, baseline SUVR by visit interaction, baseline MMSE, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. ApoE, apolipoprotein E; MMRM, mixed model for repeated measure; MMSE, Mini Mental State Examination; PET, positron emission tomography; SE, standard error; SUVR, standardized uptake value ratio.

ENGAGE: CSF biomarkers of tau pathology and neurodegeneration

CSF p-tau



CSF total tau

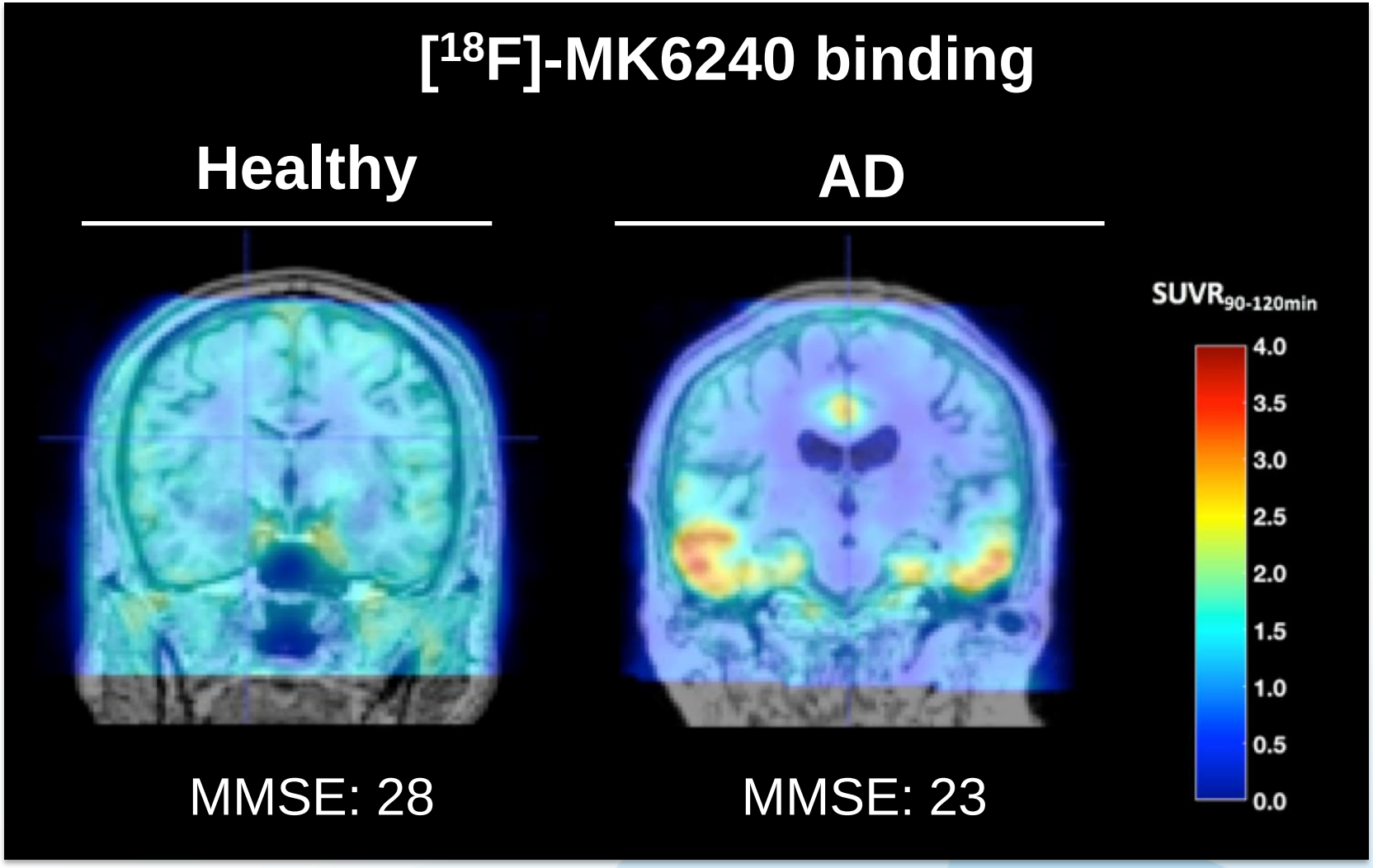


CSF modified analysis population (patients with both baseline and post-baseline CSF assessments). **p<0.01 compared with placebo (nominal). Values were based on an ANCOVA model at Week 78, fitted with change from baseline as the dependent variable, and with categorical treatment, baseline biomarker value, baseline age, and laboratory ApoE ε4 status (carrier and non-carrier) as the independent variables. ANCOVA, analysis of covariance; ApoE, apolipoprotein E; CSF, cerebrospinal fluid; SE, standard error.

Phase 3 Results

Tau PET data

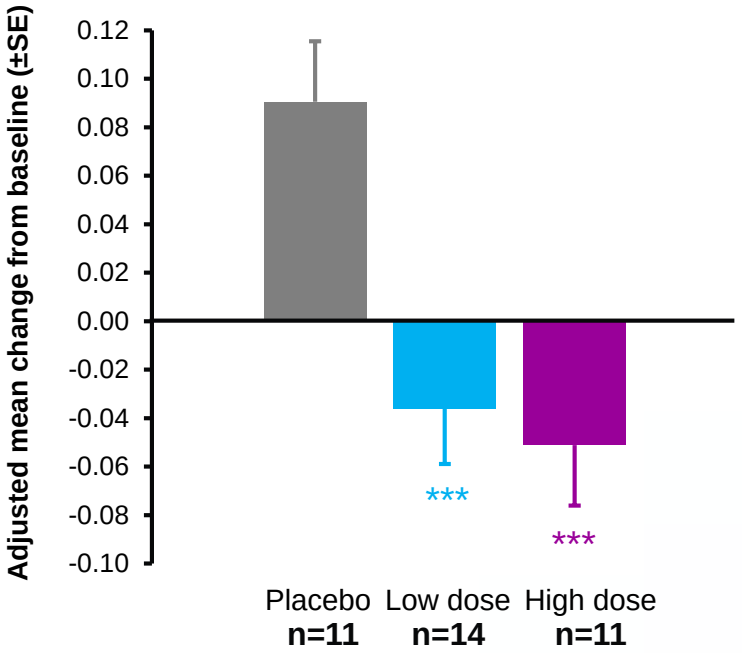
[18F]-MK6240 was used as the tau PET ligand



Salinas C, et al. Data presented at HAI 2017.
AD, Alzheimer's disease; MMSE, Mini-Mental State Examination; PET, positron emission tomography; SUVR, standardized uptake value ratio.

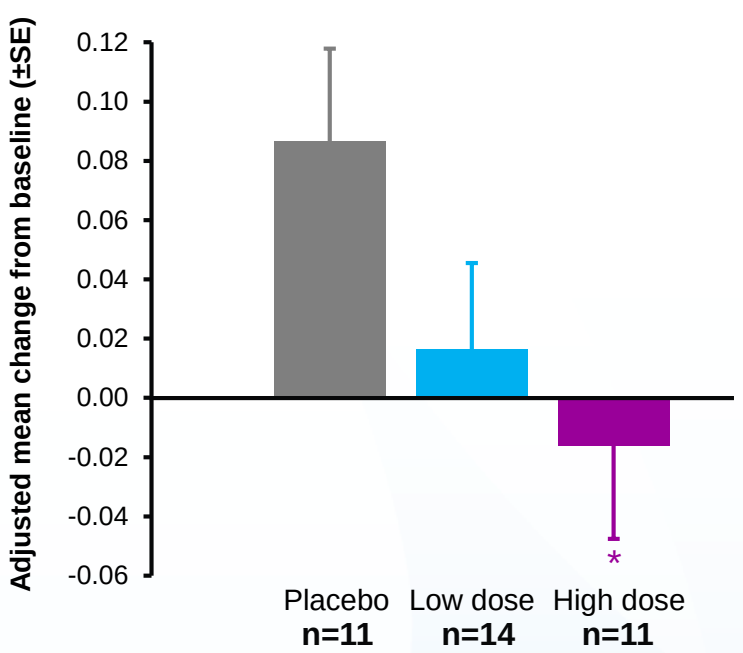
EMERGE and ENGAGE: Composite SUVR change from baseline

Medial temporal composite



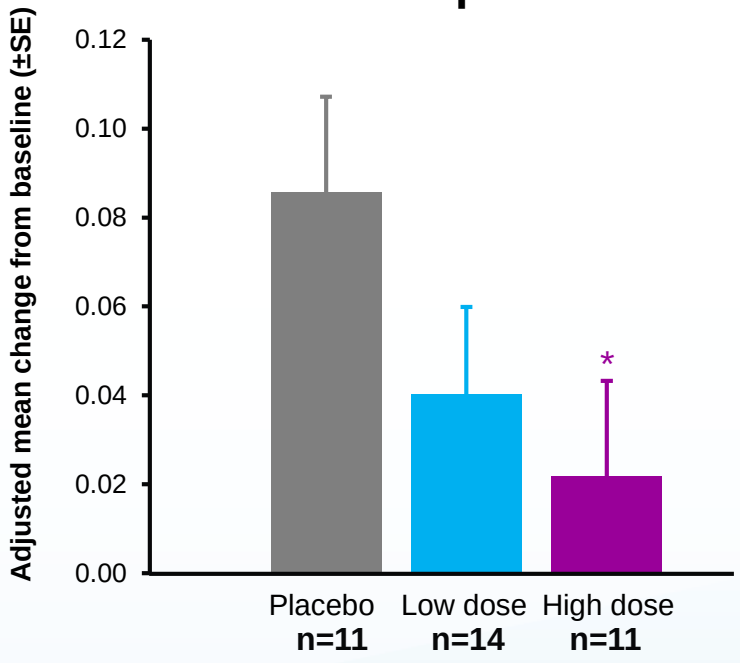
HIPPOCAMPUS
PARAHIPPOCAMPAL
TEMPORAL LOBE ANTERIOR MEDIAL
(includes Entorhinal and Amygdala)
TEMPORAL LOBE ANTERIOR LATERAL

Temporal composite



TEMPORAL LOBE Comprised of:
SUPERIOR, POSTERIOR, MIDDLE INFERIOR
POSTERIOR, SUPERIOR ANTERIOR,
FUSIFORM GYRUS

Frontal composite

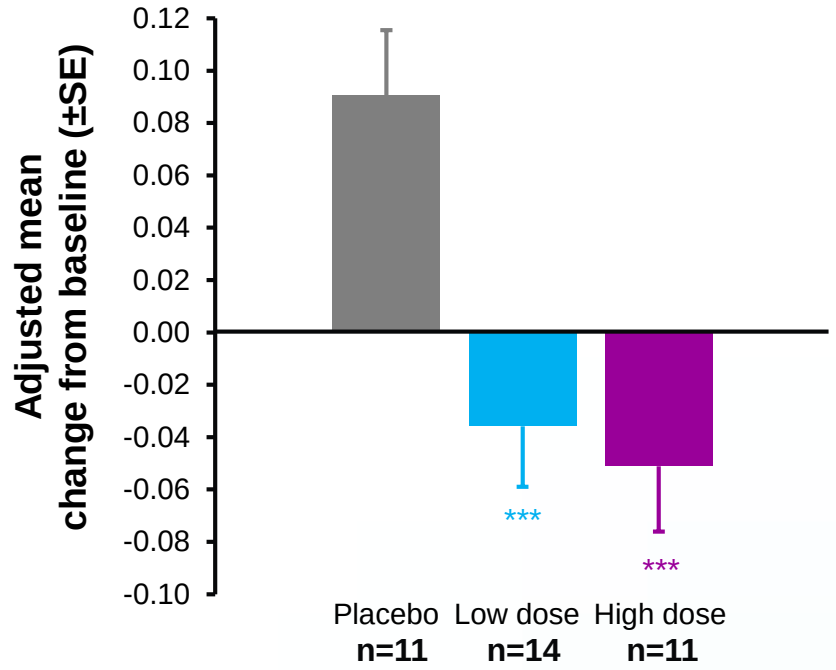


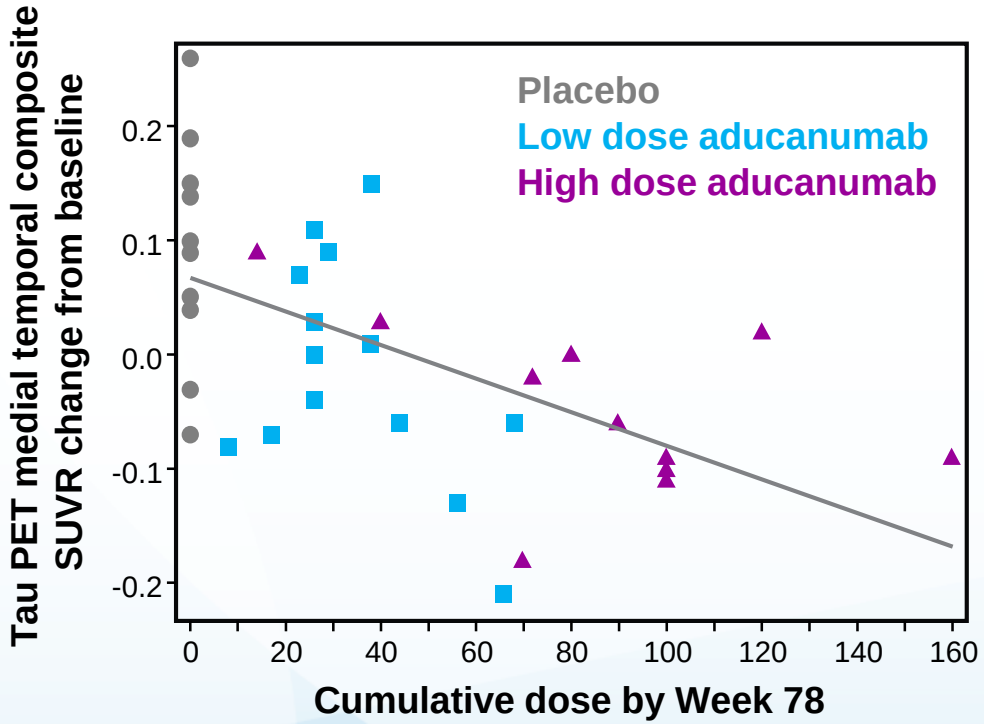
FRONTAL LOBE Comprised of:
MIDDLE, PRECENTRAL, STRAIGHT GYRUS
INFERIOR, SUPERIOR
ORBITOFRONTAL CORTEX Comprised of:
ANTERIOR, MEDIAL, LATERAL, POSTERIOR

Tau PET modified analysis population (patients with both baseline and post-baseline tau PET assessments). *P <0.05, ***P<0.001 compared with placebo (nominal). Values based on an ANCOVA model, fitted with change from baseline as dependent variable, and with categorical treatment, baseline tau PET value and laboratory ApoE ε4 status (carrier and non-carrier) as independent variables. Due to the early termination of the studies, all the post-baseline tau PET assessments were performed within a range of 9 to 20 months post-baseline in the placebo-controlled period.
ANCOVA, analysis of covariance; PET, positron emission tomography; SUVR, standardized uptake value ratio.

Tau deposition in the medial temporal composite

Change from baseline correlation to cumulative dose



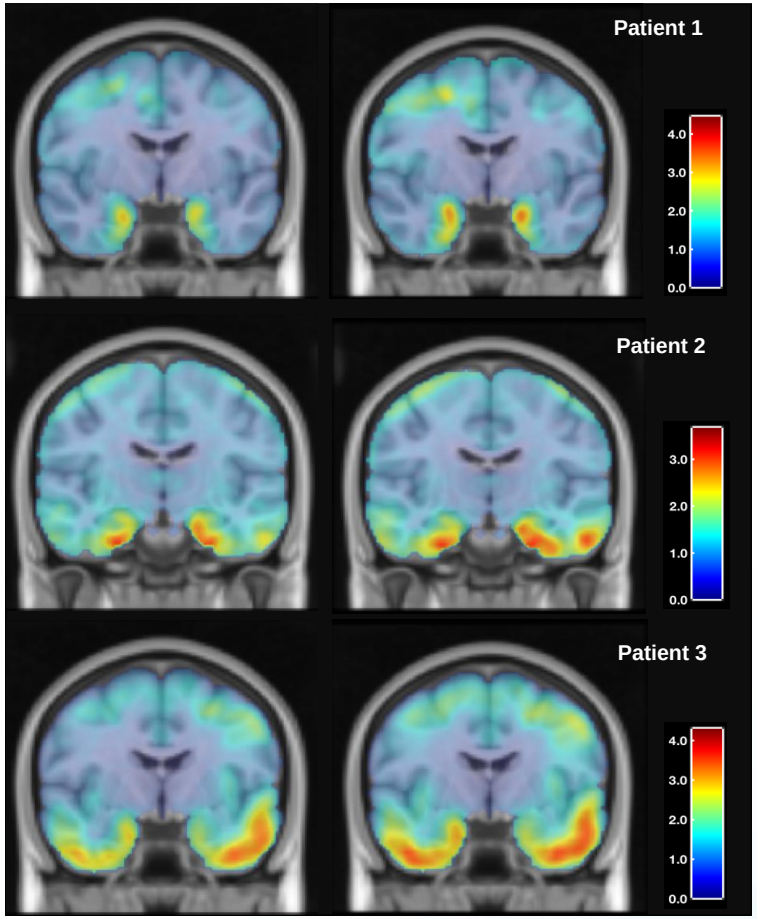


Tau PET modified analysis population (patients with both baseline and post-baseline tau PET assessments). ***P<0.001 compared with placebo (nominal). Values on left graph based on an ANCOVA model, fitted with change from baseline as dependent variable, and with categorical treatment, baseline tau PET value and laboratory ApoE ε4 status (carrier and non-carrier) as independent variables. Due to the early termination of the studies, all the post-baseline tau PET assessments were performed within a range of 9 to 20 months post-baseline in the placebo-controlled period.
ANCOVA, analysis of covariance; PET, positron emission tomography; SUVR, standardized uptake value ratio.

Tau deposition in representative patients

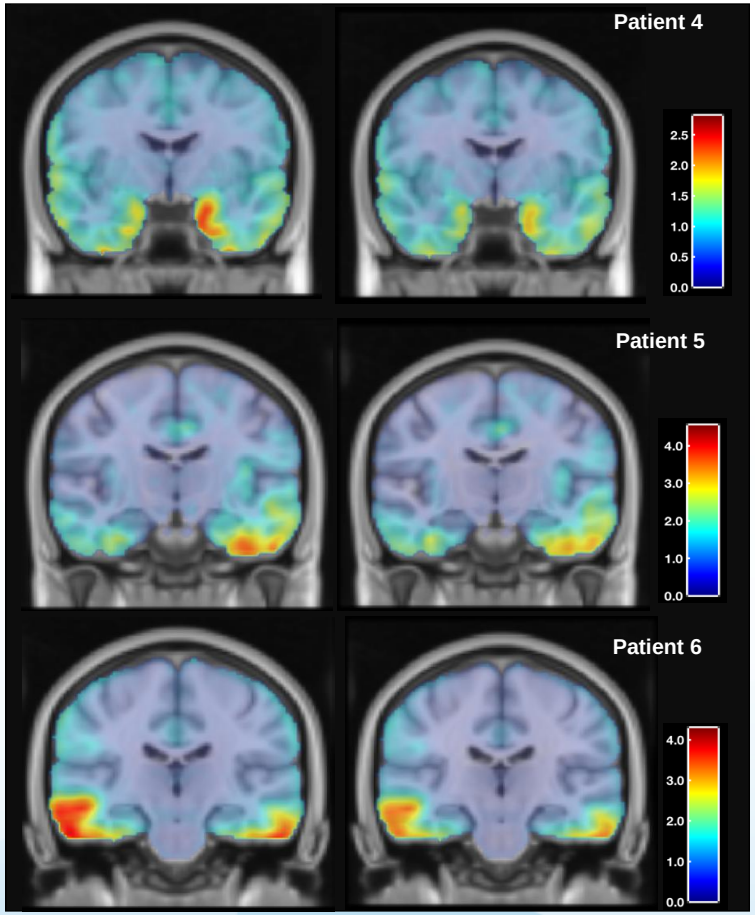
Placebo

Baseline Follow-up



Aducanumab (10 mg/kg)

Baseline Follow-up



Representative images from 3 patients in placebo group and 3 patients in aducanumab high dose group.

Phase 3 Results

Safety

EMERGE and ENGAGE: Safety summary

	EMERGE			ENGAGE		
	Placebo (n=547)	Low dose (n=544)	High dose (n=547)	Placebo (n=541)	Low dose (n=548)	High dose (n=558)
Patients with an AE, n (%)	**476** (87.0)	**477** (87.7)	**505** (92.3)	**465** (86.0)	**491** (89.6)	**500** (89.6)
Patients with an SAE, n (%)	**77** (14.1)	**69** (12.7)	**66** (12.1)	**69** (12.8)	**71** (13.0)	**71** (12.7)
Patients permanently discontinuing treatment due to AE, n (%)	**16** (2.9)	**42** (7.7)	**48** (8.8)	**28** (5.2)	**45** (8.2)	**64** (11.5)
Patients permanently discontinuing treatment due to ARIA, n (%)	**1** (0.2)	**25** (4.6)	**36** (6.6)	**6** (1.1)	**27** (4.9)	**41** (7.3)
Number of all-cause deaths, n (%)	**5** (0.9)	**0**	**6** (1.1)	**0**	**3** (0.5)	**2** (0.4)

Safety analyses presented were based on the larger dataset and are ongoing.

Safety population. Patients randomized to placebo who accidentally received active dose are summarized under active groups (4 in ENGAGE and 1 in EMERGE).
All safety data presented are from the placebo-controlled period.
AE, adverse event; ARIA, amyloid-related imaging abnormalities; SAE, serious adverse event.

EMERGE and ENGAGE: Adverse events with incidence >10%

	EMERGE			ENGAGE		
	Placebo (n=547)	Low dose (n=544)	High dose (n=547)	Placebo (n=541)	Low dose (n=548)	High dose (n=558)
Patients with any event, n (%)	**476** (87.0)	**477** (87.7)	**505** (92.3)	**465** (86.0)	**491** (89.6)	**500** (89.6)
ARIA-E (%)	**12** (2.2)	**140** (25.7)	**186** (34.0)	**16** (3.0)	**139** (25.4)	**198** (35.5)
Headache (%)	**83** (15.2)	**106** (19.5)	**106** (19.4)	**81** (15.0)	**98** (17.9)	**114** (20.4)
ARIA-H, microhemorrhage (%)	**38** (6.9)	**88** (16.2)	**102** (18.6)	**31** (5.7)	**85** (15.5)	**98** (17.6)
Nasopharyngitis (%)	**90** (16.5)	**70** (12.9)	**87** (15.9)	**67** (12.4)	**64** (11.7)	**66** (11.8)
ARIA-H, superficial siderosis (%)	**14** (2.6)	**50** (9.2)	**73** (13.3)	**10** (1.8)	**48** (8.8)	**86** (15.4)
Fall (%)	**68** (12.4)	**64** (11.8)	**69** (12.6)	**55** (10.2)	**77** (14.1)	**83** (14.9)

This table includes patients who received at least one dose of investigational treatment.

Safety population. Patients randomized to placebo who accidentally received active dose are summarized under active groups (4 in ENGAGE and 1 in EMERGE).
All safety data presented are from the placebo-controlled period.
ARIA-E, amyloid related imaging abnormality-edema/effusion; ARIA-H, amyloid related imaging abnormality-micro-hemorrhages and hemosiderin deposits.

EMERGE and ENGAGE: ARIA incidence

	EMERGE			ENGAGE		
	Placebo (n=544)	Low dose (n=537)	High dose (n=541)	Placebo (n=533)	Low dose (n=544)	High dose (n=554)
ARIA-E[a], n/total (%)	**12/544** (2.2)	**140/537** (26.1)	**186/541** (34.4)	**16/533** (3.0)	**139/544** (25.6)	**198/554** (35.7)
ApoE ε4 carriers	**7/371** (1.9)	**109/366** (29.8)	**154/362** (42.5)	**9/371** (2.4)	**112/390** (28.7)	**158/378** (41.8)
ApoE ε4 non-carriers	**5/173** (2.9)	**31/171** (18.1)	**32/179** (17.9)	**7/162** (4.3)	**27/154** (17.5)	**40/176** (22.7)
ARIA-H, microhemorrhage, n (%)	**38** (7.0)	**88** (16.4)	**102** (18.9)	**31** (5.8)	**85** (15.6)	**98** (17.7)
ARIA-H, superficial siderosis, n (%)	**14** (2.6)	**50** (9.3)	**73** (13.5)	**10** (1.9)	**48** (8.8)	**86** (15.5)
ARIA-H, macrohemorrhage, n (%)	**0**	**1** (0.2)	**3** (0.6)	**4** (0.8)	**0**	**3** (0.5)

This table includes patients who had at least one post-baseline safety MRI.

Safety MRI population (patients with at least one post-baseline MRI). [a]ARIA-E with or without ARIA-H.
All safety data presented are from the placebo-controlled period.
ARIA, amyloid-related imaging abnormalities; ARIA-E, amyloid-related imaging abnormalities due to vasogenic edema.

EMERGE and ENGAGE: ARIA incidence

	EMERGE			ENGAGE		
	Placebo (n=544)	Low dose (n=537)	High dose (n=541)	Placebo (n=533)	Low dose (n=544)	High dose (n=554)
Any ARIA (either E or H), n (%)	**56** (10.3)	**176** (32.8)	**223** (41.2)	**52** (9.8)	**167** (30.7)	**223** (40.3)
Symptomatic status, n (%)	**56**	**176**	**223**	**52**	**167**	**223**
Asymptomatic ARIA	**53** (94.6)	**138** (78.4)	**179** (80.3)	**49** (94.2)	**139** (83.2)	**158** (70.9)
Symptomatic ARIA	**3** (5.4)	**38** (21.6)	**44** (19.7)	**3** (5.8)	**28** (16.8)	**65** (29.1)

This table includes patients who had at least one post-baseline safety MRI.

- Symptoms reported in patients with ARIA included: headache, dizziness, visual disturbances, nausea and vomiting
- ARIA-E episodes generally resolved within 4-16 weeks
- The majority of patients who experienced ARIA were able to continue investigational treatment

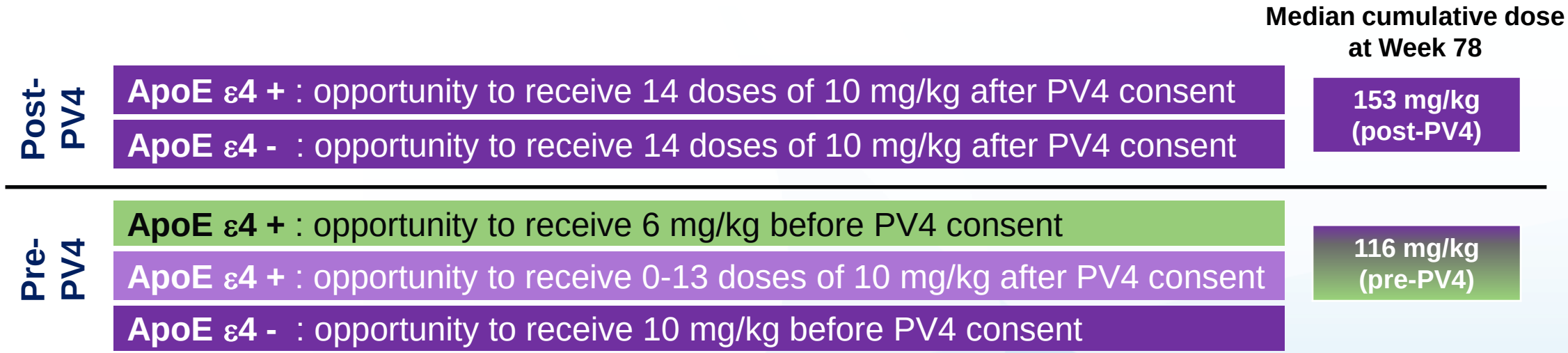
Safety MRI population (patients with at least one post-baseline MRI). All safety data presented are from the placebo-controlled period.
ARIA, amyloid-related imaging abnormalities; ARIA-E, amyloid-related imaging abnormalities due to vasogenic edema; ARIA-H, amyloid-related imaging abnormalities due to microhemorrhage, superficial siderosis or macrohemorrhage.

EMERGE and ENGAGE

Defining a population by Protocol Version 4 (PV4)

Patients selected using the cutoff related to PV4:

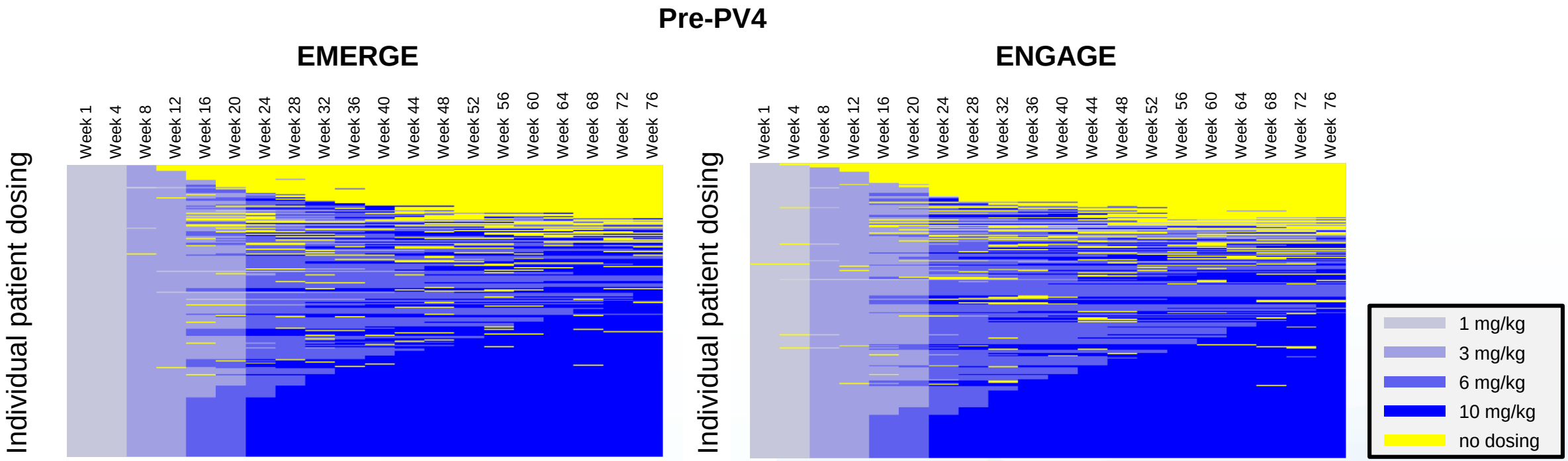
(1) To assess the treatment effect under the intended dosing regimen and ARIA management
(2) To assess the treatment effect among a representative population (i.e., ApoE ε4 carriers consist of ~2/3 of the population in AD)
(3) To preserve the randomization



ApoE, apolipoprotein E; PV4, Protocol Version 4.

EMERGE and ENGAGE: Individual-level dosing in high dose regimen

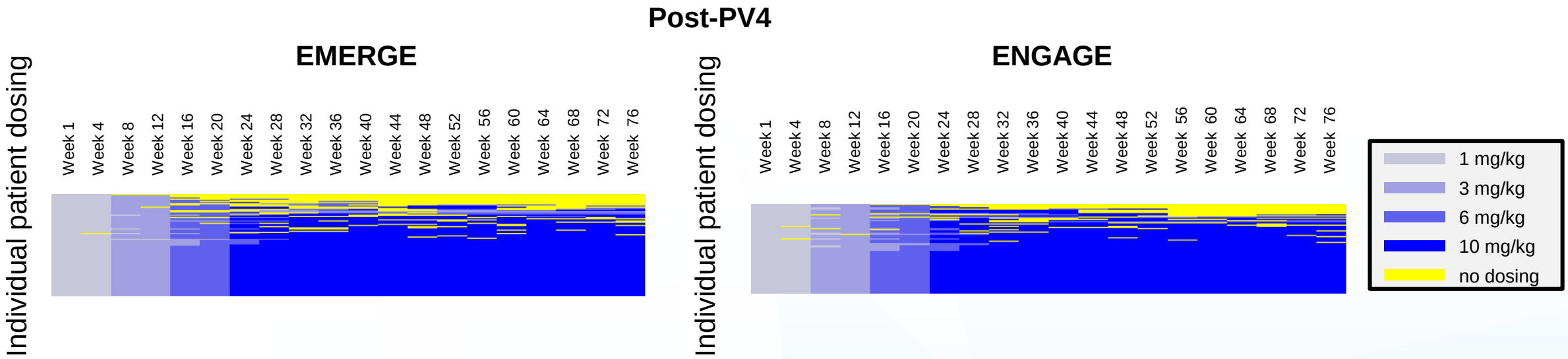
For pre-PV4 patients, 21% in EMERGE and 15% in ENGAGE received the full possible 14 doses of 10 mg/kg



OTC population. Patients who had the opportunity to complete Week 78 visit by March 20, 2019.
OTC, opportunity to complete; PV4, Protocol, Version 4.

EMERGE and ENGAGE: Individual-level dosing in the high dose regimen post-Protocol Version 4

For post-PV4 patients, 51% in EMERGE and 47% in ENGAGE received the full possible 14 doses of 10 mg/kg



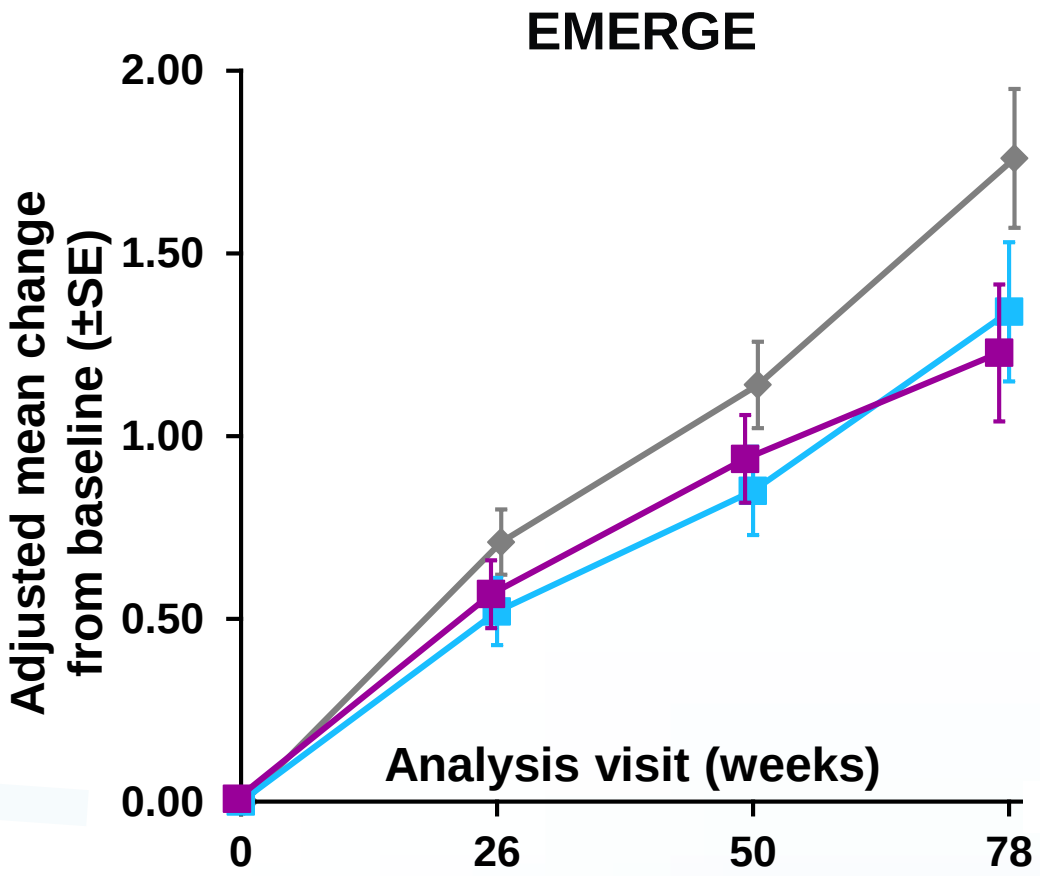
OTC population. Patients who had the opportunity to complete Week 78 visit by March 20, 2019.
OTC, opportunity to complete; PV4, Protocol, Version 4.

CDR-SB for ITT population compared with Post-PV4 population for EMERGE and ENGAGE at Week 78

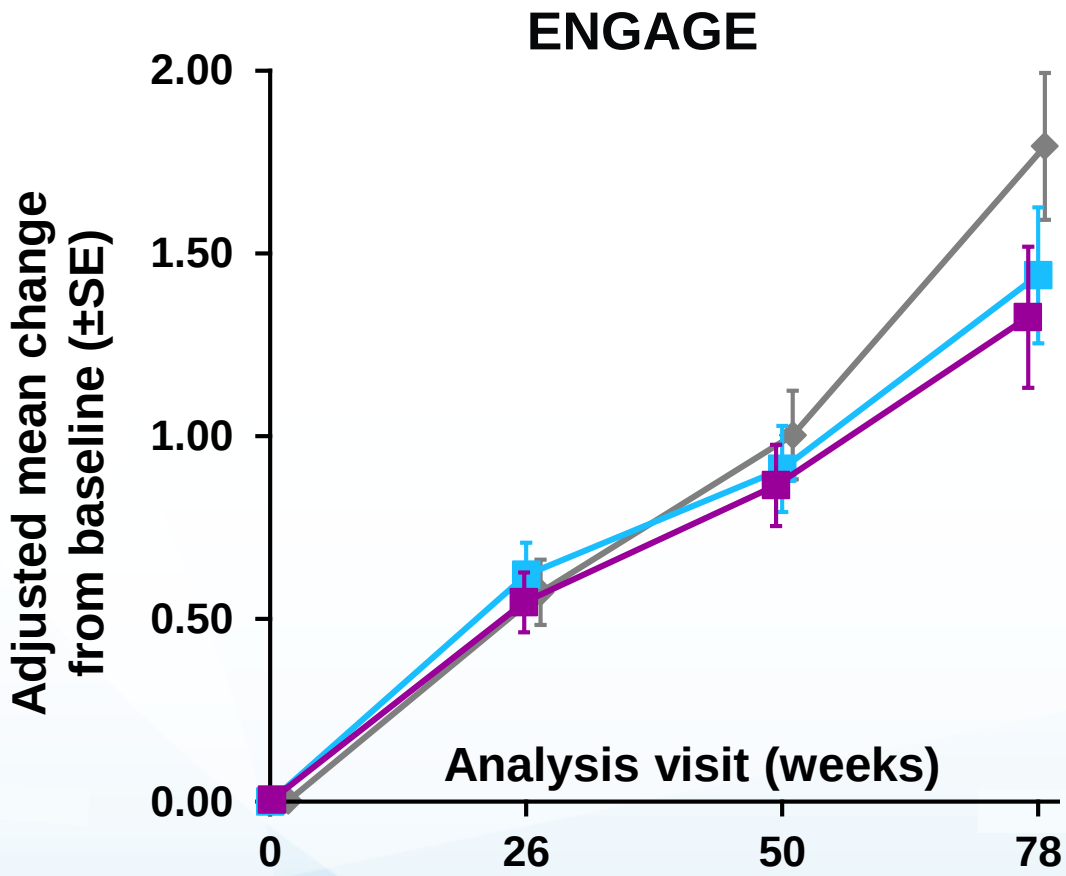
	ITT			Post-PV4[a,b]		
EMERGE	**Placebo decline (n=548)**	**Low dose (n=543)** diff vs. placebo, 95% CI (%)[c]	**High dose (n=547)** diff vs. placebo 95% CI (%)[c]	**Placebo decline (n=304)**	**Low dose (n=295)** diff vs. placebo 95% CI (%)[c]	**High dose (n=288)** diff vs. placebo 95% CI (%)[c]
CDR-SB	1.74	**-0.25** -0.55, 0.06 (-14%)	**-0.40** -0.71, -0.10 (-23%)	1.76	**-0.42** -0.94, 0.10 (-24%)	**-0.53** -1.05, -0.02 (-30%)
ENGAGE	**Placebo decline (n=545)**	**Low dose (n=547)**	**High dose (n=555)**	**Placebo decline (n=247)**	**Low dose (n=261)**	**High dose (n=282)**
CDR-SB	1.55	**-0.18** -0.47, 0.12 (-12%)	**0.03** -0.26, 0.33 (2%)	1.79	**-0.35** -0.88, 0.18 (-20%)	**-0.48** -1.02, 0.06 (-27%)

[a]MMRM model was fitted separately for pre- and post-Protocol Version 4 set; [b]Patients who consented to PV4 or higher version prior to Week 16 in ITT population; [c]Difference vs placebo at Week 78. Negative percentage means less progression in the treated arm; N denotes the number of all randomized and dosed patients that were included in the ITT analysis.
CDR-SB, Clinical Dementia Rating–Sum of Boxes; ITT, intent to treat.

Post PV4[a,b]: Longitudinal change from baseline in CDR-SB



Placebo	n=303	293	198	74
Low dose aducanumab	n=295	280	197	76
High dose aducanumab	n=288	271	200	80



Placebo	n=247	236	174	66
Low dose aducanumab	n=261	251	185	82
High dose aducanumab	n=282	276	204	69

[a]MMRM model was fitted separately for pre- and post-Protocol Version 4 set; [b]Patients who consented to PV4 or higher version prior to Week 16 in ITT population.
CDR-SB, Clinical Dementia Rating–Sum of Boxes; PV4, Protocol Version 4; SE, standard error.

Summary of aducanumab Phase 3 topline results

Following study termination based on futility, analysis of a larger dataset showed:

- In EMERGE, high dose aducanumab reduced clinical decline as measured by primary and secondary endpoints
- In ENGAGE, aducanumab did not reduce clinical decline
  - In a post hoc analysis, data from a subset of patients exposed to high dose aducanumab support the positive findings of EMERGE
- In sub-studies, aducanumab showed an effect on disease related biomarkers
- The most common AEs were ARIA-E and headache
- We are finalizing the details of a re-dosing study with the aim to offer access to aducanumab to eligible patients previously enrolled in the aducanumab clinical studies

AE, adverse event; ARIA, amyloid-related imaging abnormalities; ARIA-E, amyloid-related imaging abnormalities due to vasogenic edema.

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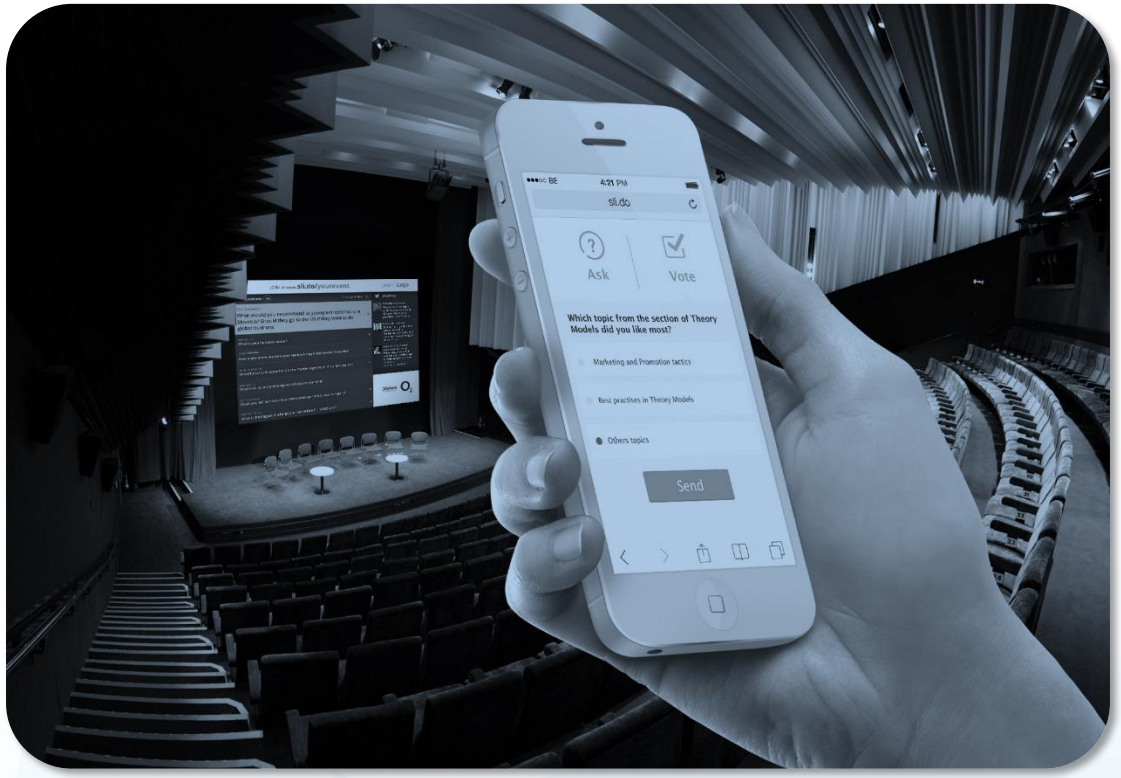

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