Bapineuzumab Phase 3 trials in mild to moderate Alzheimer's disease dementia in *apolipoprotein E ε4* carriers (Study 302) and non-carriers (Study 301)

Clinical Outcomes

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On Behalf of the Bapineuzumab Study Investigators

Disclosures

- Dr. Salloway is the Chair of 301/302 Steering Committee, is a bapineuzumab IV P3 study investigator, serves on the scientific advisory boards of Janssen AI and Pfizer, and receives honoraria from Janssen AI and Pfizer.
- Dr. Sperling serves on the 301/302 Steering Committee, is a consultant to Janssen AI (unpaid), and was a site investigator in Janssen AI and Pfizer trials for bapineuzumab IV. She is also a consultant for Roche, Merck, Bristol-Myers-Squibb, Eli-Lilly, Satori, Eisai, and Biogen..
- Dr. Raskind serves on and is a paid member of the 301/302 Steering Committee, and is a bapineuzumab IV P3 study investigator for Janssen AI and Eli Lilly.
- Dr. Ferris serves on the 301/302 Steering Committee,and is a consultant to Pfizer, Eisai, Bristol Myers-Squibb, Eli Lilly, Merck and Baxter.
- Dr. Honig serves on and is a paid member of the Study 301/302 Steering Committee, and is a bapineuzumab IV P3 study investigator.
- Dr. Porsteinsson serves on the Study 301/302 Steering Committee, is a bapineuzumab IV P3 study investigator, and receives honoraria from Janssen AI.
- Dr. Sabbagh serves on the Study 301/302 Steering Committee, is a bapineuzumab IV P3 study investigator, and previously served on speaker's bureau for Pfizer.
- Prof. Fox served on the scientific advisory boards of Alzheimer's Research Form, GE Healthcare, Janssen AI, and Wyeth. He is a paid consultant for Eli Lilly, Abbott Laboratories, Eisai, Elan, Wyeth, Janssen AI, GE Healthcare, Sanofi-Aventis, and Lundbeck, and received research support from GlaxoSmithKline, Elan, Wyeth, Janssen AI, Lundbeck, Sanofi-Aventis, IXICO and Pfizer Inc for contracted image analysis
- E Liu, E Yuen, Y Lu, D Wang, B Nejadnik, V Guenzler, J Lull, M Miloslavsky, C Tudor, M Reichert, N Ketter, and B Brashear are employees of Janssen Alzheimer Immunotherapy R&D, LLC.
- R Black was an employee of Pfizer Inc.
- M Grundman is a consultant to Janssen Alzheimer Immunotherapy R&D, LLC.

Study funding:
Janssen Alzheimer Immunotherapy and Pfizer Inc

Bapineuzumab Background

- A humanized N-terminus anti-amyloid-β monoclonal antibody in development for the treatment of Alzheimer's disease (AD)
- Phase 3 clinical trial program designed to evaluate safety and efficacy as a potential disease modifier based on a combination of clinical and biomarker evidence
- Based on results in Phase 2, separate Phase 3 trials were designed for apolipoprotein E (APOE) ε4 allele carriers and non-carriers with mild to moderate AD dementia
- These presentations report the primary efficacy, key biomarkers and safety results for both trials, pooled analyses across the studies, pre-specified mild (MMSE ≥ 21) and moderate (MMSE ≤ 20) subgroup analyses

Trial Design

- Multi-center randomized double-blind, placebo-controlled, 18-month clinical trials in mild-moderate AD dementia (MMSE 16-26)
- APOE ε4 carriers: Bapineuzumab 0.5 mg/kg or placebo (ratio 3:2)
- Non-carriers: Bapineuzumab 0.5 mg/kg, 1.0 mg/kg or placebo (ratio 3:3:4)
  - 2 mg/kg dose terminated early in Phase 3 due to amyloid-related imaging abnormalities (ARIA)
- **Primary Clinical Endpoints:**
  - Alzheimer's Disease Assessment Scale – Cognitive (ADAS-Cog 11)
  - Disability Assessment for Dementia (DAD)
- **Key Biomarker Secondary Endpoints:**
  - Brain amyloid burden on PiB PET
  - CSF phospho-tau
  - MRI brain volume
- **Schedule of Events:**
  - 6 infusions every 13 weeks
  - MRI monitoring for ARIA ~6 weeks after each infusion

Analysis Populations

Study 302
APOE ε4 Carriers
Total Randomized
N = 1121

Population	Placebo N (%)	Bapineuzumab 0.5 mg/kg N (%)
Randomized (Safety population)	**448** (100.0)	**673** (100.0)
mITT	**432** (96.4)	**658** (97.8)
PiB PET	**40** (8.9)	**75** (11.1)
CSF	**85** (19.0)	**127** (18.9)
vMRI	**238** (53.1)	**352** (52.3)

Study 301
Non-Carriers
Total Randomized
N = 1331

Population	Placebo N=524 (%)	Bapineuzumab 0.5 mg/kg N=337 (%)	Bapineuzumab 1.0 mg/kg N=329 (%)
Randomized (Safety population)	**524** (100.0)	**337** (100.0)	**329** (100.0)
mITT	**493** (94.1)	**314** (93.2)	**307** (93.3)
PiB PET	**15** (2.9)	**12** (3.6)	**12** (3.6)
CSF	**77** (14.7)	**47** (13.9)	**54** (16.4)
vMRI	**244** (46.6)	**169** (50.1)	**146** (44.4)

Baseline Demographics – mITT Population
Study 302 APOE ε4 Carriers

Total Randomized N = 1121

	Placebo (N=432)	Bapineuzumab (N=658)
Age, y (SD)	**72.3** (8.4)	**72.0** (8.0)
Gender (% female)	**242** (56.0)	**358** (54.4)
Race (% Caucasian)	**420** (97.2)	**624** (94.8)
APOE ε4: **% heterozygote ε4** **% homozygote ε4**	 **325** (75.2) **107** (24.8)	 **495** (75.2) **163** (24.8)
AChEI or memantine use (%)	**400** (92.6)	**606** (92.1)
MMSE total score (SD)	**20.7** (3.2)	**20.8** (3.1)
ADAS-Cog 11 total score (SD)	**23.9** (9.5)	**23.5** (9.4)
DAD total score (SD)	**79.4** (18.9)	**80.9** (17.3)

Baseline Demographics – mITT Population
Study 301 APOE ε4 Non-Carriers

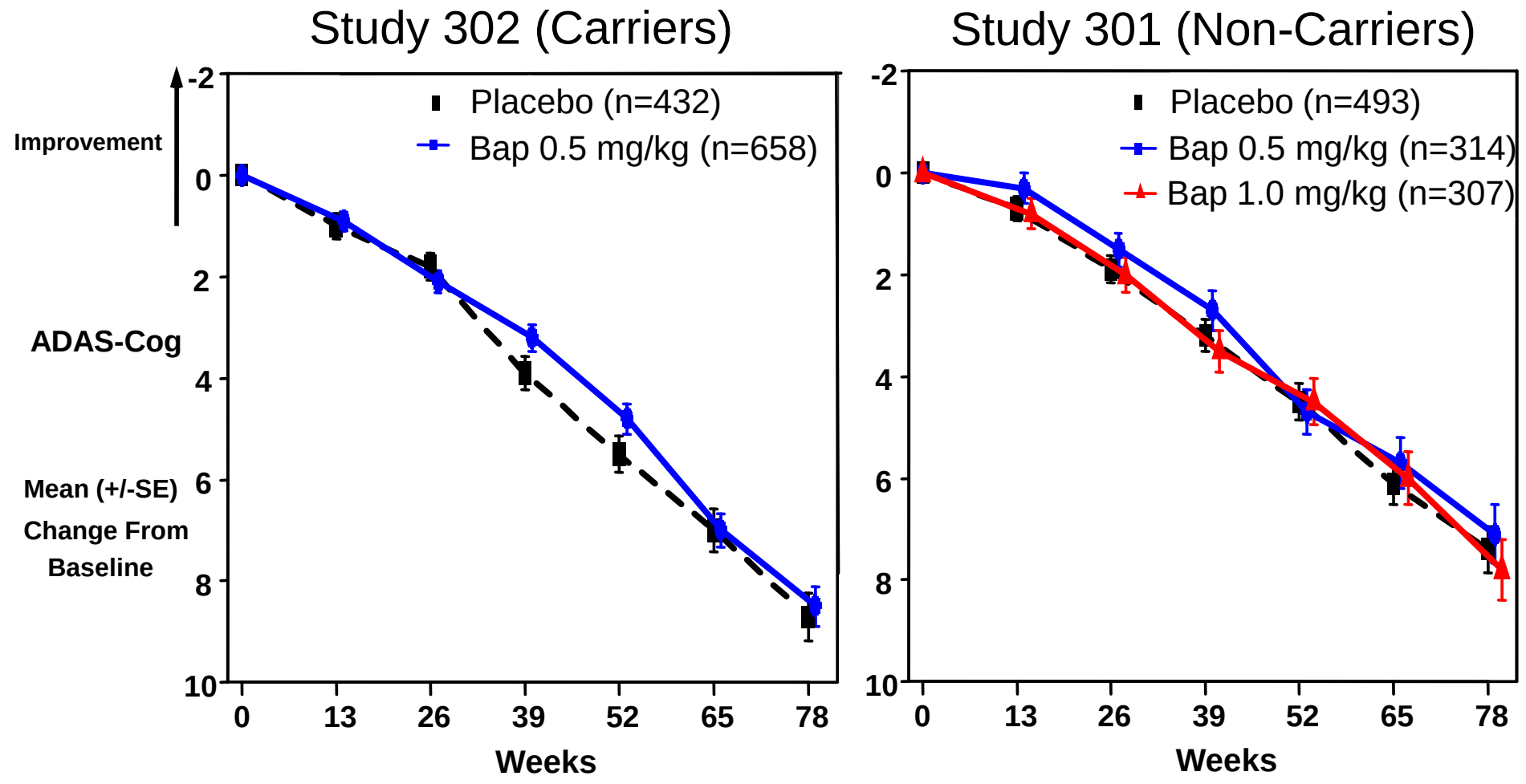
Total Randomized N = 1331*

	Placebo (N=493)	Bapineuzumab 0.5 mg/kg (N=314)	Bapineuzumab 1.0 mg/kg (N=307)
Age, y (SD)	**71.9** (10.1)	**73.1** (9.3)	**73.5** (9.1)
Gender (% female)	**248** (50.3)	**165** (52.5)	**175** (57.0)
Race (% Caucasian)	**469** (95.1)	**298** (94.9)	**292** (95.1)
AChEI or memantine use, (%)	**442** (89.7)	**281** (89.5)	**278** (90.6)
MMSE total score (SD)	**21.2** (3.2)	**21.2** (3.4)	**21.2** (3.3)
ADAS-Cog 11 total score (SD)	**22.2** (10.1)	**22.4** (9.7)	**22.2** (10.0)
DAD total score (SD)	**80.5** (19.2)	**80.0** (18.1)	**80.4** (18.8)

*Bapineuzumab 2.0 mg/kg group (n=141) discontinued early in the course of study; primary cognitive and functional outcomes will not be presented

Results: Clinical Endpoints

Change in ADAS-Cog 11 by Treatment Group Over 78 Weeks (mITT population)

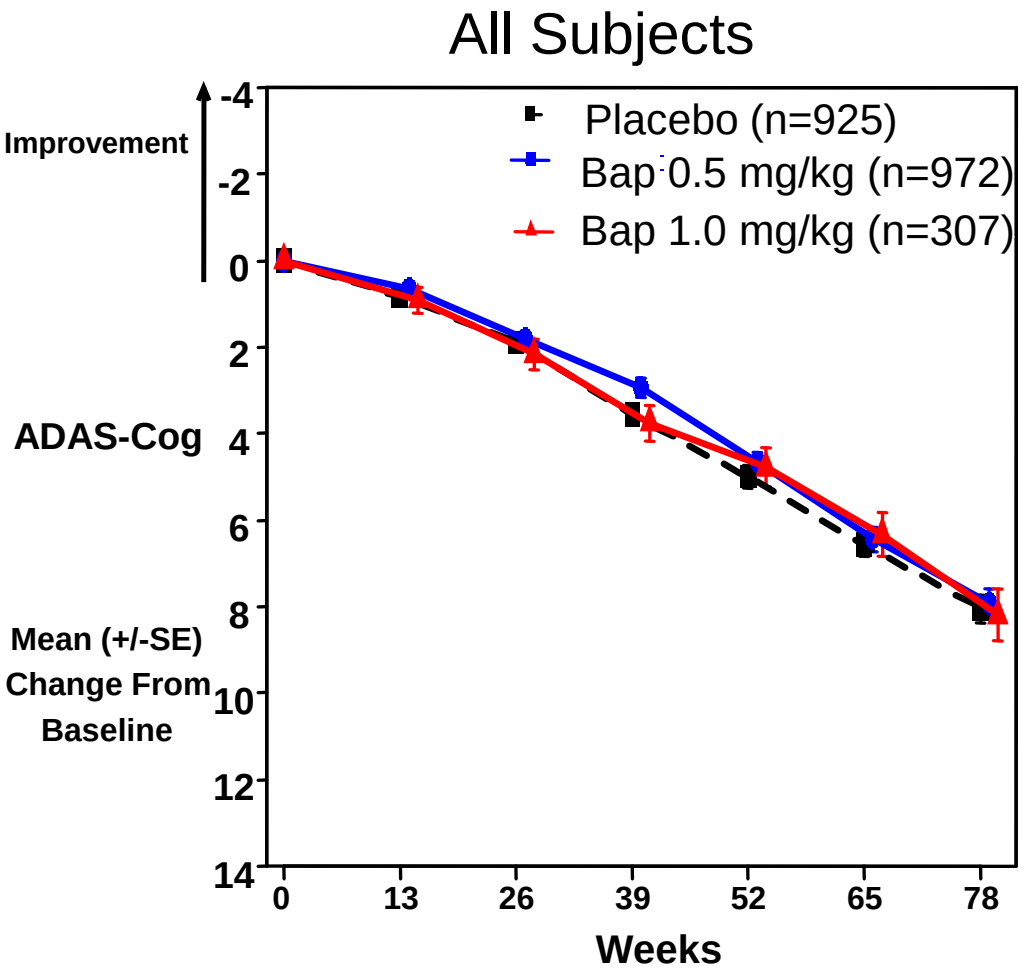


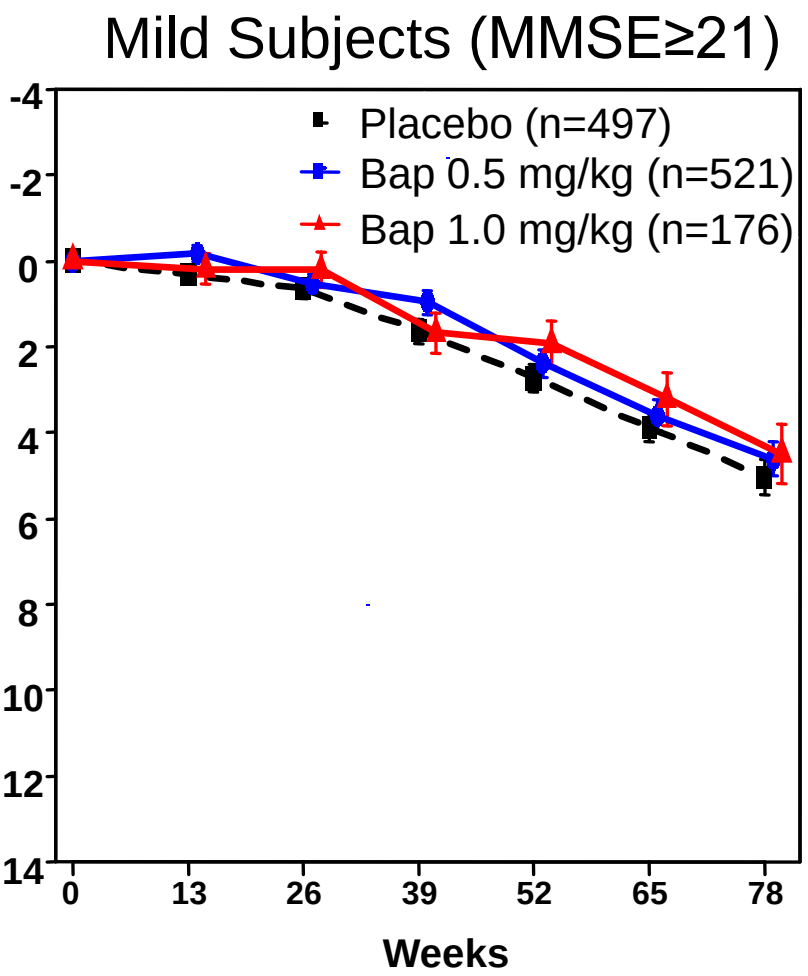
Placebo vs Bap 0.5 mg/kg **p=0.798**

Placebo vs Bap 0.5 mg/kg **p=0.642**
Placebo vs Bap 1.0 mg/kg **p=0.620**

MMRM (mixed model for repeated measures) analysis. Error bars represent 1 SE.

Pooled 302/301: Change in ADAS-Cog 11 by Treatment Group Over 78 Weeks (mITT population)

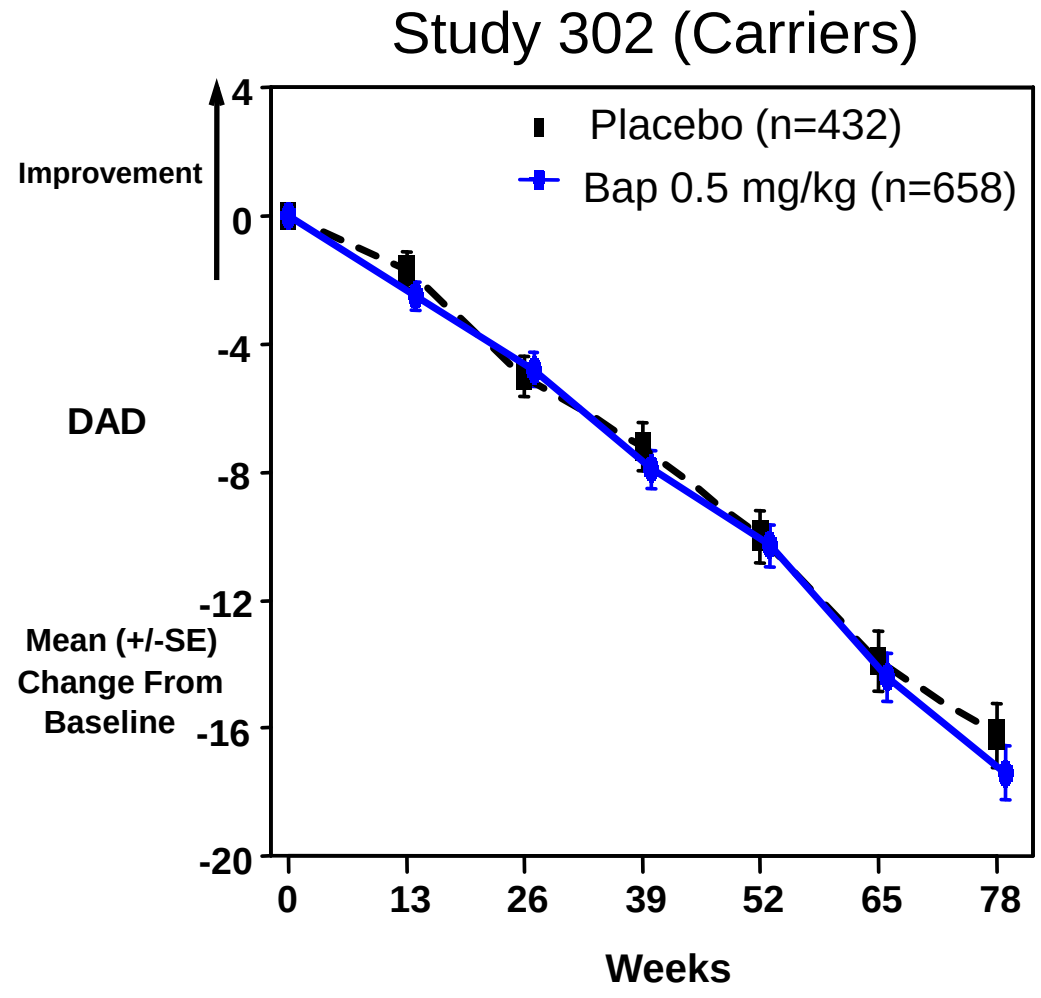


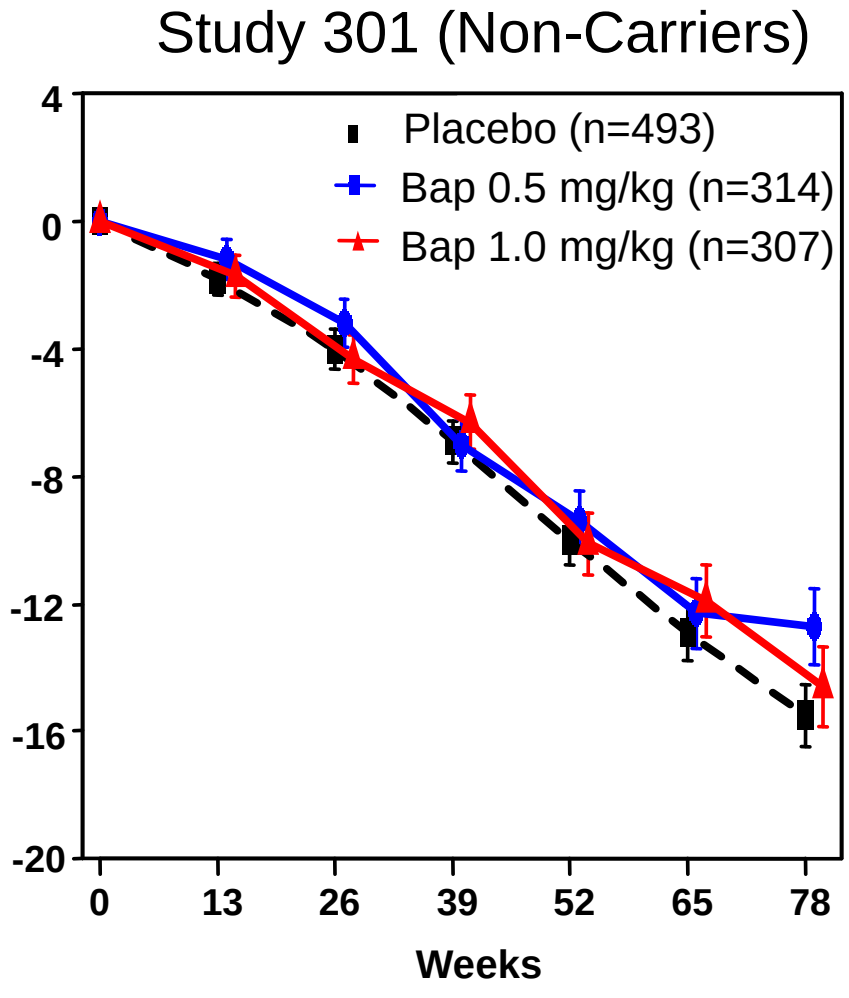


Placebo vs Bap 0.5 mg/kg **p=0.793**
Placebo vs Bap 1.0 mg/kg **p=0.842**

Placebo vs Bap 0.5 mg/kg **p=0.465**
Placebo vs Bap 1.0 mg/kg **p=0.513**

Change in DAD by Treatment Group Over 78 Weeks (mITT population)



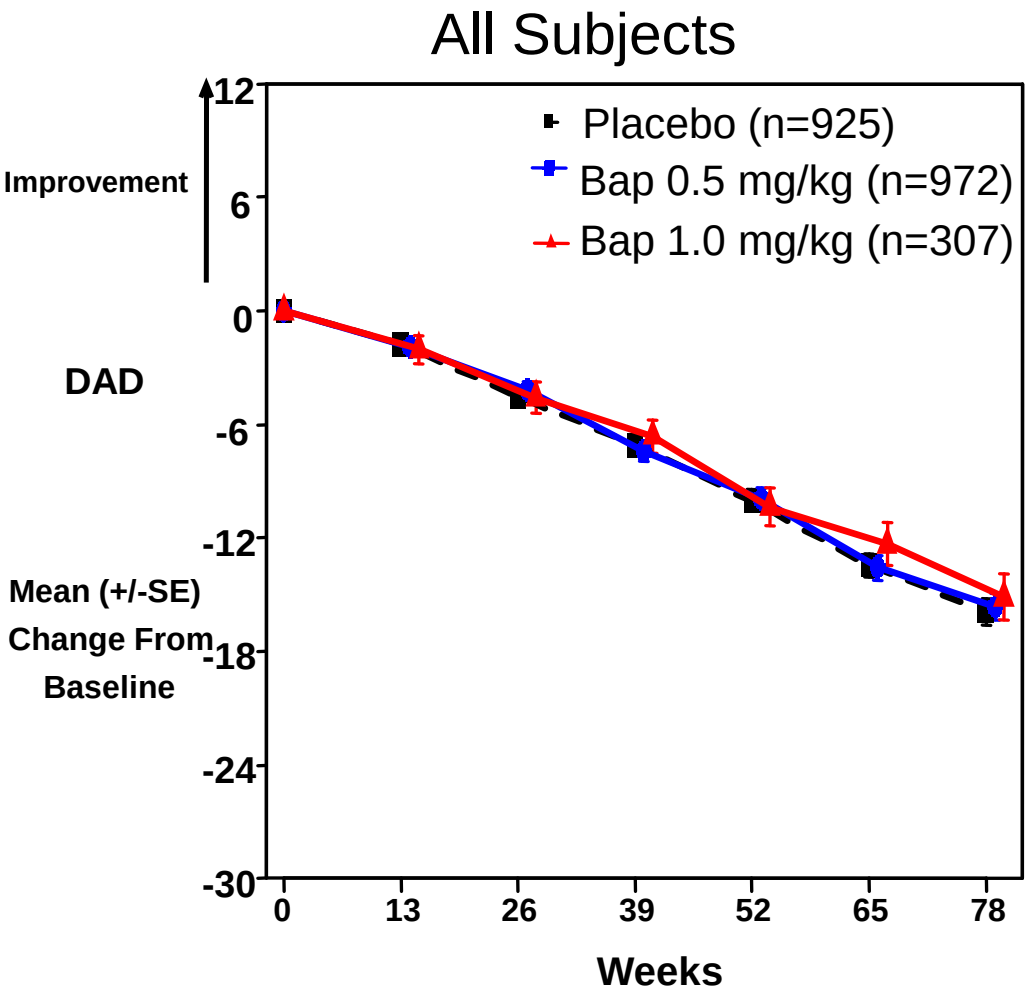


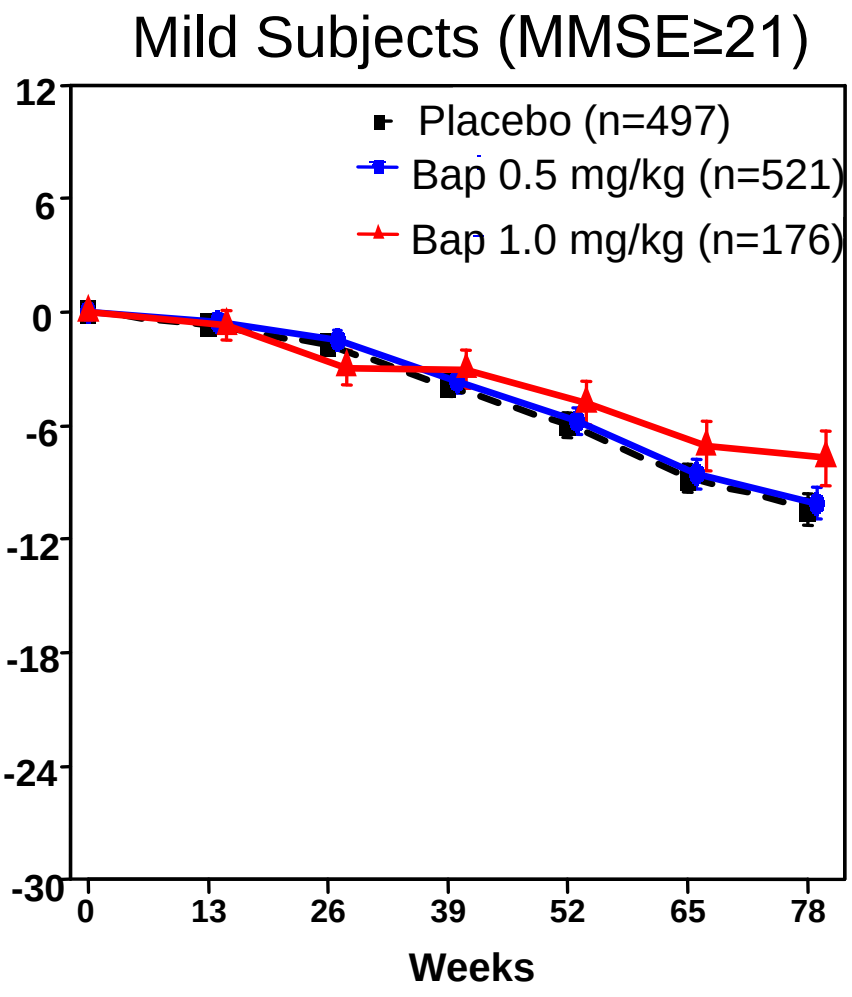
Placebo vs Bap 0.5 mg/kg **p=0.343**

Placebo vs Bap 0.5 mg/kg **p=0.067**
Placebo vs Bap 1.0 mg/kg **p=0.550**

MMRM (mixed model for repeated measures) analysis. Error bars represent 1 SE.

Pooled 302/301: Change in DAD by Treatment Group Over 78 Weeks (mITT population)



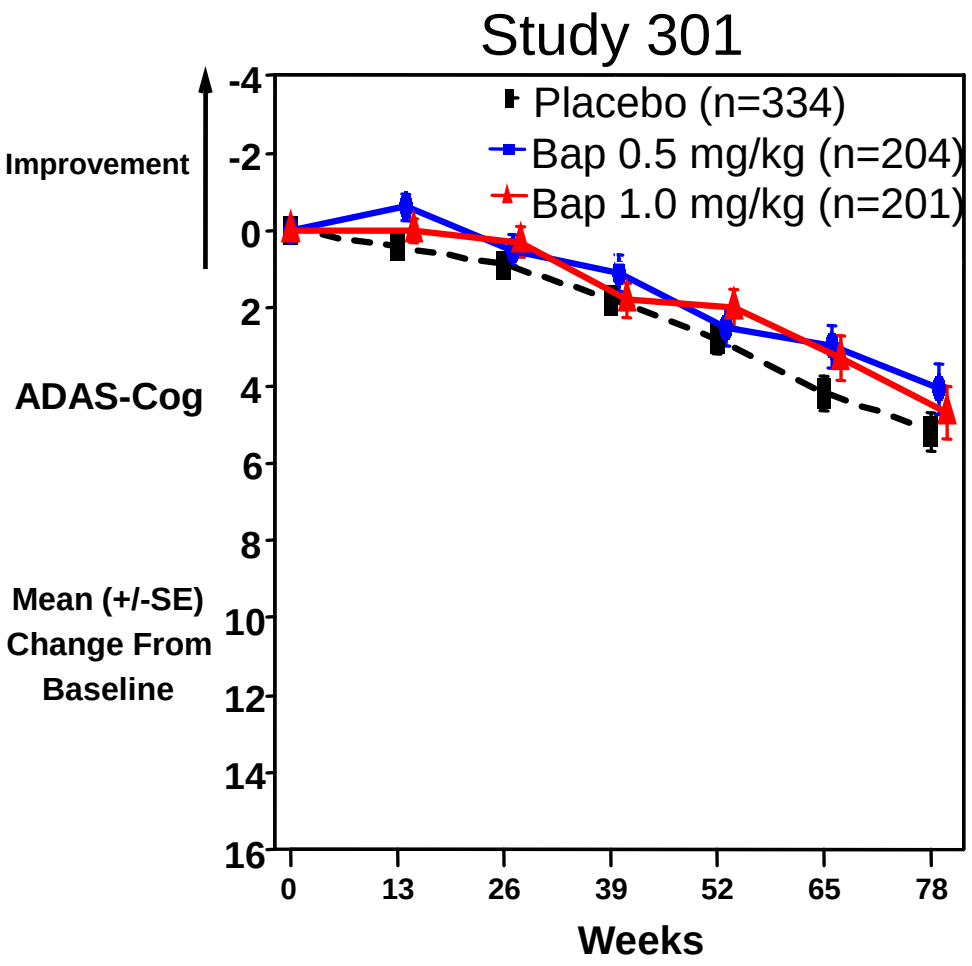


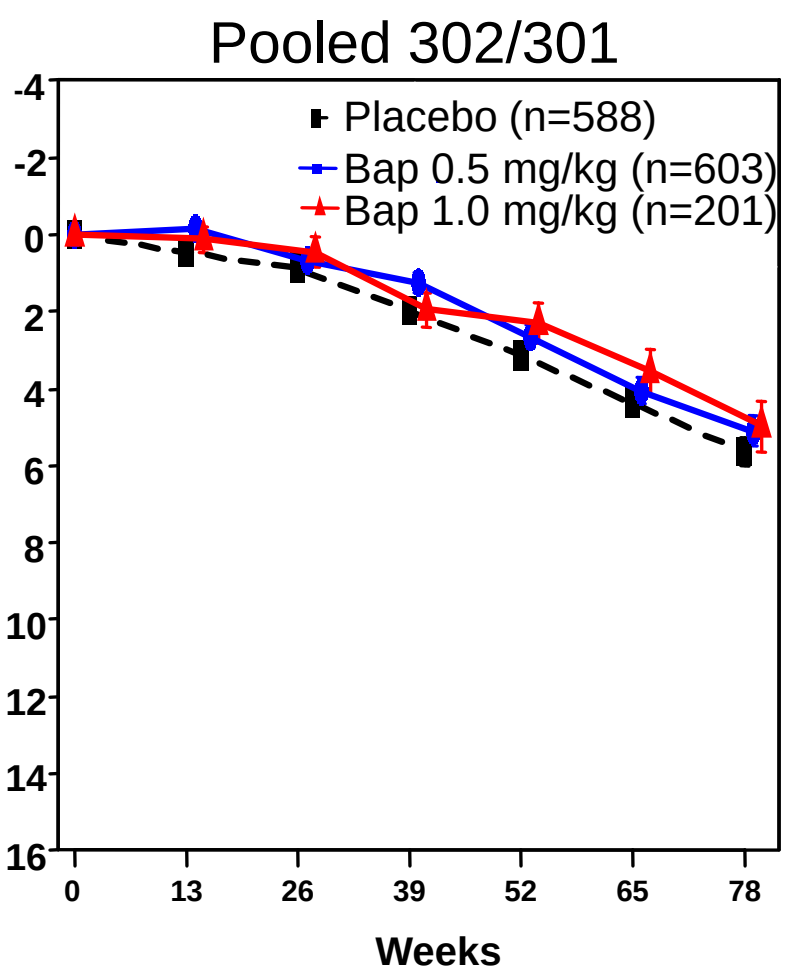
Placebo vs Bap 0.5 mg/kg **p=0.798**
Placebo vs Bap 1.0 mg/kg **p=0.567**

Placebo vs Bap 0.5 mg/kg **p=0.802**
Placebo vs Bap 1.0 mg/kg **p=0.098**

Analyses on ADAS-COG and DAD in Mild Subjects with MMSE≥20

Study 301 and Pooled 302/301: Change in ADAS-COG by Treatment Group Over 78 Weeks (mITT population) in Mild Subjects (MMSE≥20)



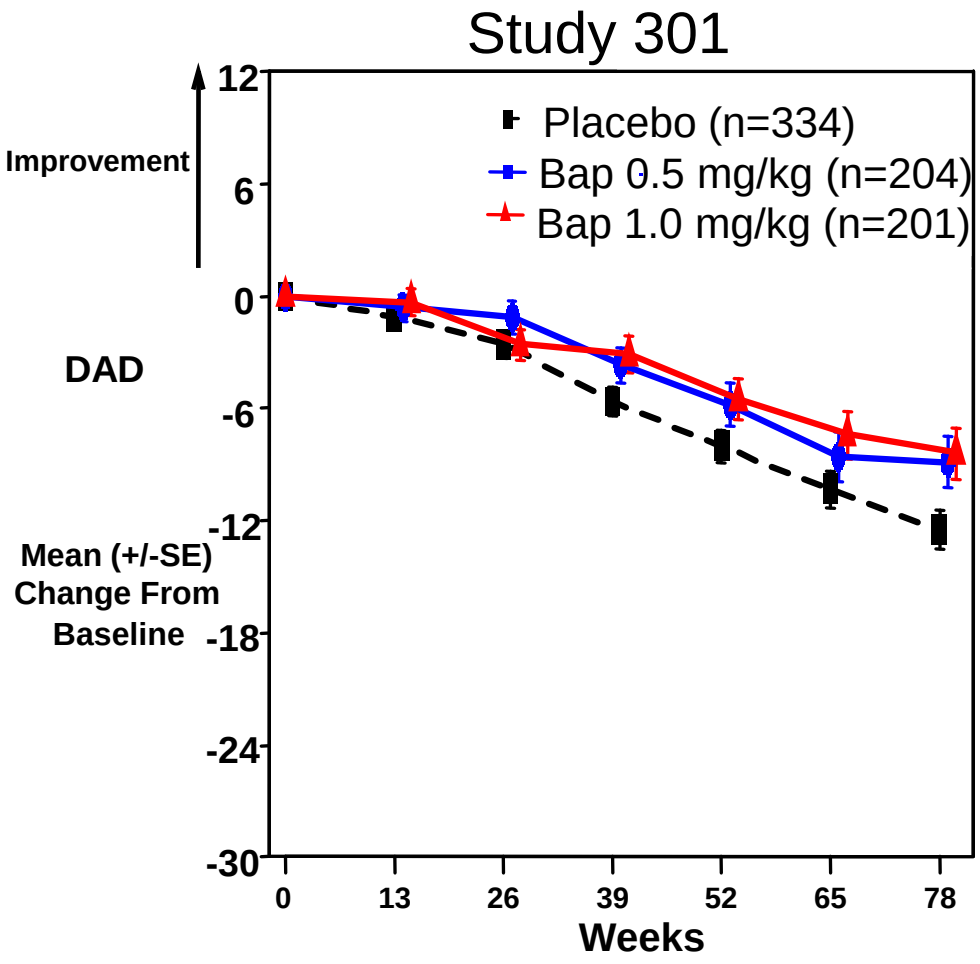


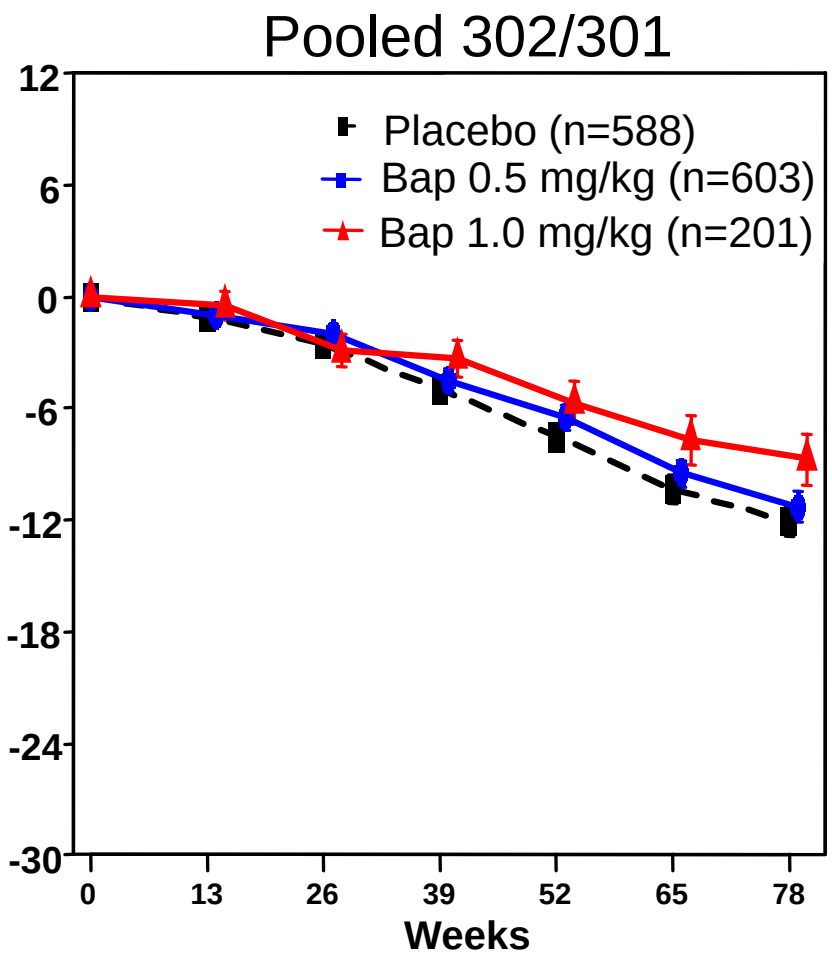
Placebo vs Bap 0.5 mg/kg **p=0.188**
Placebo vs Bap 1.0 mg/kg **p=0.513**

Placebo vs Bap 0.5 mg/kg **p=0.325**
Placebo vs Bap 1.0 mg/kg **p=0.389**

No differences observed in 302 study mild subjects (MMSE ≥20)

Study 301 and Pooled 302/301: Change in DAD by Treatment Group Over 78 Weeks (mITT population) in Mild Subjects (MMSE≥20)





Placebo vs Bap 0.5 mg/kg **p=0.042**
Placebo vs Bap 1.0 mg/kg **p=0.018**

Placebo vs Bap 0.5 mg/kg **p=0.505**
Placebo vs Bap 1.0 mg/kg **p=0.039**

No differences observed in 302 study mild subjects (MMSE≥20)

Secondary Clinical Endpoints

- **In the overall study population, no differences were seen in NTB, MMSE or CDR-SB in either study 302 or 301**
- **Analyses in mild and moderate subgroups are ongoing**

Data Summary

Co-Primary Clinical Endpoints:

- No treatment differences on ADAS-Cog or DAD compared to placebo among carriers, non-carriers, pooled studies, or pre-specified mild or moderate subgroups (MMSE≥21)

- Using an alternative mild/moderate MMSE cutpoint (MMSE≥20; pre-specified in SAP), potential treatment differences were observed on DAD ($p<0.05$) in non-carriers for both doses and when pooled across 302/301 for 1.0 mg/kg dose