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

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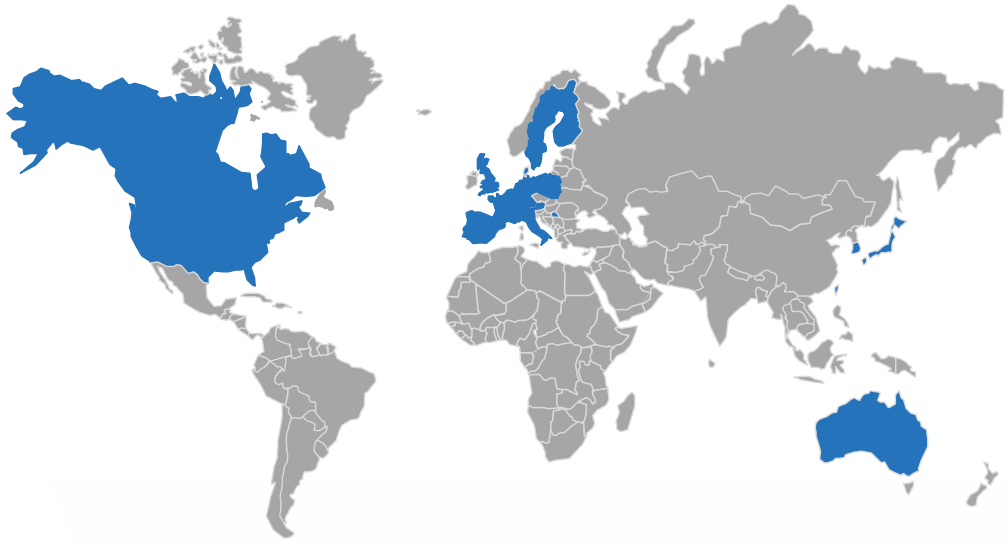
Aducanumab Phase 3 studies EMERGE and ENGAGE

Studies	Two identical,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

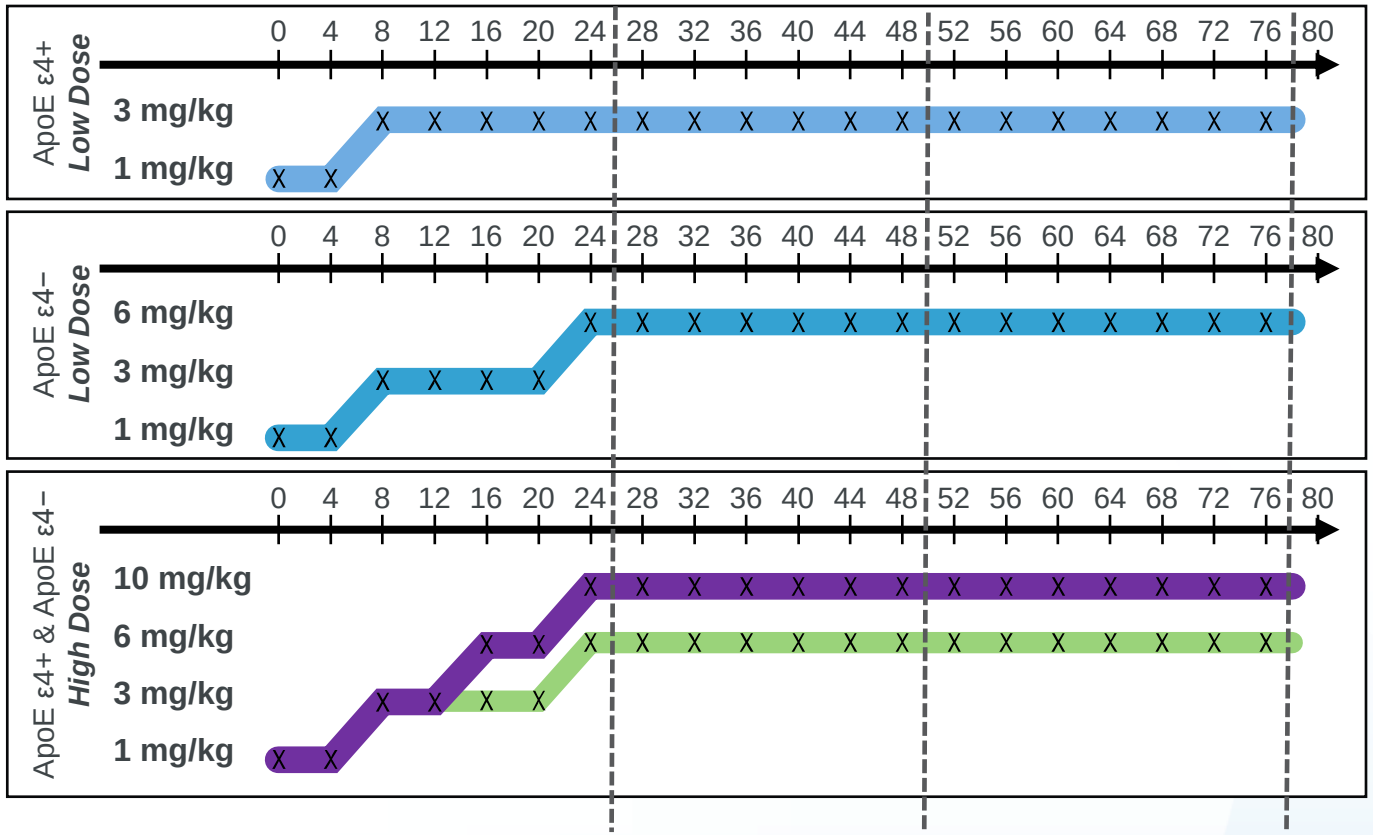


Countries with active sites included:
Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Italy, Japan, the Netherlands, Poland, Portugal, South Korea, Spain, Sweden, Switzerland, Taiwan, United Kingdom, United States

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

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



Expected # of 10 mg/kg in high dose group

***by Week 26*: 1 dose**

***by Week 50*: 7 doses**

***by Week 78*: 14 doses**

Median <u>cumulative</u> dose at Week 78

56 mg/kg

98 mg/kg

116 mg/kg (pre-PV4)

153 mg/kg (post-PV4)

<u>Low dose</u>

- **Titrated to 3 or 6 mg/kg**
- **Maintained throughout study**

<u>High dose</u>

- **Titrated to 6 or 10 mg/kg in Protocol Versions 1-3**
- **Titrated to 10 mg/kg in Protocol Version 4 and higher**

ApoE, apolipoprotein E; PV3, Protocol Version 3; PV4, Protocol Version 4.

EMERGE and ENGAGE Topline Results

Baseline demographics

	EMERGE			ENGAGE		
	Placebo (n=548)	Low dose (n=543)	High dose (n=547)	Placebo (n=545)	Low dose (n=547)	High dose (n=555)
Age in years, mean ± SD	70.8±7.40	70.6±7.45	70.6±7.47	69.8±7.72	70.4±6.96	70.0±7.65
Female, n (%)	290 (52.9)	269 (49.5)	284 (51.9)	287 (52.7)	284 (51.9)	292 (52.6)
Race, n (%) Asian White	 47 (8.6) 415 (75.7)	 38 (7.0) 418 (77.0)	 41 (7.5) 405 (74.0)	 55 (10.1) 413 (75.8)	 55 (10.1) 412 (75.3)	 65 (11.7) 413 (74.4)
Education years, mean ± SD	14.5±3.82	14.5±3.63	14.6±3.74	14.7±3.66	14.6±3.77	14.6±3.72
Alzheimer's disease medications used, n (%)	279 (50.9)	277 (51.0)	277 (50.6)	293 (53.8)	307 (56.1)	307 (55.3)
ApoE ε4, n (%) Carriers Non-carriers	 367 (67.0) 178 (32.5)	 362 (66.7) 178 (32.8)	 365 (66.7) 181 (33.1)	 376 (69.0) 167 (30.6)	 391 (71.5) 156 (28.5)	 378 (68.1) 176 (31.7)
Clinical stage, n (%) MCI due to Alzheimer's disease Mild Alzheimer's disease	 446 (81.4) 102 (18.6)	 452 (83.2) 91 (16.8)	 438 (80.1) 109 (19.9)	 443 (81.3) 102 (18.7)	 440 (80.4) 107 (19.6)	 442 (79.6) 113 (20.4)
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)	1.38±0.198 (203)	1.39±0.186 (198)	1.41±0.177 (181)

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.

Baseline disease characteristics

	EMERGE			ENGAGE		
	Placebo (n=548)	Low dose (n=543)	High dose (n=547)	Placebo (n=545)	Low dose (n=547)	High dose (n=555)
RBANS delayed memory score, mean ± SD	60.5±14.23	60.0±14.02	60.7±14.15	60.0±13.65	59.5±14.16	60.6±14.09
MMSE score, mean ± SD	26.4±1.78	26.3±1.72	26.3±1.68	26.4±1.73	26.4±1.78	26.4±1.77
CDR global score, n (%) 0.5 1	 544 (99.3) 3 (0.5)	 543 (100) 0	 546 (99.8) 1 (0.2)	 544 (99.8) 1 (0.2)	 546 (99.8) 1 (0.2)	 554 (99.8) 0
CDR-SB score, mean ± SD	2.47±0.999	2.46±1.011	2.51±1.053	2.40±1.012	2.43±1.014	2.40±1.009
ADAS-Cog 13 score, mean ± SD	21.9±6.73	22.5±6.76	22.2±7.08	22.5±6.56	22.5±6.30	22.4±6.54
ADCS-ADL-MCI score, mean ± SD	42.6±5.73	42.8±5.48	42.5±5.82	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.

Patient disposition

	EMERGE (N=1643)			ENGAGE (N=1653)		
Randomized						
Dosed	n=1638			n=1647		
	Placebo n=548	Low dose n=543	High dose n=547	Placebo n=545	Low dose n=547	High dose n=555
Discontinued treatment[a], n (%)	82 (15.0)	108 (19.9)	131 (23.9)	96 (17.6)	105 (19.2)	148 (26.7)
Adverse event	16 (2.9)	41 (7.6)	46 (8.4)	26 (4.8)	43 (7.9)	64 (11.5)
Consent withdrawn	6 (1.1)	22 (4.1)	18 (3.3)	14 (2.6)	11 (2.0)	15 (2.7)
Death	5 (0.9)	0	5 (0.9)	0	3 (0.5)	1 (0.2)
Study visit burden	2 (0.4)	7 (1.3)	5 (0.9)	4 (0.7)	3 (0.5)	9 (1.6)
Site terminated by sponsor	21 (3.8)	10 (1.8)	14 (2.6)	16 (2.9)	16 (2.9)	24 (4.3)
Other	23 (4.2)	23 (4.2)	28 (5.1)	28 (5.1)	22 (4.0)	28 (5.0)
Withdrew from study[a], n (%)	39 (7.1)	54 (9.9)	66 (12.1)	58 (10.6)	60 (11.0)	78 (14.1)
Adverse event	10 (1.8)	11 (2.0)	18 (3.3)	16 (2.9)	23 (4.2)	26 (4.7)
Consent withdrawn	8 (1.5)	28 (5.2)	22 (4.0)	21 (3.9)	14 (2.6)	23 (4.1)
Death	5 (0.9)	0	6 (1.1)	0	3 (0.5)	2 (0.4)
Study visit burden	2 (0.4)	7 (1.3)	5 (0.9)	5 (0.9)	3 (0.5)	11 (2.0)
Site terminated by sponsor	0	0	1 (0.2)	2 (0.4)	1 (0.2)	0
Other	3 (0.5)	4 (0.7)	3 (0.5)	5 (0.9)	5 (0.9)	9 (1.6)
Completed placebo-controlled period, n (%)	275 (50.2)	274 (50.5)	285 (52.1)	319 (58.5)	314 (57.4)	275 (49.5)

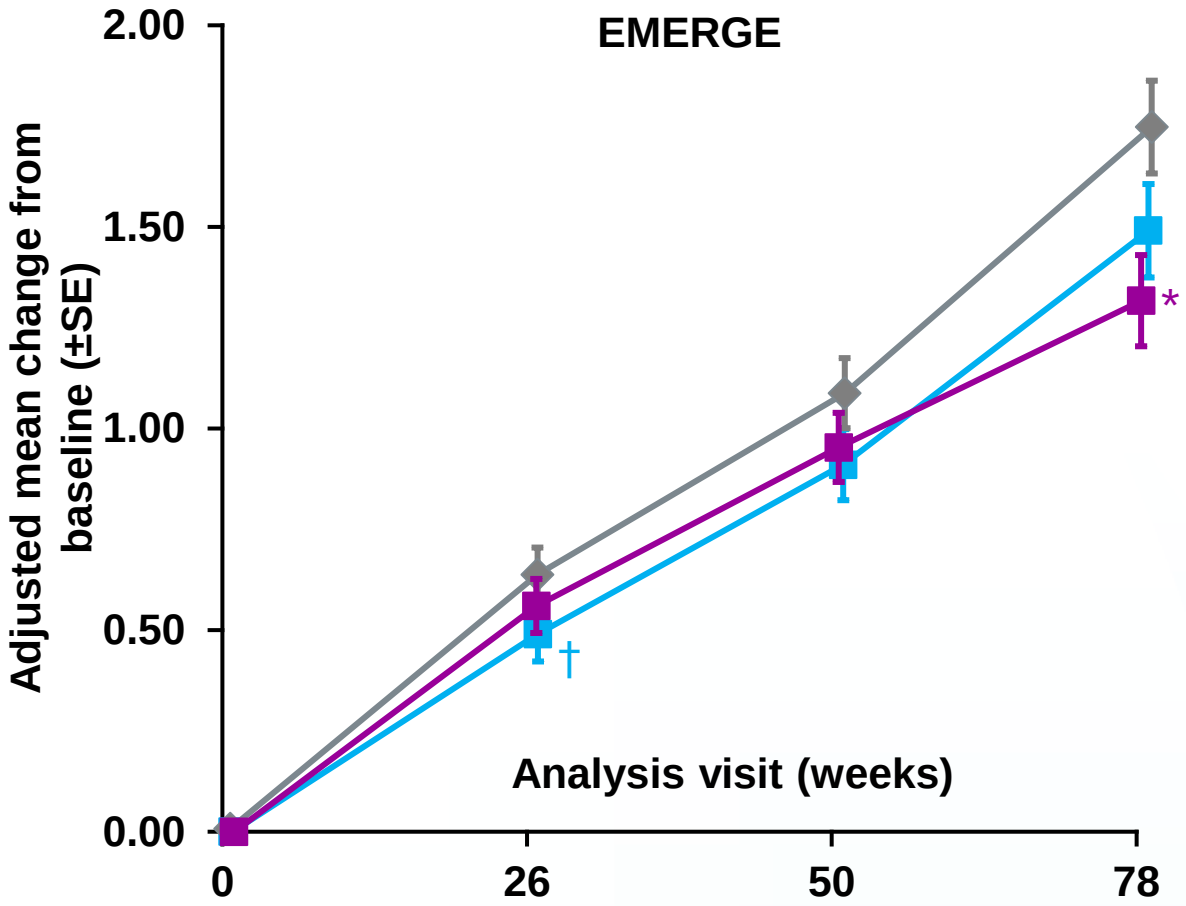
ITT population. [a]Some categories with less than 1% patients are not displayed, including lost to follow-up, disease progression, pregnancy, investigator decision, relocation, change of treatment, withdrawal by parent/guardian, protocol amendment, site terminated by investigator and loss of capacity.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

Prespecified primary and secondary endpoints at Week 78

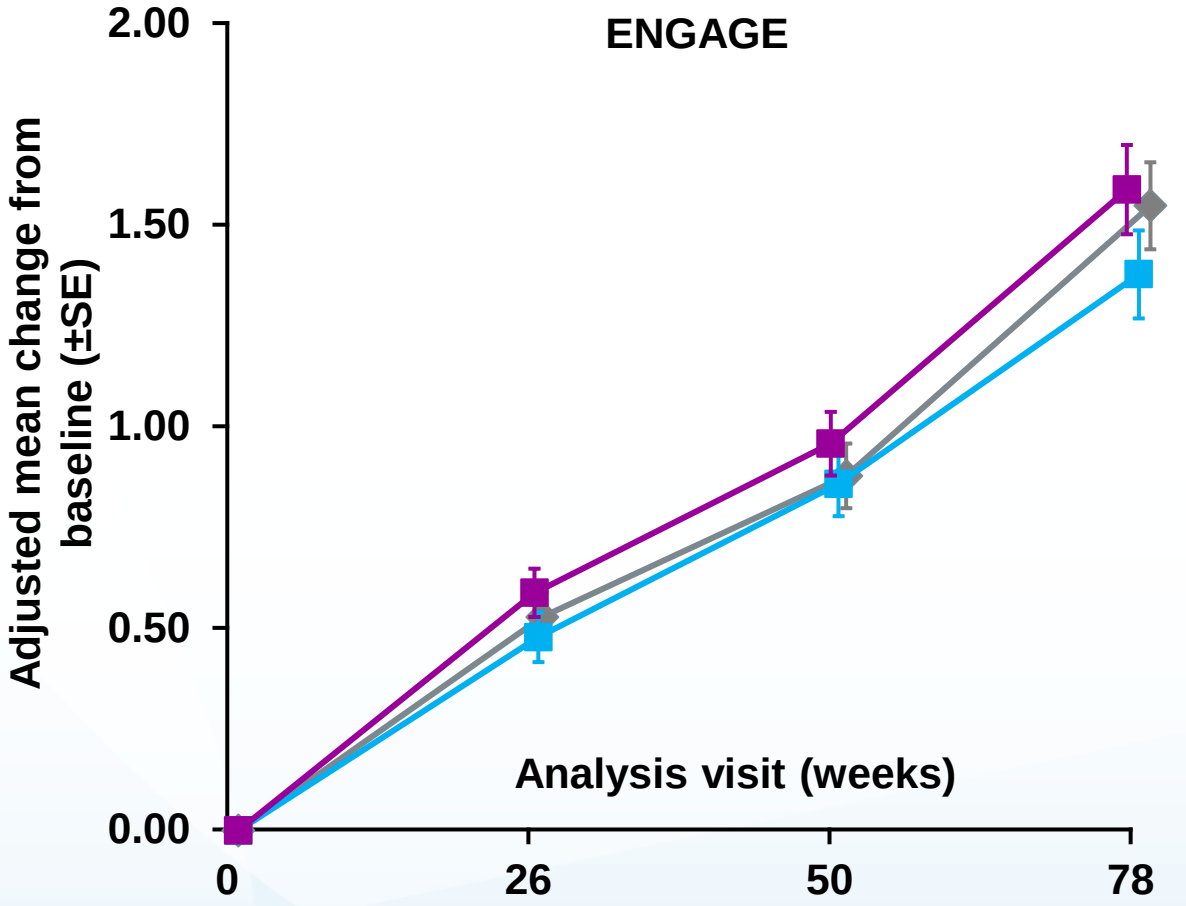
	EMERGE			ENGAGE		
	Placebo decline (n=548)	Difference vs. placebo (%)[a] p-value		Placebo decline (n=545)	Difference vs. placebo (%)[a] p-value[b]	
		Low dose (n=543)	High dose (n=547)		Low dose (n=547)	High dose (n=555)
CDR-SB	1.74	**-0.26** (-15%) 0.0901	**-0.39** (-22%) 0.0120	1.56	**-0.18** (-12%) 0.2250	**0.03** (2%) 0.8330
MMSE	-3.3	**-0.1** (3%) 0.7578	**0.6** (-18%) 0.0493	-3.5	**0.2** (-6%) 0.4795	**-0.1** (3%) 0.8106
ADAS-Cog 13	5.162	**-0.701** (-14%) 0.1962	**-1.400** (-27%) 0.0097	5.140	**-0.583** (-11%) 0.2536	**-0.588** (-11%) 0.2578
ADCS-ADL-MCI	-4.3	**0.7** (-16%) 0.1515	**1.7** (-40%) 0.0006	-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.
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.

Longitudinal change from baseline in CDR-SB



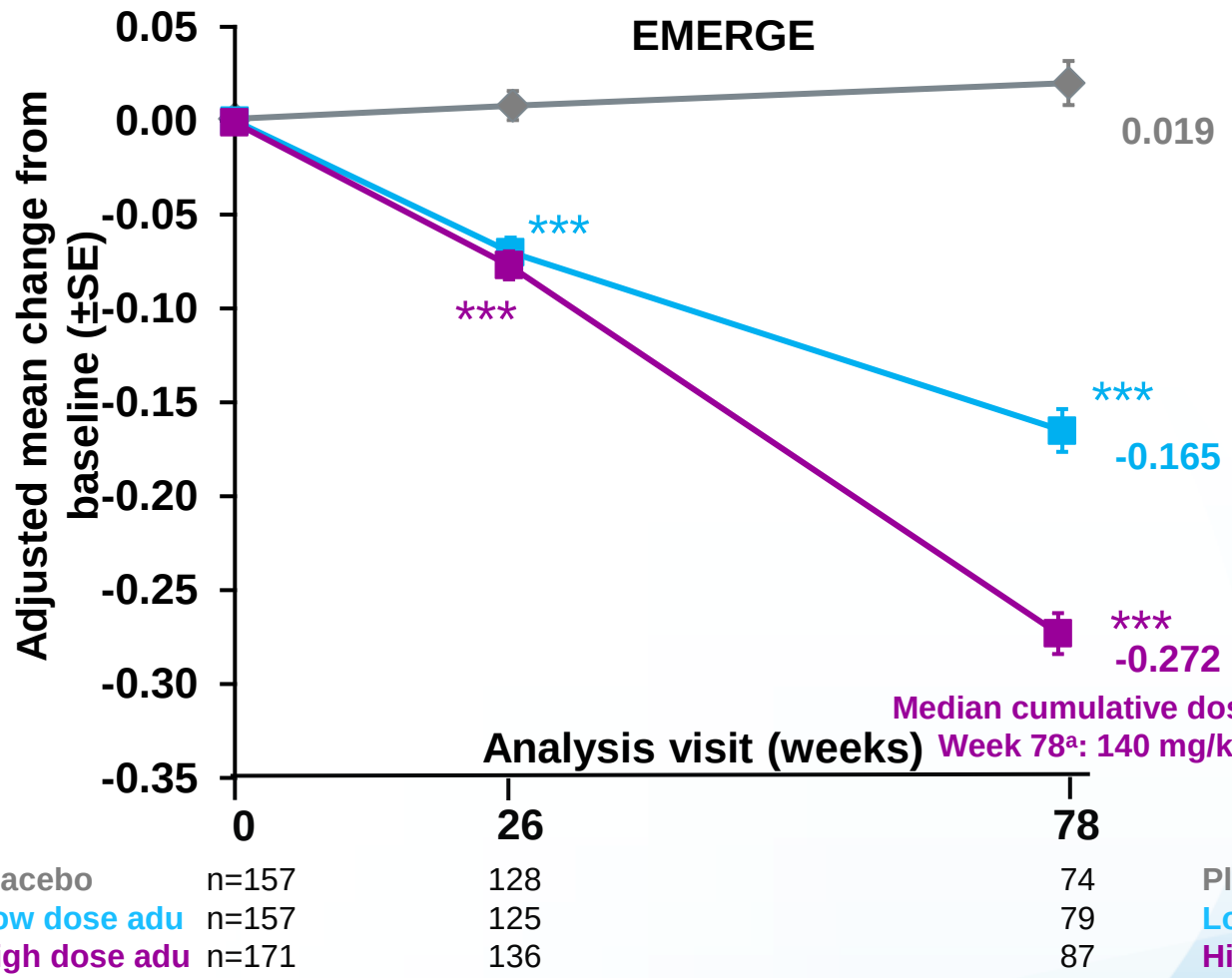
Placebo	n=547	531	429	288
Low dose adu	n=543	512	420	289
High dose adu	n=547	513	431	299



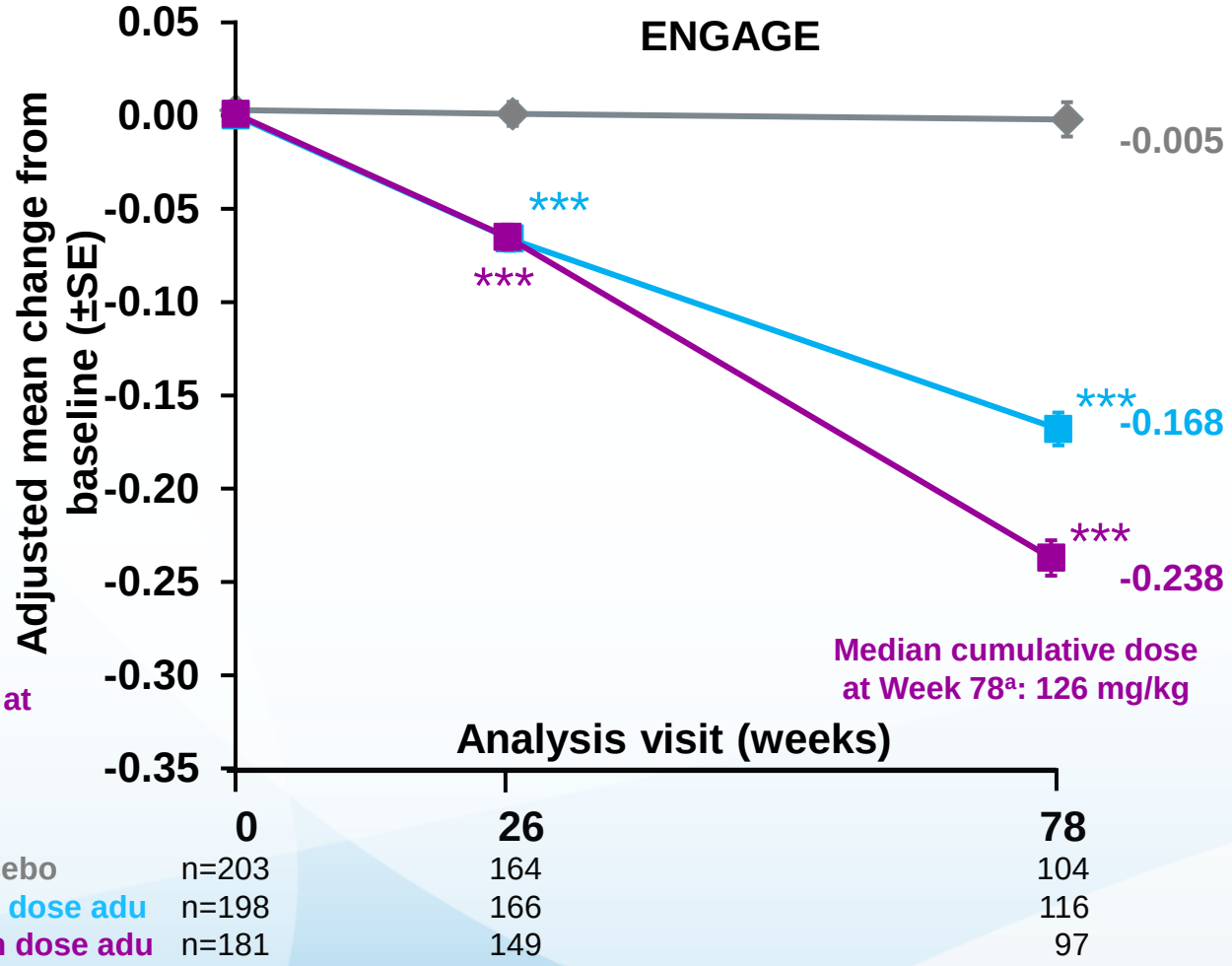
Placebo	n=545	522	455	333
Low dose adu	n=547	529	454	331
High dose adu	n=554	532	448	293

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.

Longitudinal change from baseline in amyloid PET SUVR



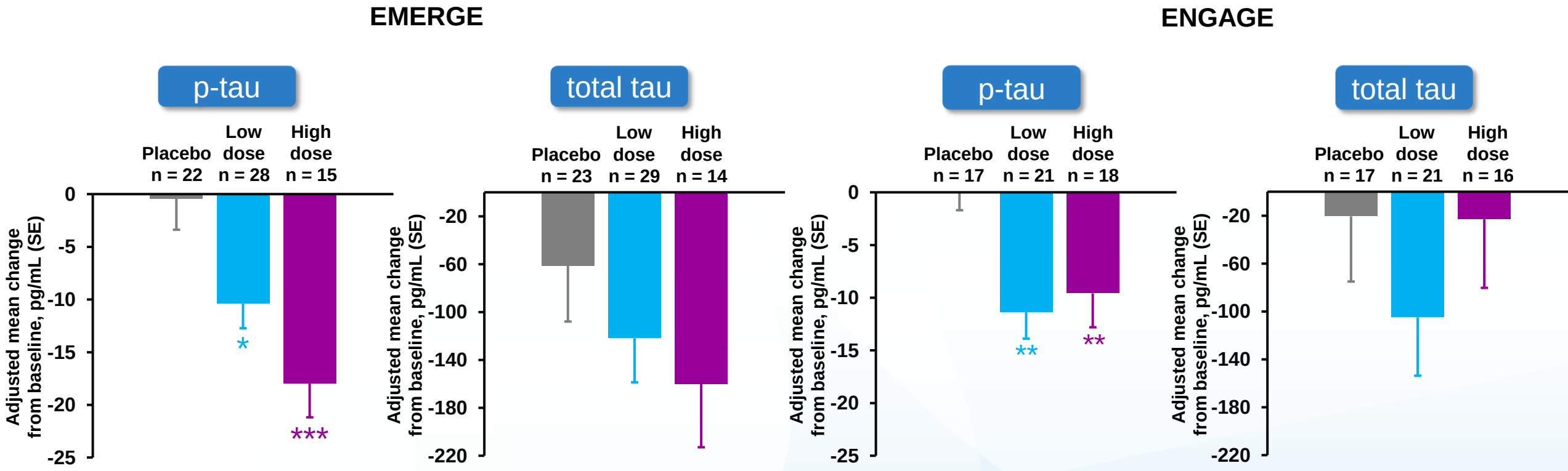
Placebo	n=157	128	74
Low dose adu	n=157	125	79
High dose adu	n=171	136	87



Placebo	n=203	164	104
Low dose adu	n=198	166	116
High dose adu	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.

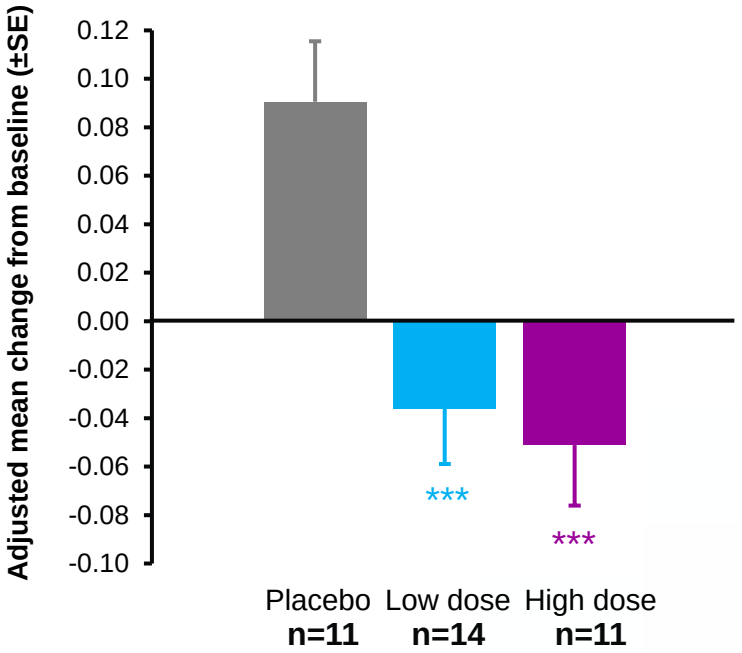
CSF biomarkers of tau pathology and neurodegeneration



CSF modified analysis population (patients with both baseline and post-baseline CSF assessments). *p<0.05, **p<0.01, ***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.

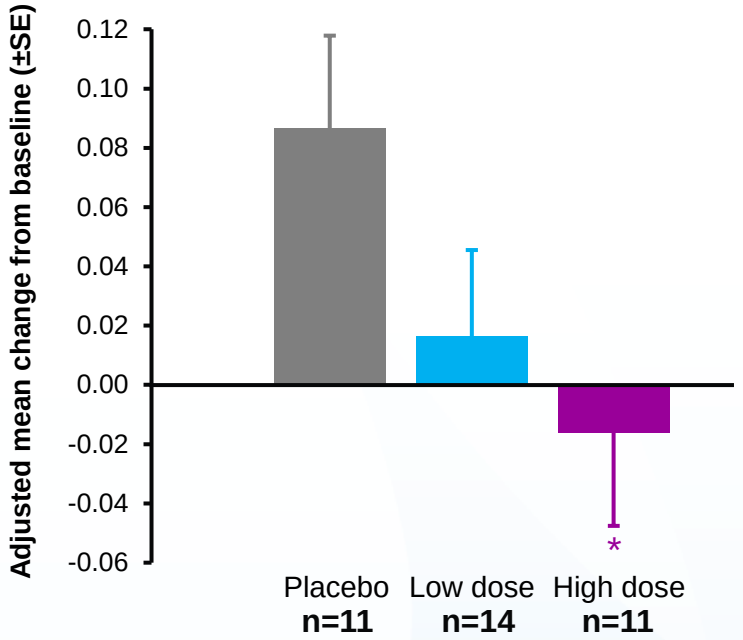
EMERGE and ENGAGE: tau PET composite SUVR change from baseline

Medial temporal composite



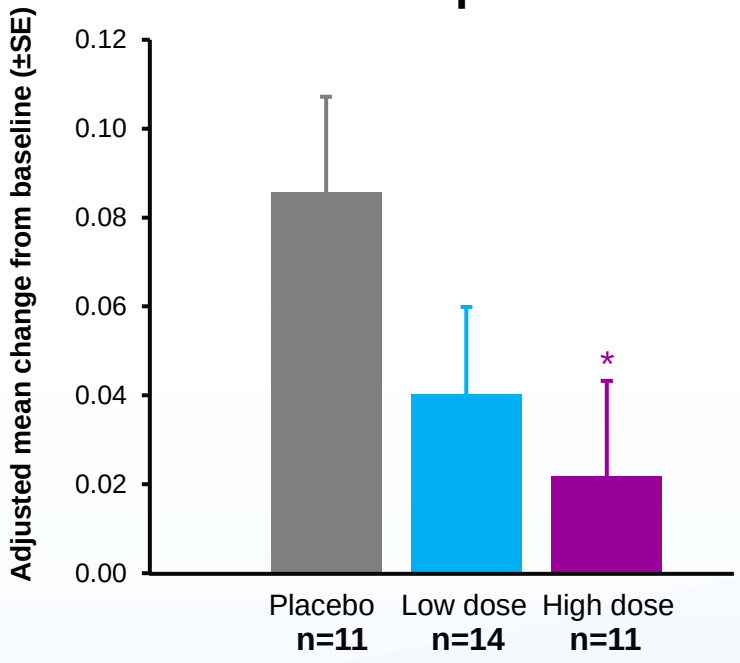
HIPPOCAMPUS
PARAHIPPOCAMPAL
TEMPORAL LOBE ANTERIOR MEDIAL
(includes Entorhinal and Amygdala)
TEMPORAL LOBE ANTERIOR LATERAL

Temporal composite



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

Frontal composite



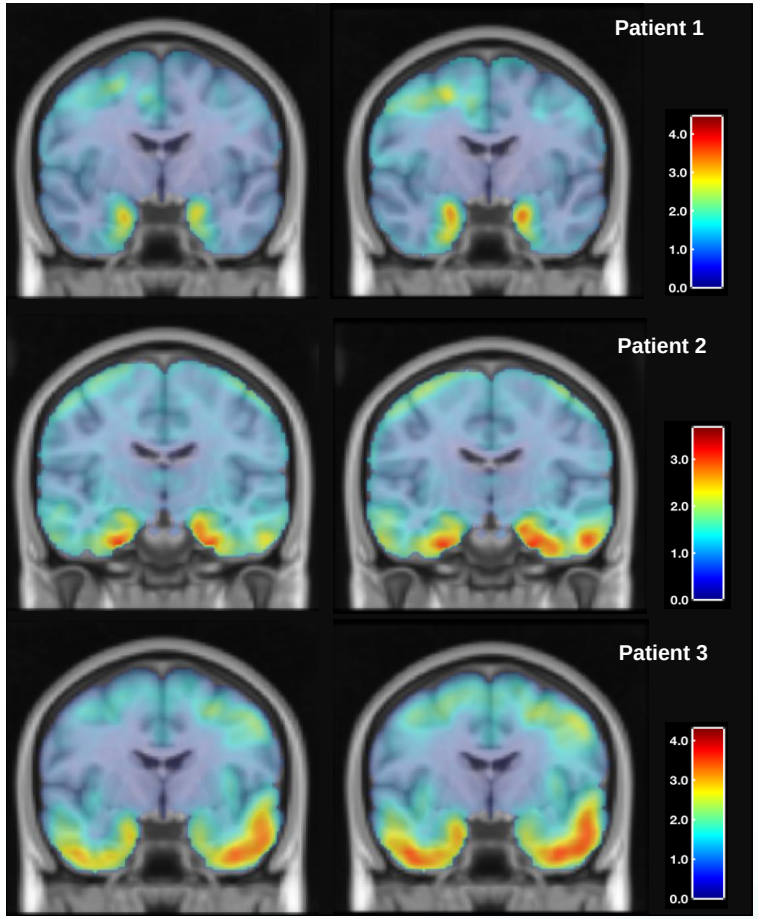
FRONTAL LOBE Comprised of:
MIDDLE, PRECENTRAL, STRAIGHT GYRUS
INFERIOR, SUPERIOR
ORBITOFRONTAL CORTEX Comprised of:
ANTERIOR, MEDIAL, LATERAL, POSTERIOR

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 representative patients

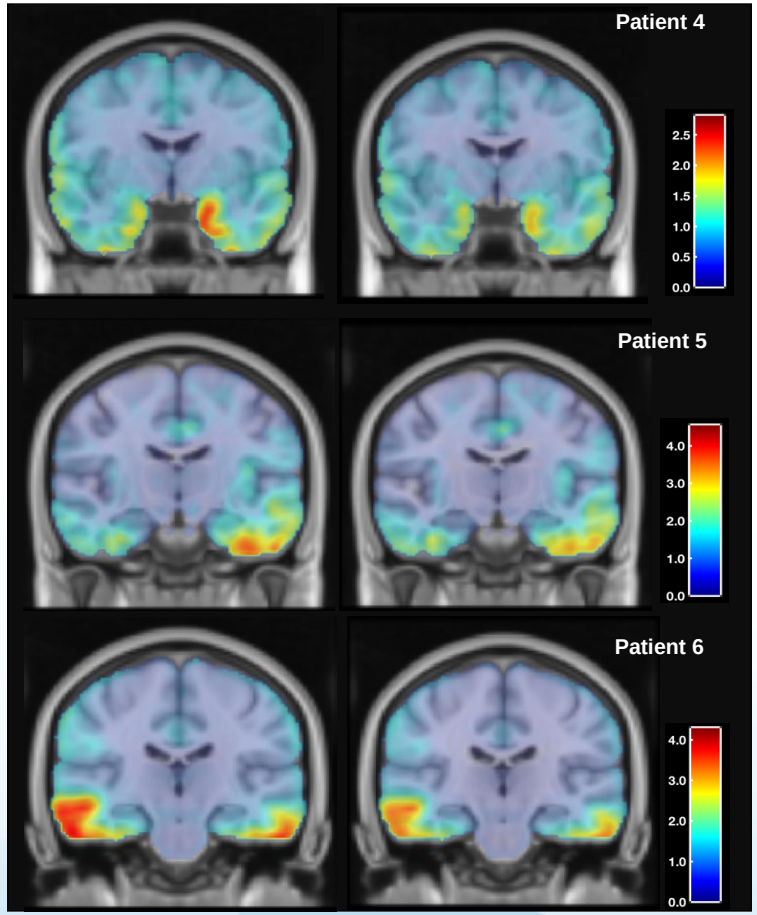
Placebo

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.

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 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.

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.

ARIA incidence

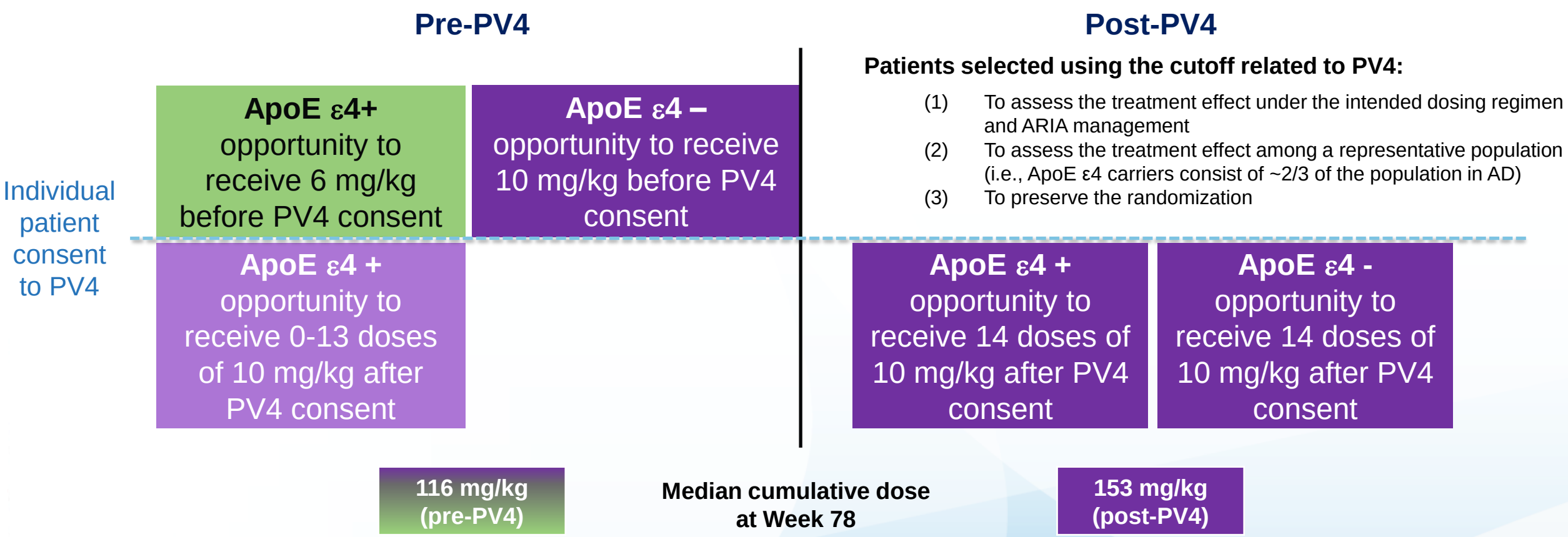
	EMERGE			ENGAGE		
	Placebo (n=544)	Low dose (n=537)	High dose (n=541)	Placebo (n=533)	Low dose (n=544)	High dose (n=554)
ARIA-E[a], n/total (%)	**12/544** (2.2)	**140/537** (26.1)	**186/541** (34.4)	**16/533** (3.0)	**139/544** (25.6)	**198/554** (35.7)
ApoE ε4 carriers	**7/371** (1.9)	**109/366** (29.8)	**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)
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). [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; ARIA-H, amyloid-related imaging abnormalities due to microhemorrhage, superficial siderosis or macrohemorrhage.

Defining a population by a randomized cohort who had the opportunity for all 14 doses of 10 mg/kg



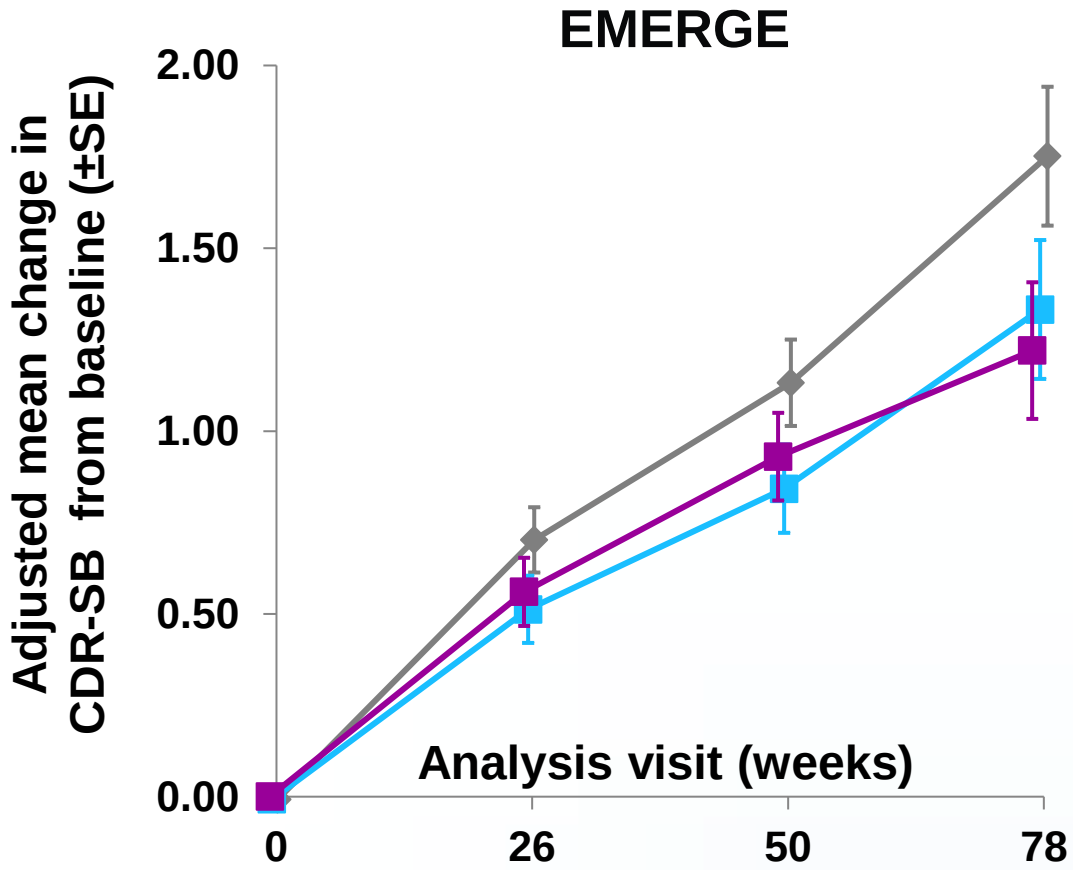
ApoE, apolipoprotein E; PV4, Protocol Version 4.

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

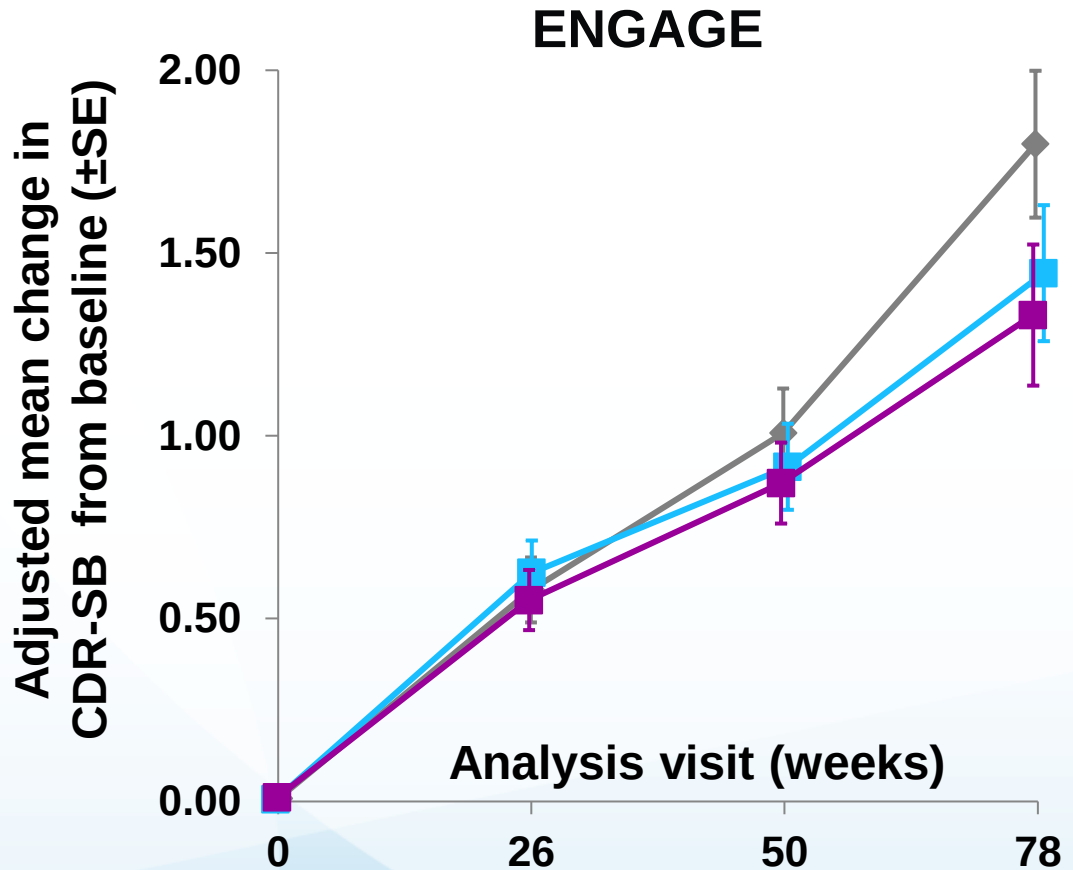
	ITT			Post-PV4[a,b]		
EMERGE	**Placebo decline (n=548)**	**Low dose (n=543)** diff vs. placebo, (%)[c]	**High dose (n=547)** diff vs. placebo (%)[c]	**Placebo decline (n=304)**	**Low dose (n=295)** diff vs. placebo (%)[c]	**High dose (n=288)** diff vs. placebo (%)[c]
CDR-SB	1.74	**-0.26** (-15%)	**-0.39** (-22%)	1.76	**-0.42** (-24%)	**-0.53** (-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	1.56	**-0.18** (-12%)	**0.03** (2%)	1.79	**-0.35** (-20%)	**-0.48** (-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.

Population[a,b] randomized with the opportunity to receive 14 doses of 10 mg/kg



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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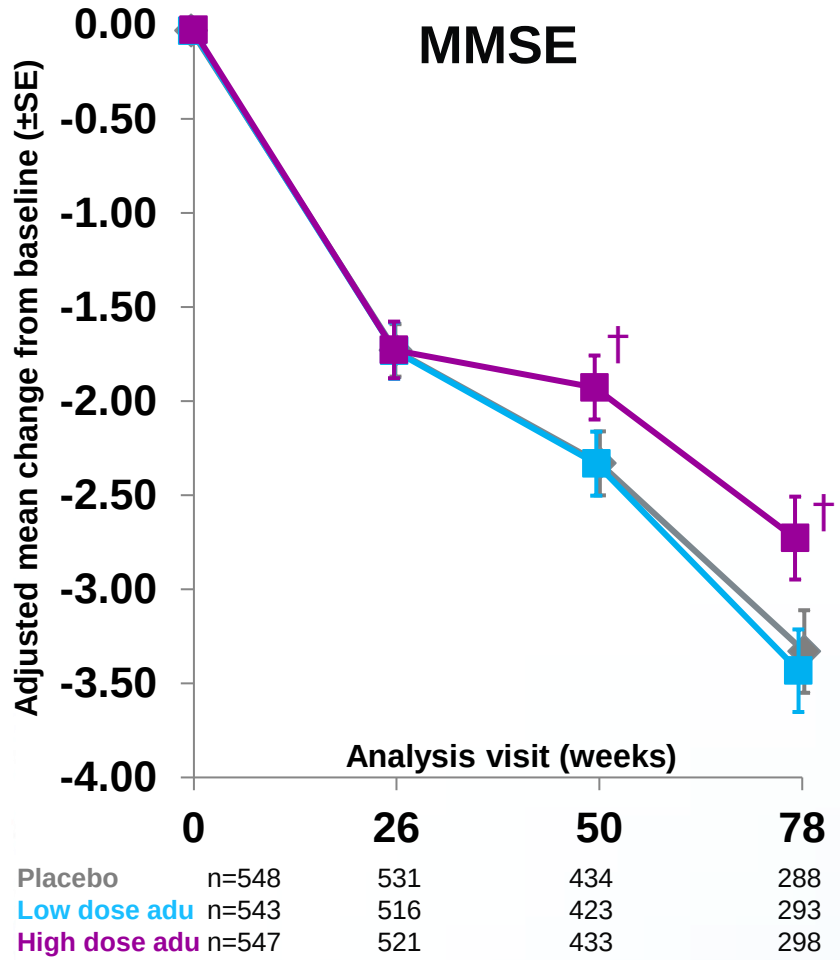
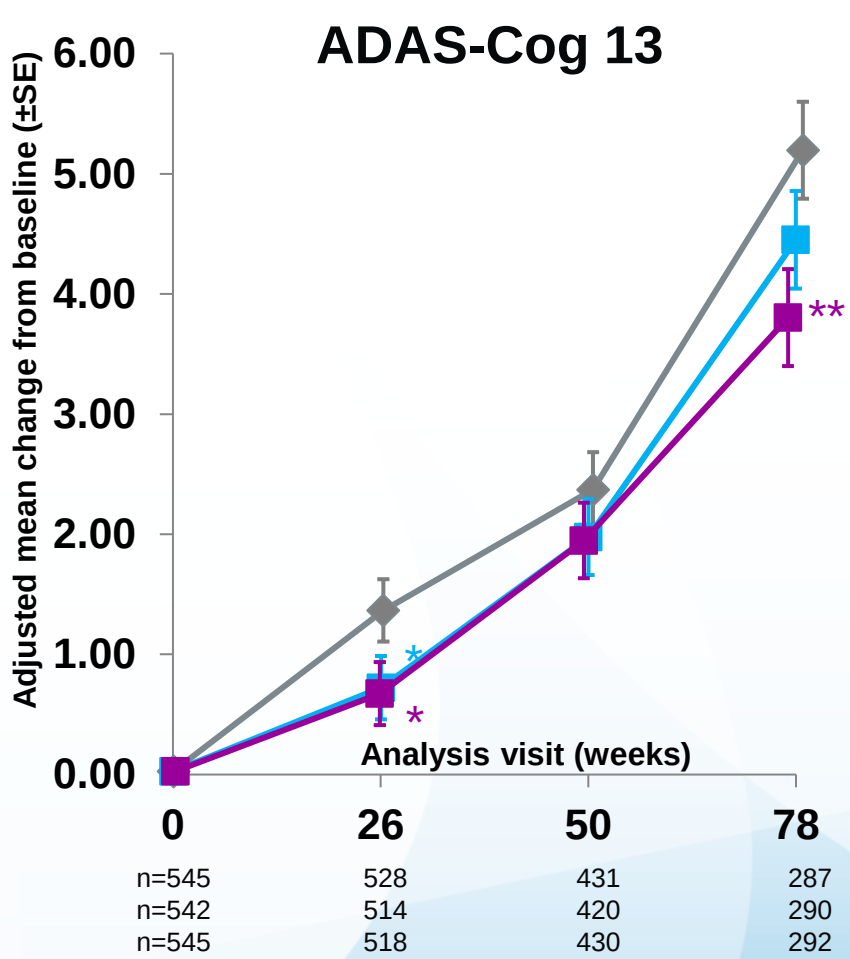
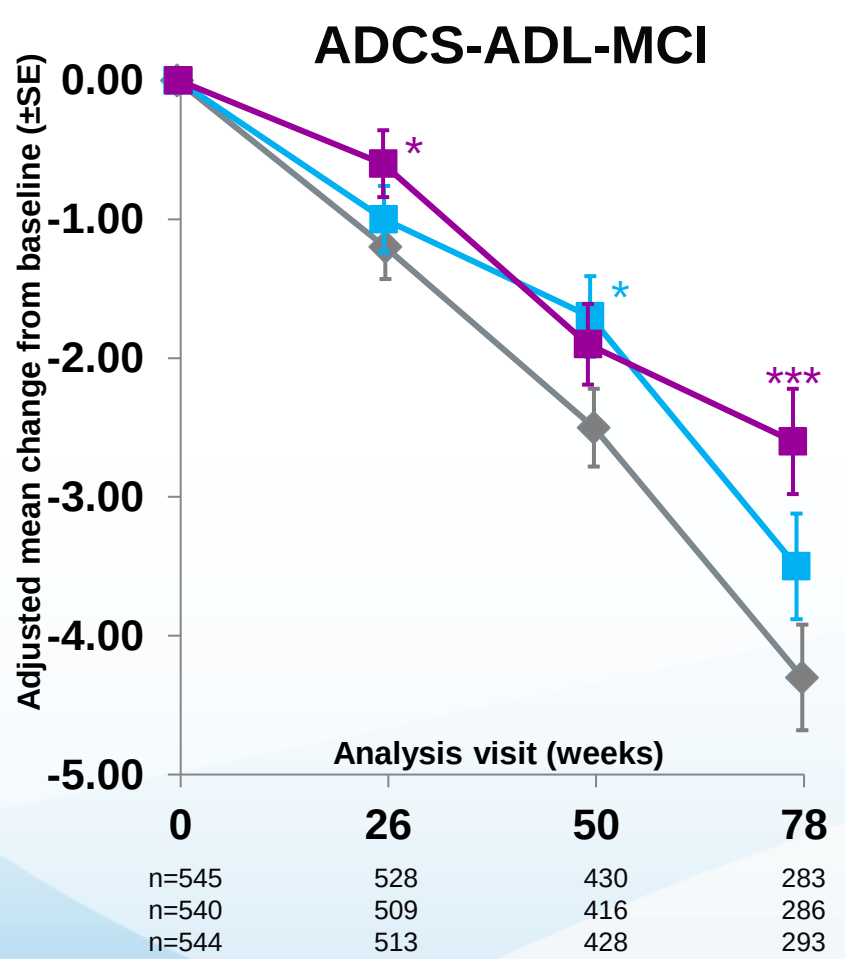
- We thank all patients and family members who participated in the aducanumab studies and the investigators and staff who conducted these studies, DSMB, and steering committee members
- We also thank those who contributed to this work, including Kimberly Umans, Stacy Lindborg, John O’Gorman, Xiaopeng Miao, Charlie Cao, Carmen Castrillo-Viguera, Ping He, Carol Yurgalevitch, Ivana Rubino, and Eric Ponton

BACK-UP

EMERGE: Longitudinal change from baseline in MMSE, ADAS-Cog 13 and ADSC-ADL-MCI

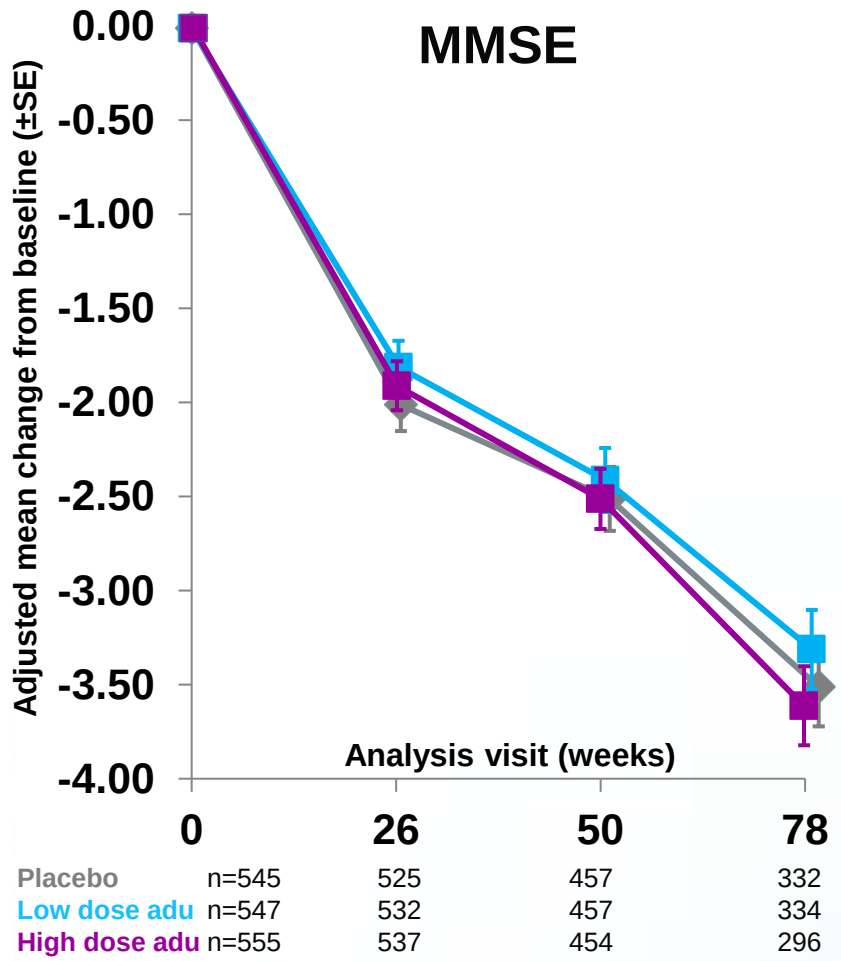


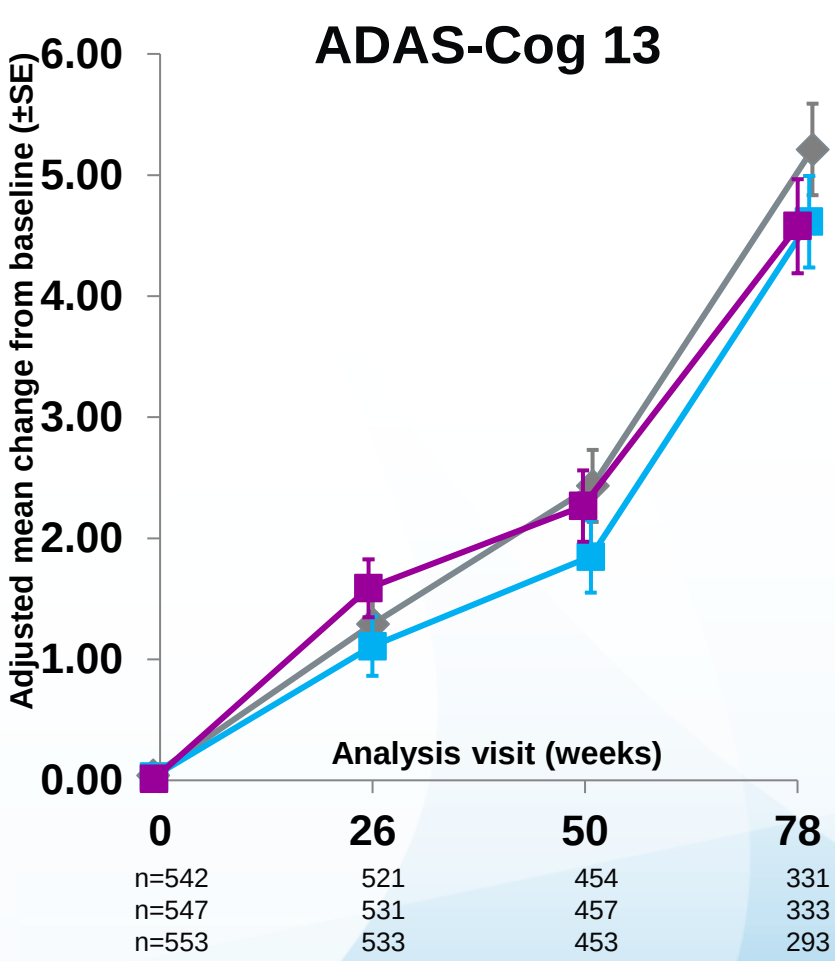


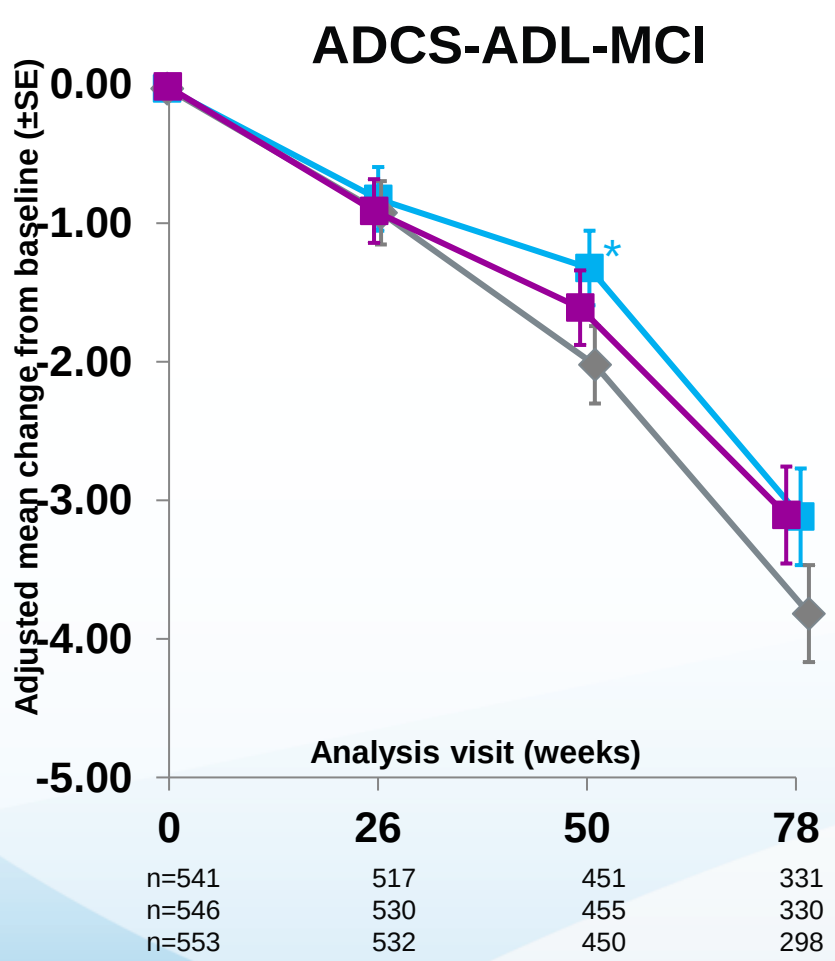


ITT population. †p<0.1 and ≥0.05, *p<0.05, **p<0.01, ***p<0.001 compared with placebo (nominal). Values at each time point were based on an MMRM model, with change from baseline in MMSE, ADAS-Cog 13, or ADCS-ADL-MCI as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline measure, baseline measure by visit interaction, Alzheimer's disease symptomatic medication use at baseline, region, and laboratory ApoE ε4 status. 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); 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 MMSE, ADAS-Cog 13 and ADSC-ADL-MCI







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