16th Clinical Trials on Alzheimer's Disease Conference (CTAD2023)

Evaluating the Efficacy of AR1001 on Plasma pTau-181 Levels and ADAS-Cog 13 in Mild to Moderate Alzheimer's Disease: Results from the Phase 2 Trial

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Disclosure : David R. Greeley, MD, is the consulting Chief Medical Officer of AriBio Co., Ltd.

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AR1001 Phase 2 Study (AR1001-ADP2-US01)

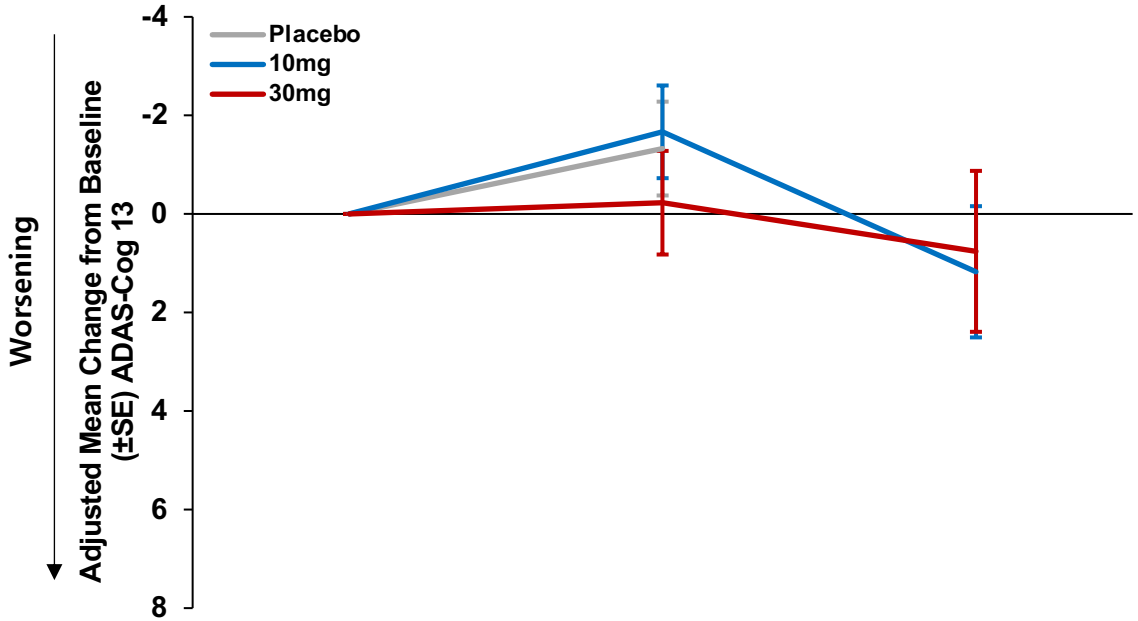
AR1001 Alzheimer's disease Phase 2 Study		
Study	26-Week, Randomized, Double-blind, Placebo-controlled, Phase II Study	
Objective	Safety and Tolerability	
	Preliminary Efficacy	
Population	55-80 years old (Total of 210 participants)	
	Mild to Moderate Alzheimer's disease : MMSE 16-26, NIA-AA dementia stage 4-5	
Doses	**Part I : Main 26 Week Study** • AR1001 10 mg, AR1001 30 mg, Placebo (1:1:1 randomized) **Part II : Optional 26 Week Extension Study** • AR1001 10 mg and 30 mg arms continue the same dose • Placebo arm is randomized into 10 mg or 30 mg	
Endpoints	Co-Primary Endpoints	**ADAS-Cog 13, ADCS-CGIC**
	Secondary Endpoint	**MMSE, NPI, GDS, QoL-AD**
	Plasma Biomarkers	**pTau-181, GFAP, NfL, Aβ42/40**

Baseline Demographics and Characteristics

Variable	Placebo (n = 70) N (%)	Low Dose 10 mg (n = 70) N (%)	High Dose 30 mg (n=70) N (%)
Age (years), mean (SD)	70.4 (5.5)	70.9 (6.5)	70.4 (6.8)
Gender, n (%) · Male · Female	 22 (31.4) 48 (68.6)	 27 (38.6) 43 (61.4)	 23 (32.9) 47 (67.1)
Race, n (%) **· Black or African American** **· White** **· Multiple Races Reported** **· Unknown**	 **12 (17.1)** **58 (82.9)** **0** **0**	 **8 (11.4)** **60 (85.7)** **1 (1.4)** **1 (1.4)**	 **8 (11.4)** **62 (88.6)** **0** **0**
Ethnicity, n (%) · Hispanic or Latino · Not Hispanic or Latino · Not Reported · Unknown	 13 (18.6) 56 (80.0) 0 1 (1.4)	 13 (18.6) 57 (81.4) 0 0	 16 (22.9) 52 (74.3) 1 (1.4) 1 (1.4)
BMI, Mean (SD)	28.07 (5.49)	29.55 (6.94)	28.74 (6.53)
AD medication used, n (%)	36 (51.4)	40 (57.1)	46 (65.7)
Clinical Stage, n (%) · Mild (MMSE 21 – 26) · Moderate (MMSE 16 – 20)	 52 (74.3) 18 (25.7)	 52 (74.3) 18 (25.7)	 47 (67.1) 23 (32.9)

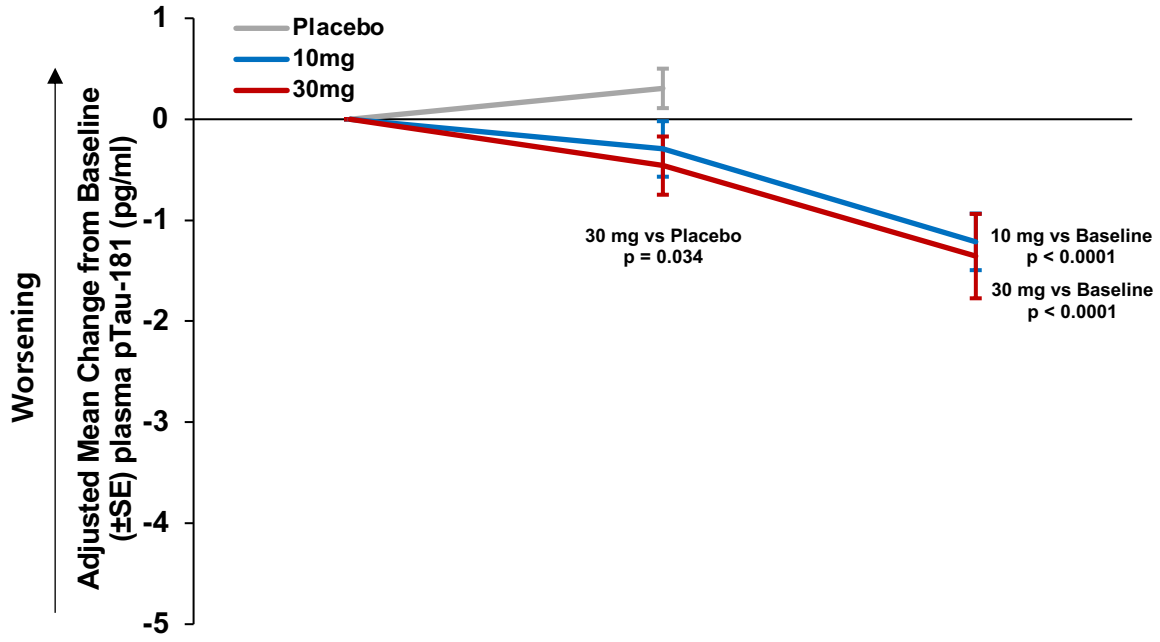
ITT Analysis

- **ADAS-Cog 13**



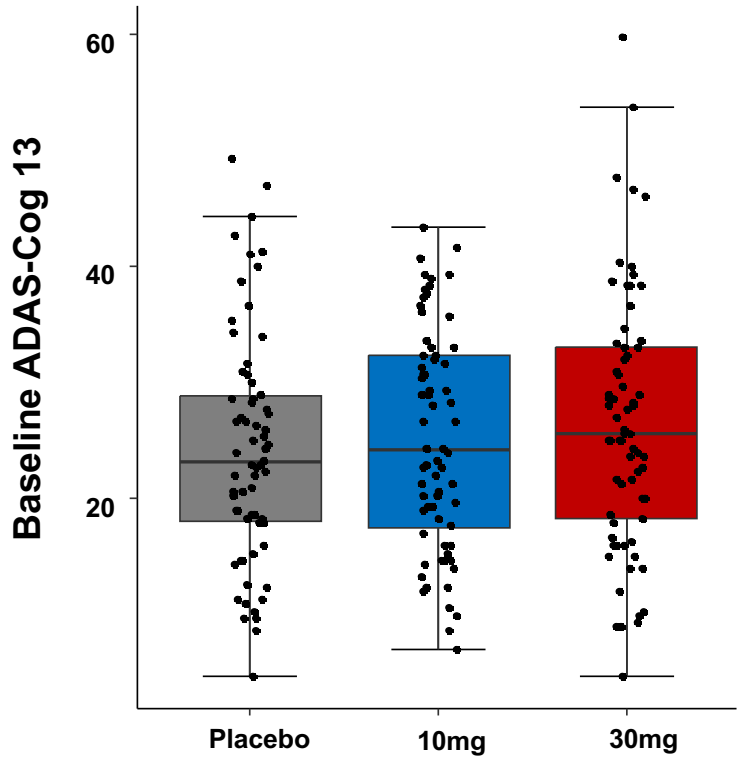
	Week 0	Week 26	Week 52
(N) Placebo	67	51	-
(N) 10 mg	68	59	48
(N) 30 mg	69	57	36

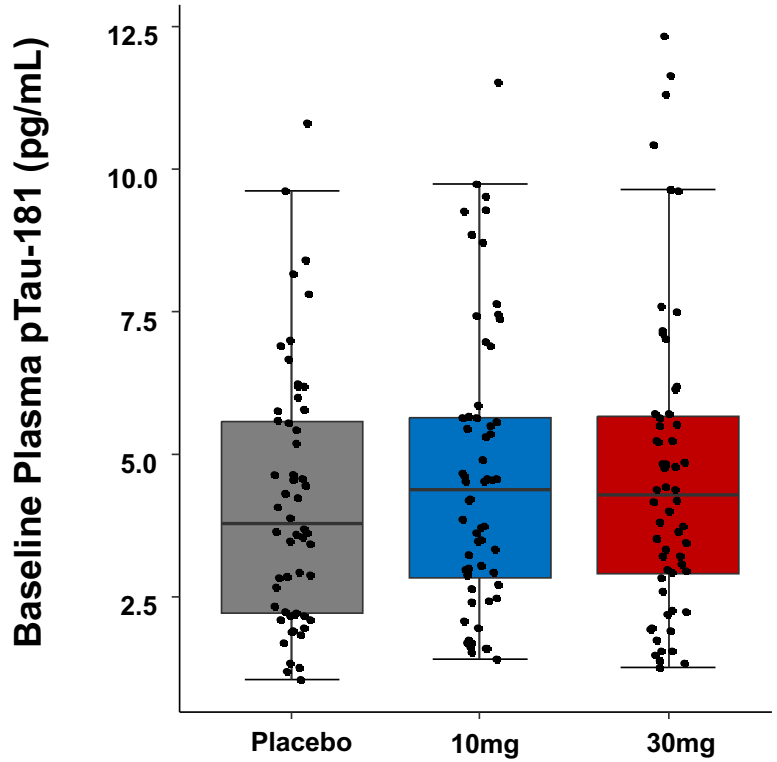
- **Plasma pTau-181**



	Week 0	Week 26	Week 52
(N) Placebo	61	41	-
(N) 10 mg	62	51	41
(N) 30 mg	61	45	30

Baseline ADAS-Cog 13 & plasma pTau-181





ADAS-Cog 13			
	Placebo	AR1001 10 mg	AR1001 30 mg
Baseline, n	67	68	69
Mean (SD)	24.179 (10.062)	25.103 (9.459)	26.411 (11.073)

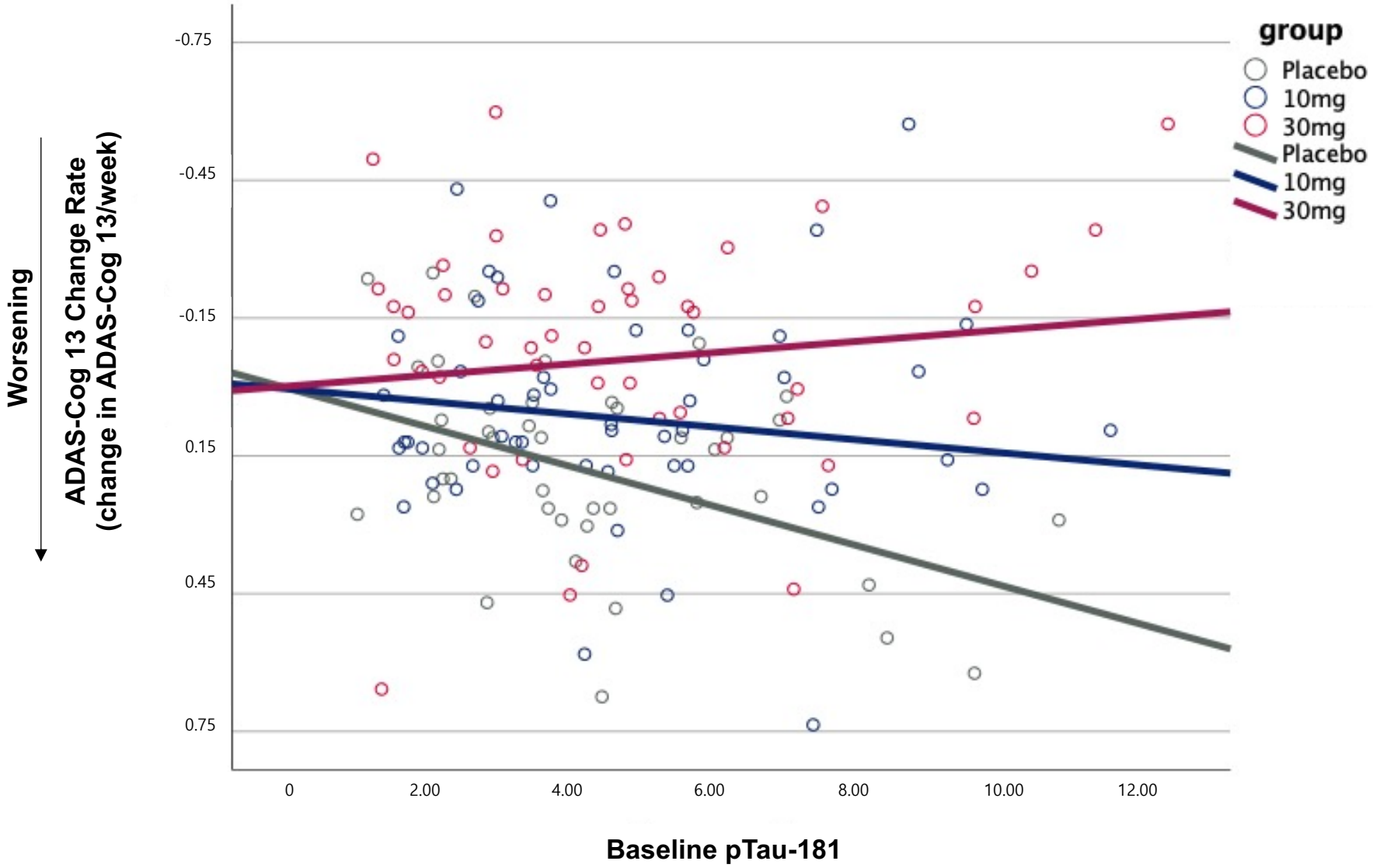
Plasma pTau-181			
	Placebo	AR1001 10 mg	AR1001 30 mg
Baseline, n	61	62	61
Mean (SE), pg/ml	4.235 (0.277)	4.645 (0.309)	4.648 (0.340)

Effect of interaction between baseline pTau-181 and time on ADAS-Cog 13

Groups	Predictor	estimate (SE)	P value
Placebo	Baseline pTau-181	2.16 (0.56)	<0.001
	Time	-1.66 (0.54)	0.004
	Baseline pTau-181*Time	**0.30 (0.11)**	**0.010**
10 mg	Baseline pTau-181	1.21 (0.49)	0.016
	Time	-0.88 (0.66)	0.185
	Baseline pTau-181* Time	**0.12 (0.12)**	**0.315**
30 mg	Baseline pTau181	1.13 (0.52)	0.033
	Time	0.64 (0.59)	0.287
	Baseline pTau-181* Time	**-0.15 (0.11)**	**0.166**

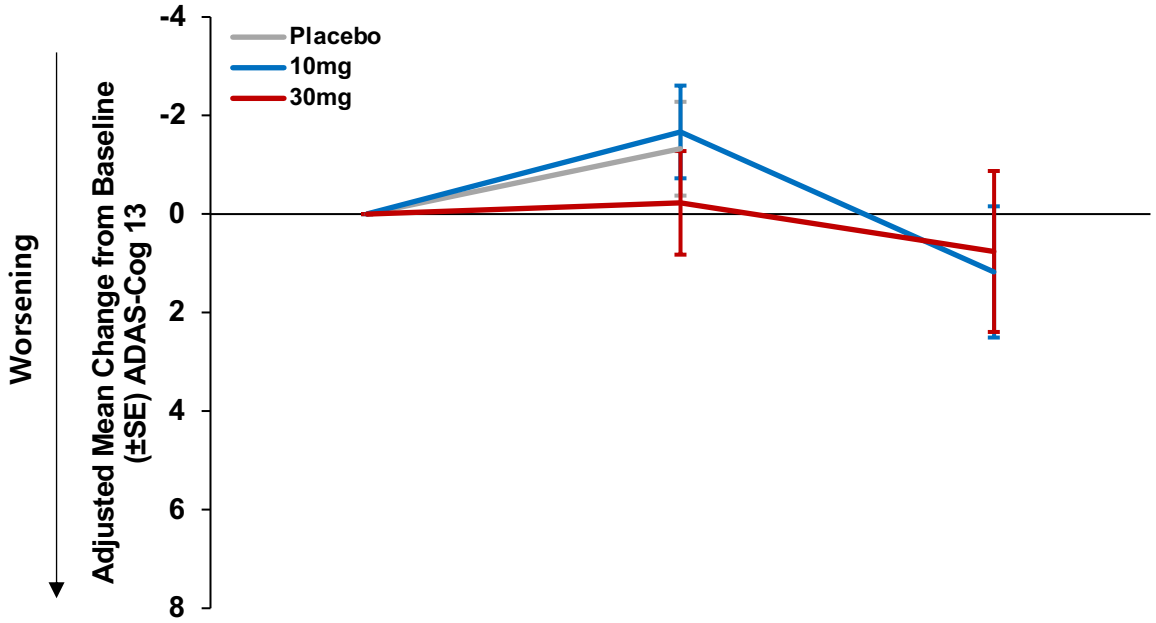
Data are results of linear mixed models for longitudinal ADAS-cog, separately performed in each AR1001 group. Predictors included group, time, baseline pTau181 and their interaction. Abbreviations: ADAS-cog = Alzheimer's Disease Assessment Scale-Cognitive Subscale; pTau-181 = tau phosphorylated at threonine 181.

Effects of Baseline pTau-181 on longitudinal ADAS-Cog 13



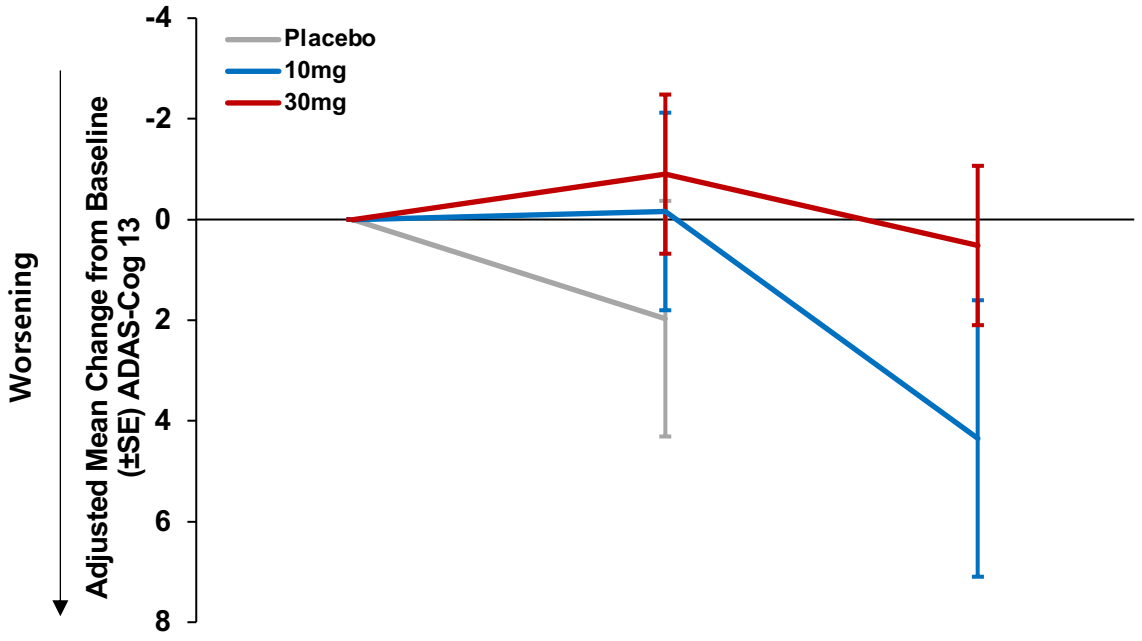
ADAS-Cog 13 (ITT vs high baseline pTau-181 group)

- ITT



	Week 0	Week 26	Week 52
(N) Placebo	67	51	-
(N) 10 mg	68	59	48
(N) 30 mg	69	57	36

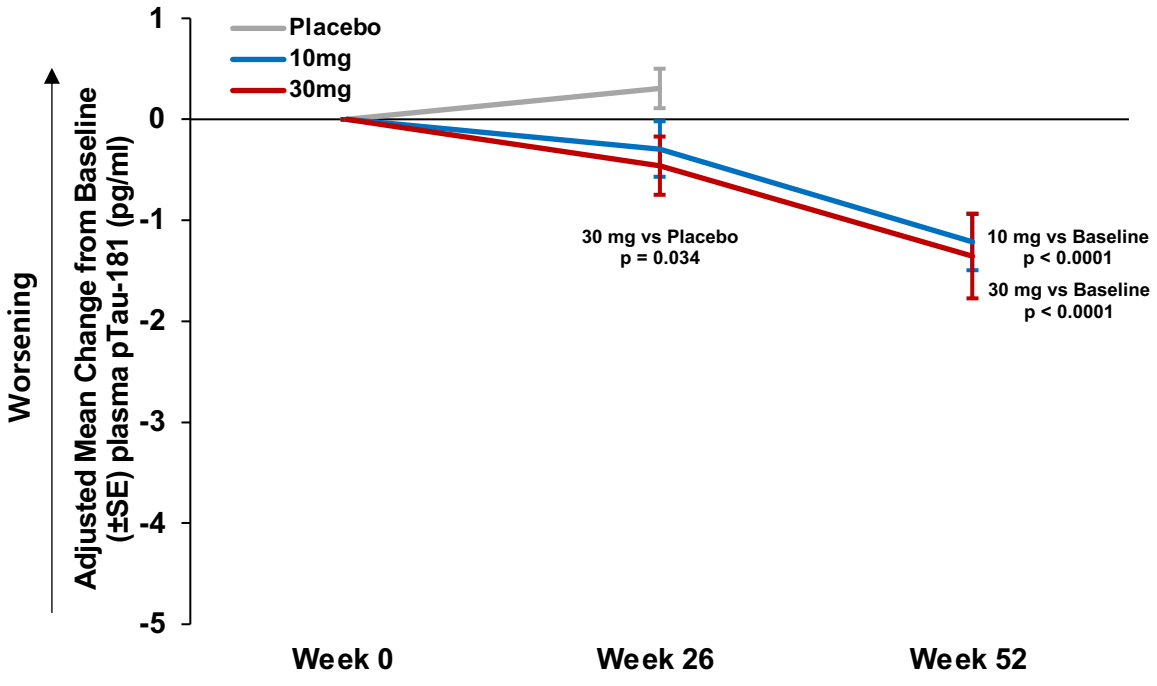
- pTau-181 > 5.0 pg/mL (Top 33%)



	Week 0 (N=60)	Week 26 (N=51)	Week 52 (N=29)
(N) Placebo	17	13	-
(N) 10 mg	22	21	18
(N) 30 mg	21	17	11

Plasma pTau-181 (ITT vs high baseline pTau-181 group)

- ITT



(N) Placebo	61	41	-
(N) 10 mg	62	51	41
(N) 30 mg	61	45	30

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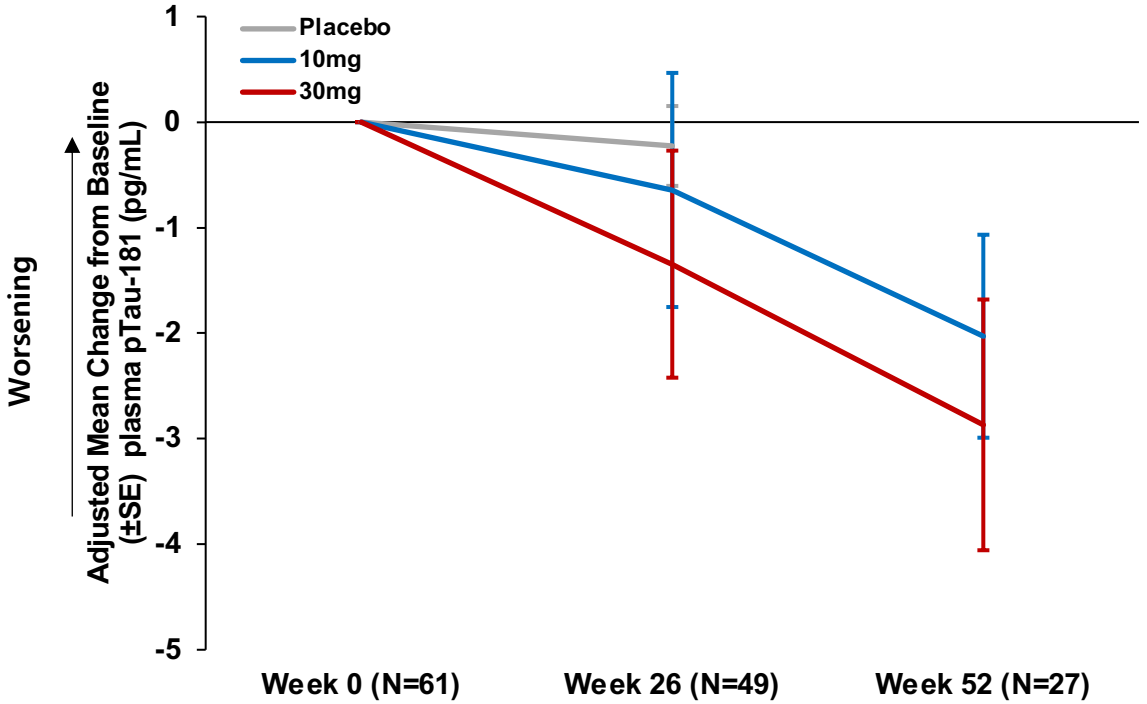

(N) Placebo	18	12	-
(N) 10 mg	22	21	17
(N) 30 mg	21	16	10


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