Clinical Trial Designs To Demonstrate Long-Term Disease Progression in AD: Learning from the Past - Looking to the Future

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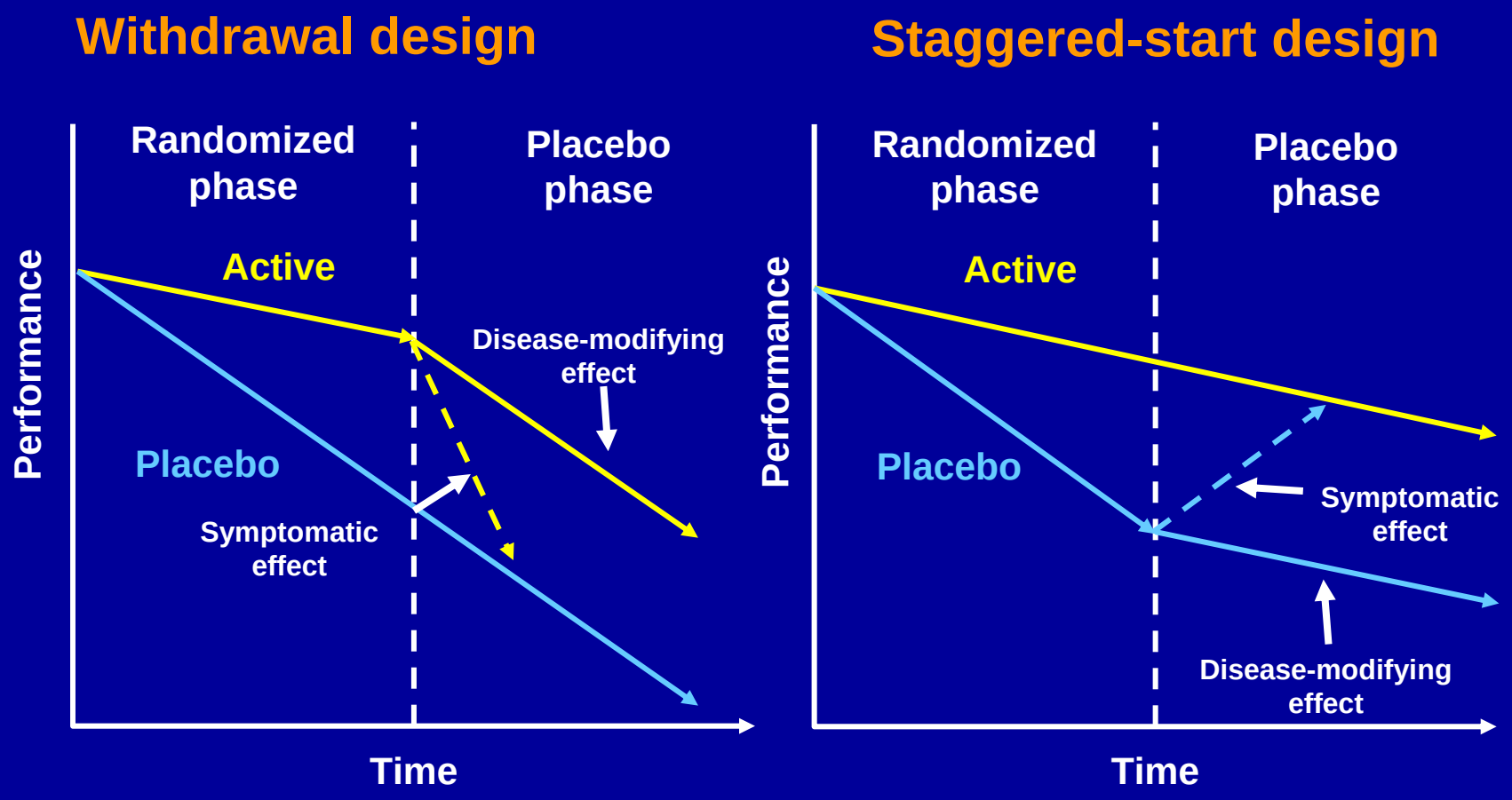
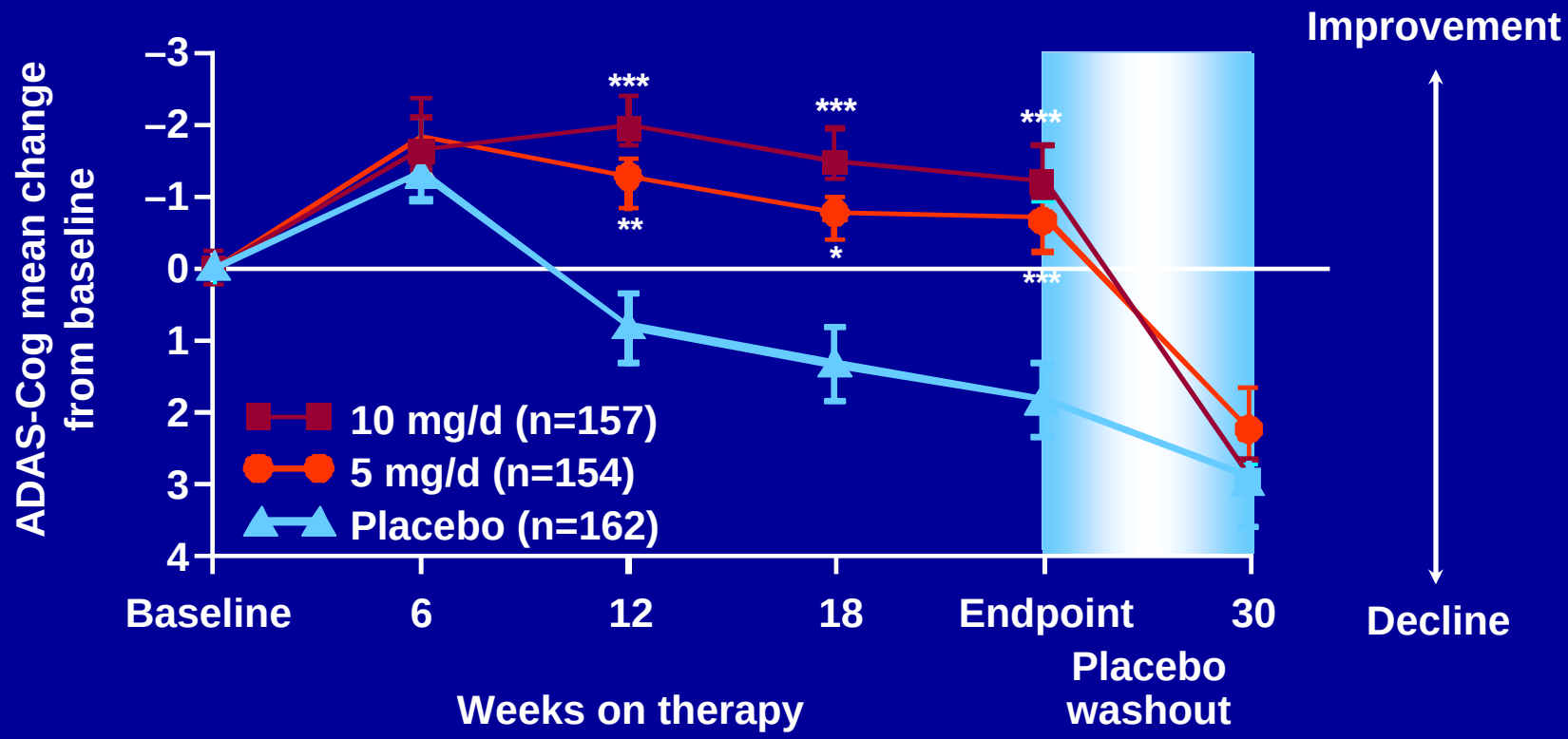
A Look Back At Methodology



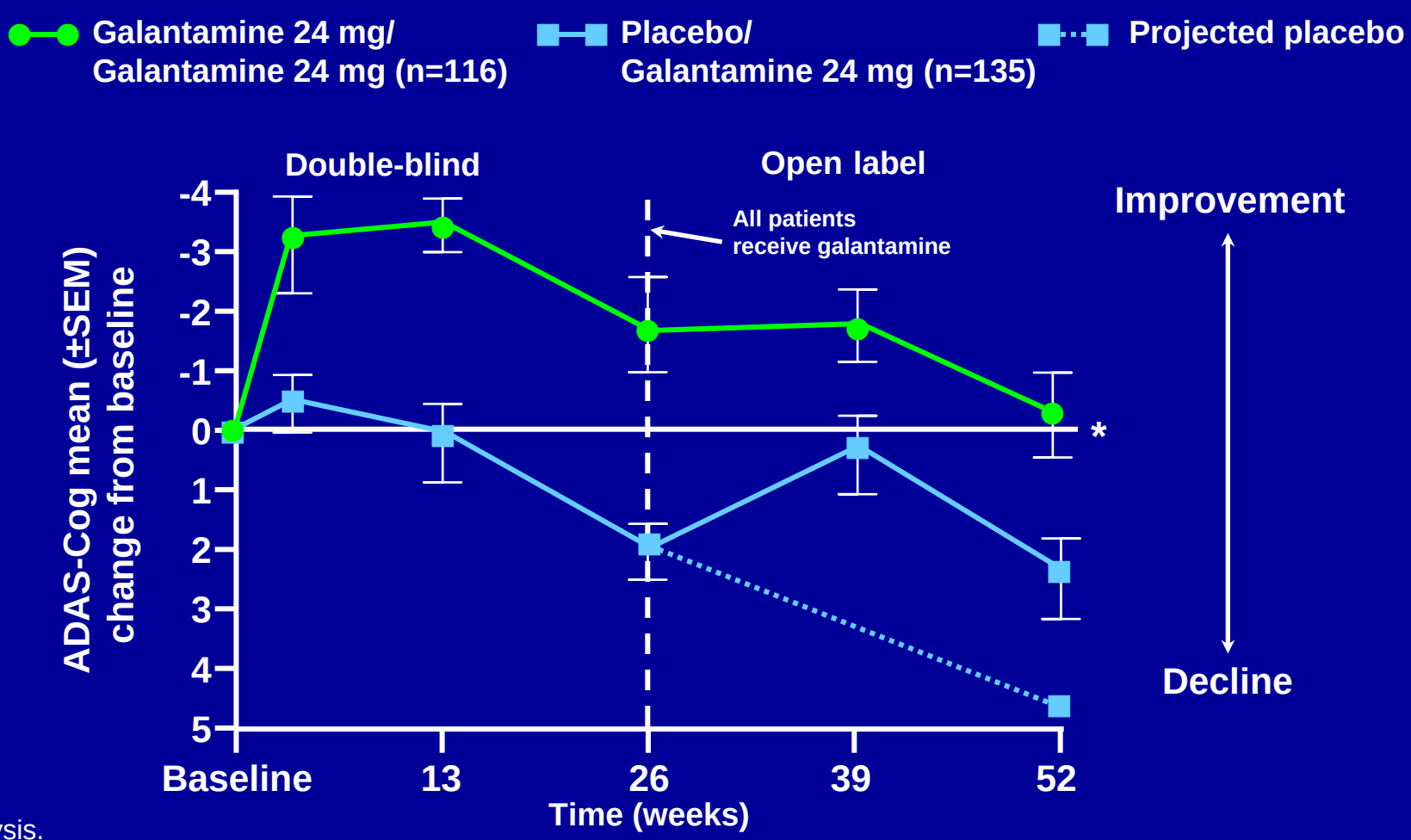
Leber, 1997

Effects of Donepezil on Cognition: ADAS-Cog (Mean MMSE 19)



*P<.0012; **P<.0007; ***P<.0001 vs placebo.
Rogers et al. 1998.

Long-Term Effects of Galantamine on Cognition: ADAS-Cog (MMSE 10-26)



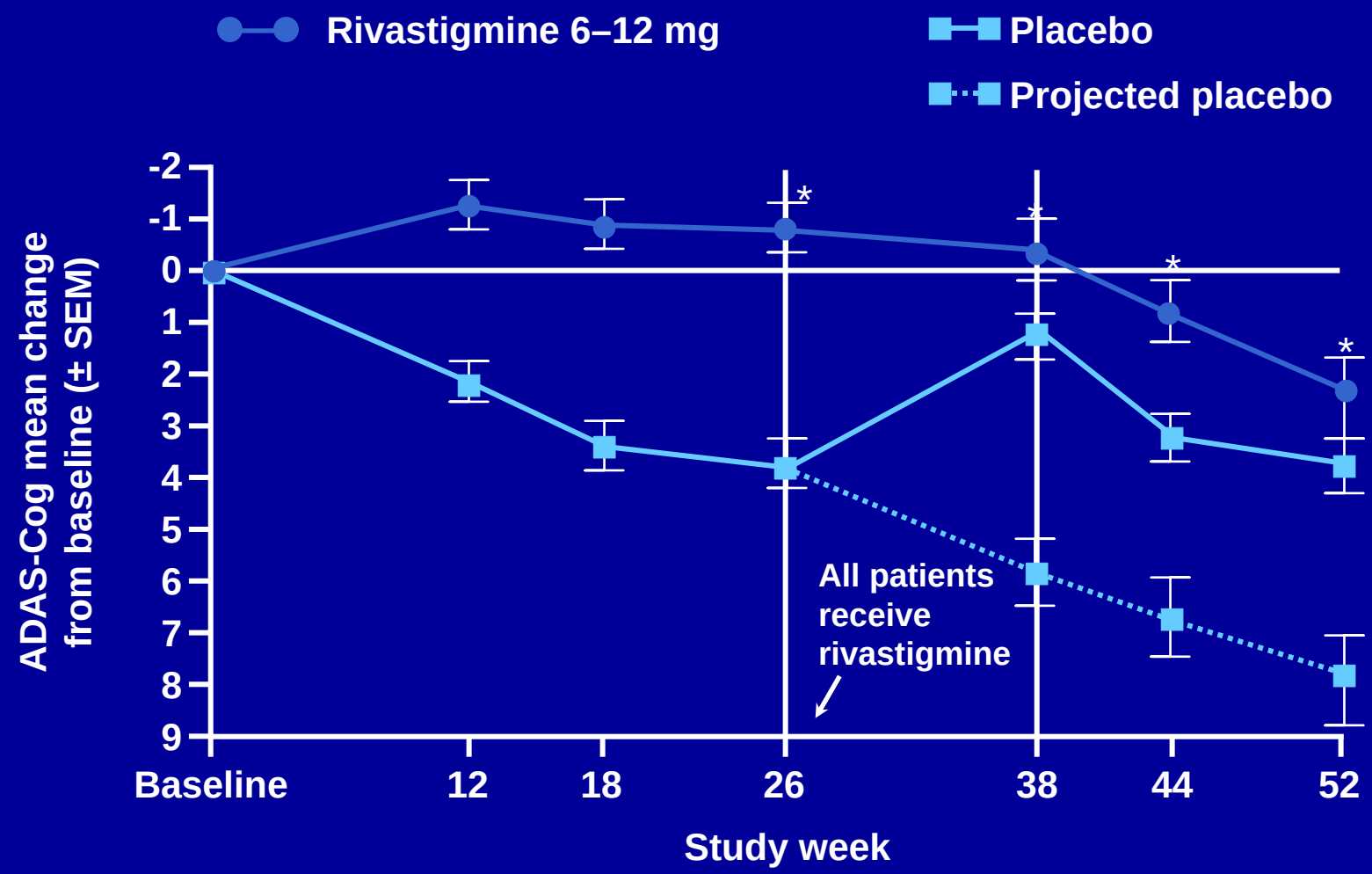
OC analysis.

*P=0.03 vs placebo/galantamine 24 mg/day.

ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive subscale.

Raskind et al, 2000.

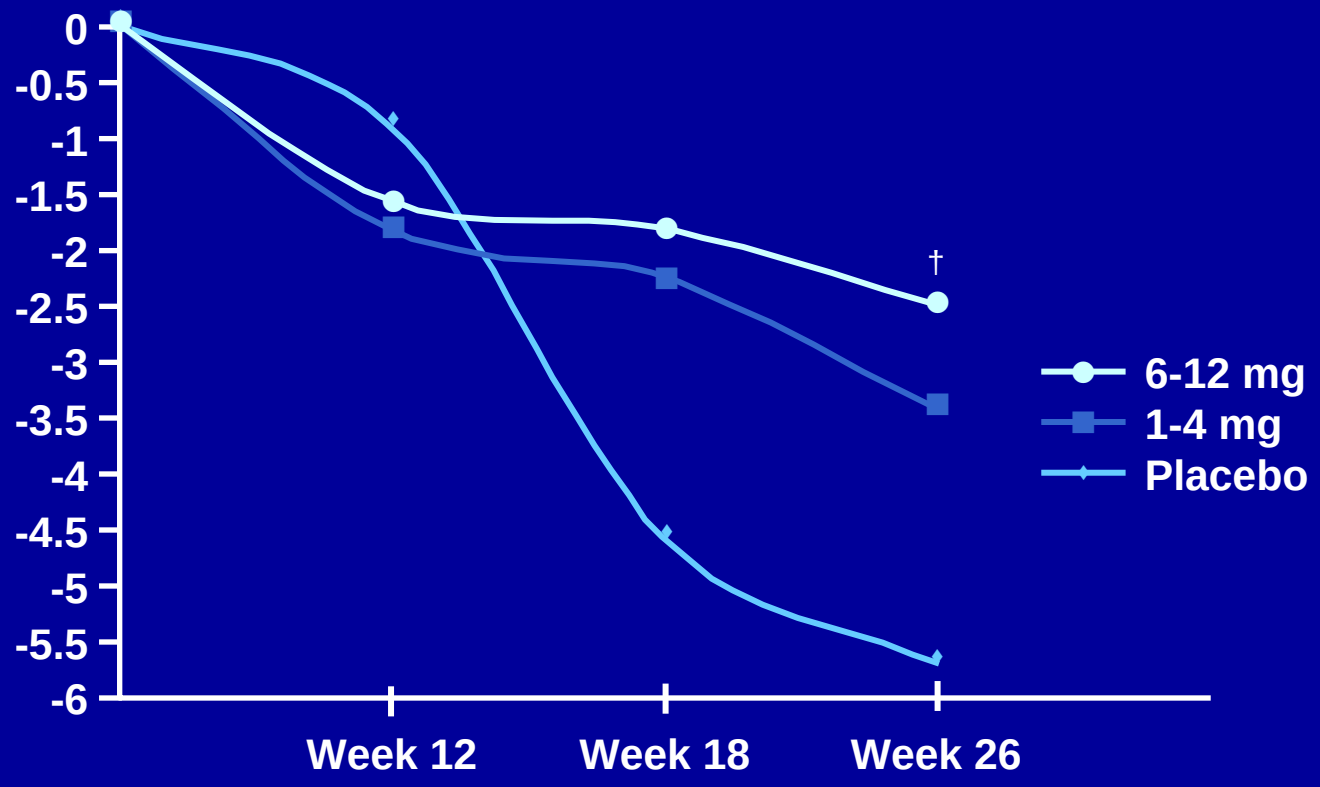
Long-Term Effects of Rivastigmine on Cognition: ADAS-Cog (MMSE 10-26)



*P<0.05 vs projected placebo.

Farlow et al, 2000.

Rivastigmine RDO Analysis: Mean Change From Baseline on ADAS-Cog



†*P*<0.05 compared to placebo.
Farlow, 2002

Looking to the Future

"We may not have the molecule or we may not have the methodology"

R. Anand MD - 2008

Challenges/Opportunities

- Need clinical measures with greater sensitivity than standard trial instruments
- Population enrichment – with risk factors – can yield more rapid progression to prespecified milestones
- Adaptive-dose response designs can shorten Phase II b studies
- Biomarkers including CSF tau & amyloid beta, amyloid + NFT PET, MRI maybe considered as alternative outcomes to clinical measures