The Food and Drug Administration's Accelerated Approval Process for New Pharmaceuticals: A Virtual Workshop

Scott S. Emerson, M.D., Ph.D.

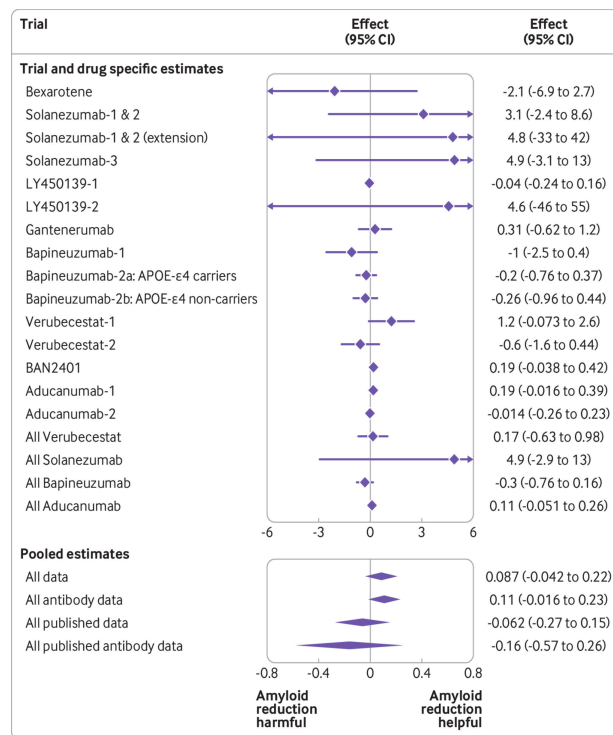Professor Emeritus of Biostatistics

University of Washington

National Academies of Sciences, Engineering and Medicine
January 30, 2023

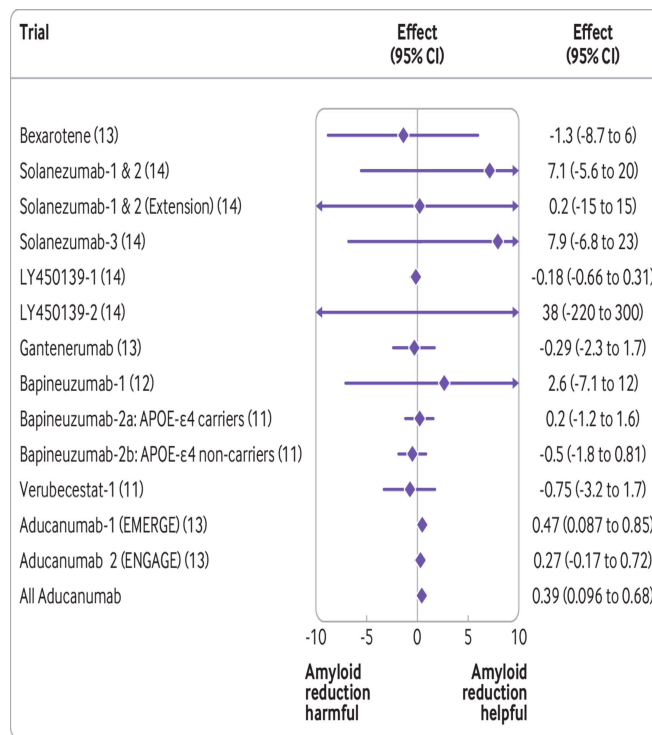# Meta-analyses cognitive decline vs amyloid reduction
- Estimated change in cognitive decline per 0.1 decrease in SUVR
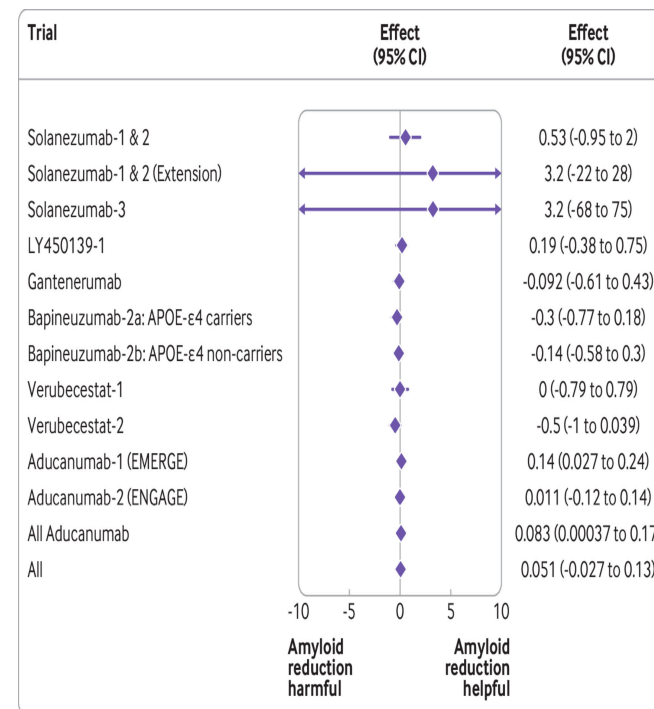
MMSE vs -0.1 SUVR (Fig 1)

ADAS-Cog vs -0.1 SUVR (fig 3)
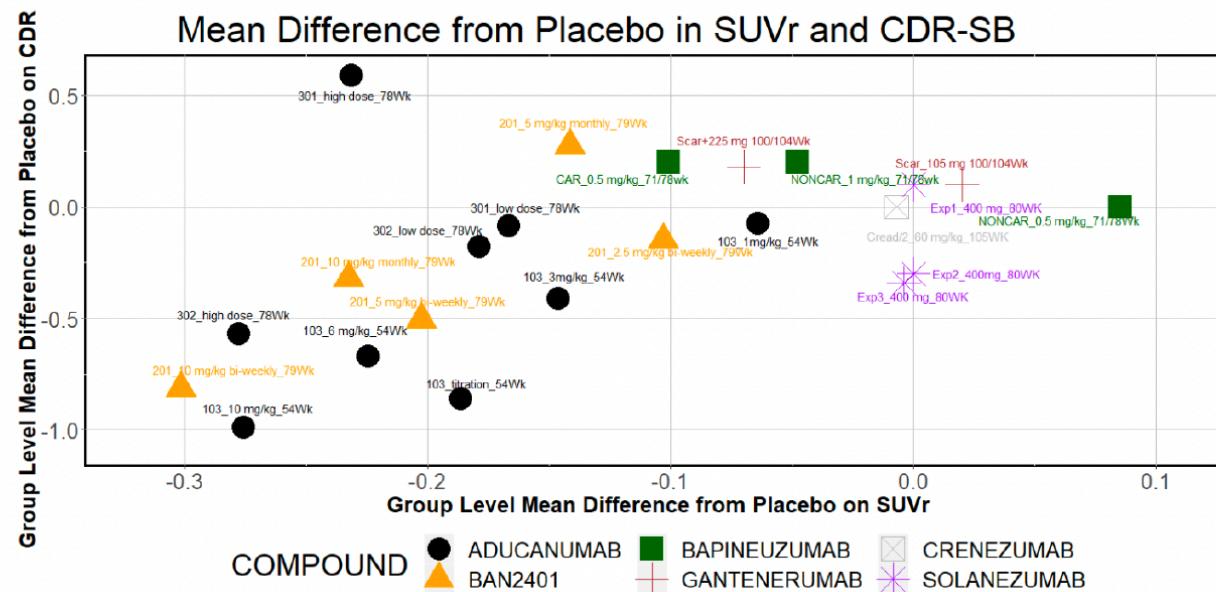
CDR-SB vs -0.1 SUVR (Fig 4)

FDA CDER Office of Clinical Pharmacology Review
- Association of Amyloid Plaque Reduction and Clinical Outcomes

https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000ClinPharm_Redacted.pdf

Figure 5 Group Level Comparison of Reduction in Aβ Plaque Burden (Described by SUVR (A.) and Centiloid (B.)) and Preserving of Clinical Function across All Available Programs of Anti-Aβ Antibodies under Development. Multiple dose levels for each drug candidate are presented.

General Comments re Surrogacy

- Best approach: Meta-analysis across (relevant?) classes of drugs
  - Surrogacy at Individual vs group level
  - Slopes, not correlation

- But still, many places to go astray, including:
  - Need to be clear on measure of clinical endpoint
  - Need to be clear on measure of surrogate
  - Need to include unbiased data from all (available) studies
  - Need to try to assess random effects of drugs / classes
  - Need to understand linearity of associations