A Placebo-controlled, Double-blind Trial of the Selective Aβ-42 Lowering Agent, MPC-7869 (*R*-flurbiprofen) in Patients with Mild to Moderate Alzheimer's Disease

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*Disclosure: In the past 2 years, GW has been a paid consultant for Eisai, Johnson & Johnson, Lundbeck, Marix Drug Development, Myriad Pharmaceuticals, Novartis, Pfizer, and Shire.

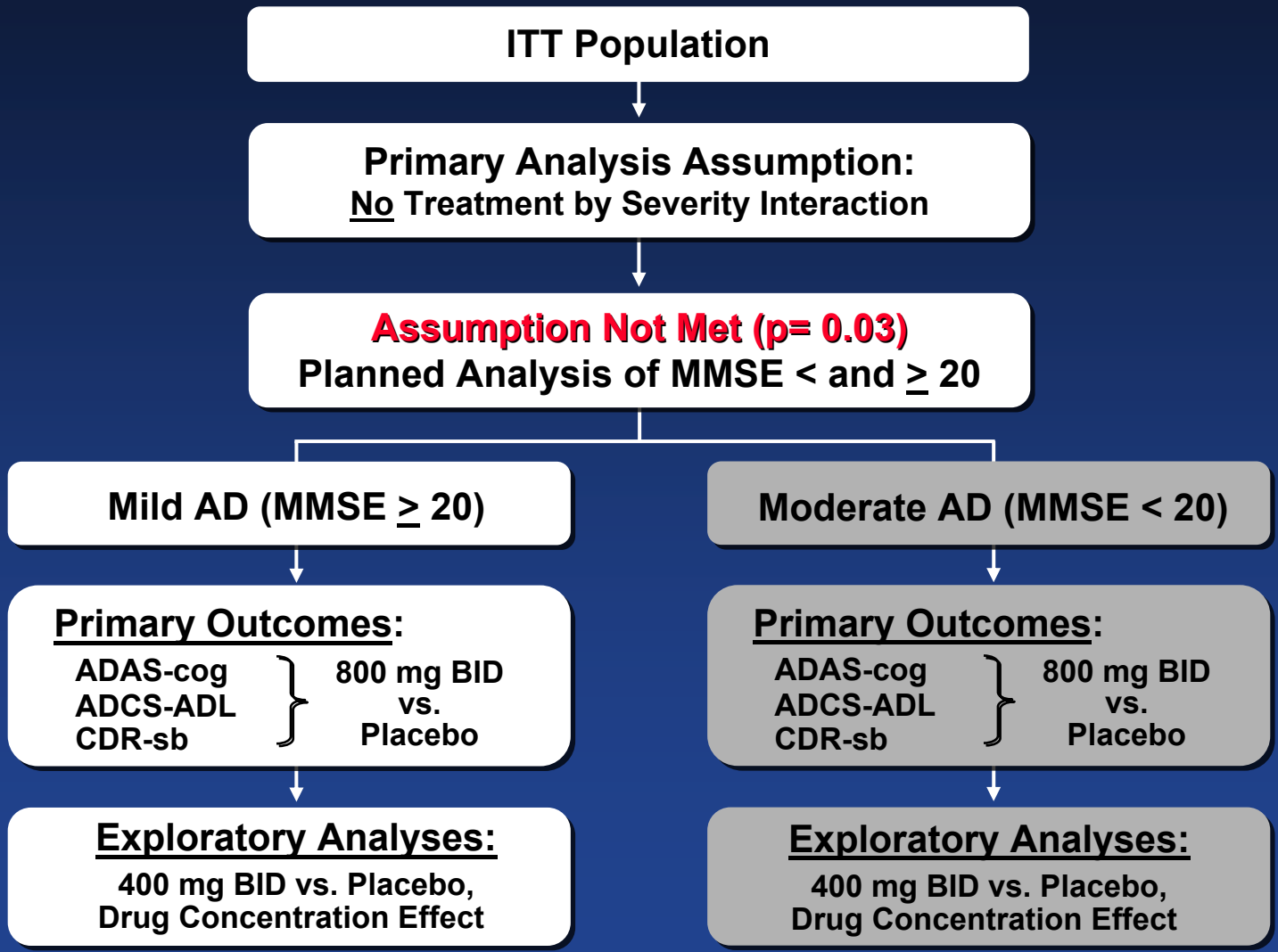
MPC-7869 Clinical Rationale

- Selective Aβ42-lowering agent *in vitro* & *in vivo*
  - Allosteric modulation of γ-secretase
- Reduces insoluble amyloid in mouse brain
- Improves spatial reference learning and memory performance in mice
- Effective concentrations achievable in humans at clinically safe doses

Phase 2 Study of MPC-7869 in Subjects with Mild to Moderate AD (MMSE 15-26)

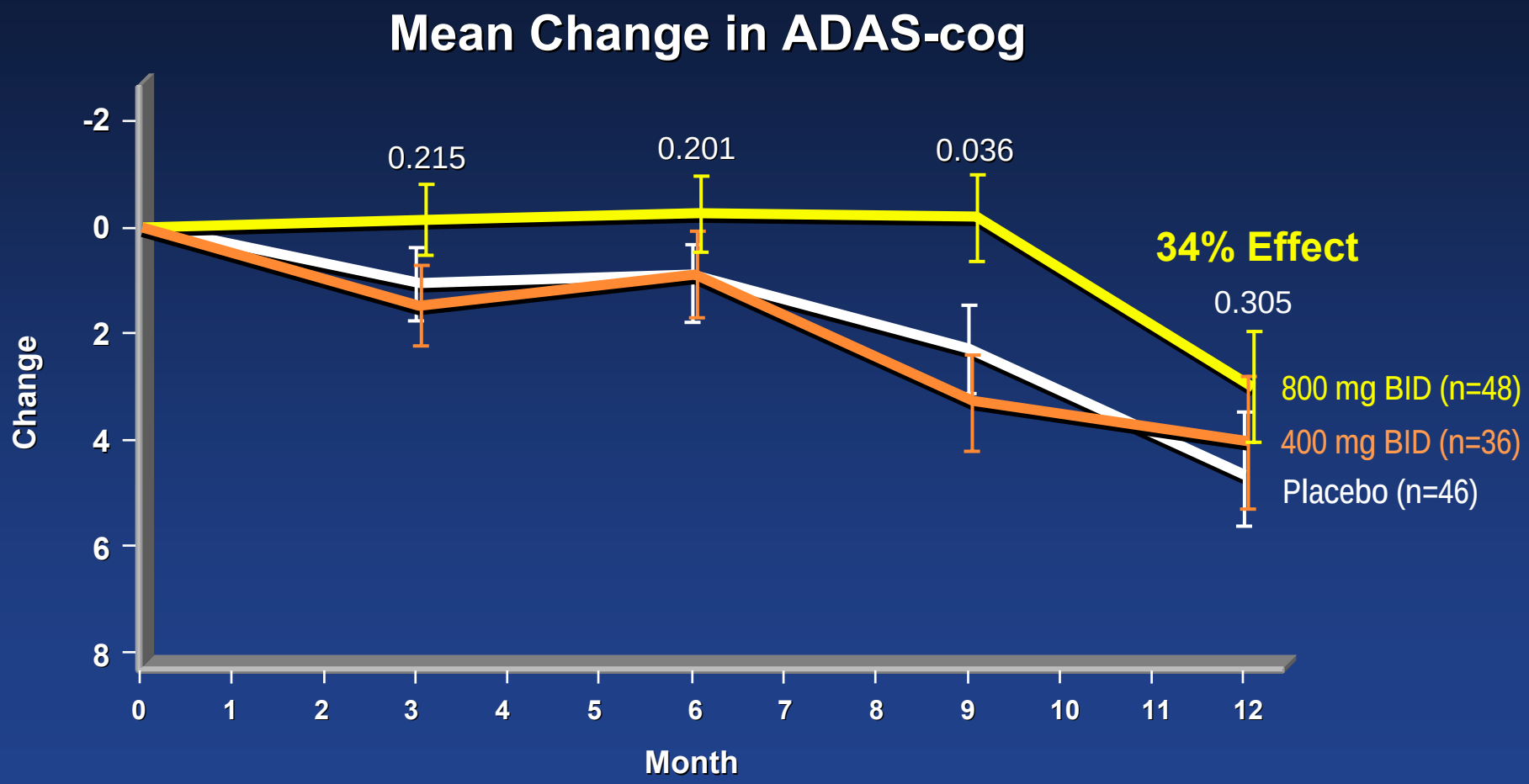
- Multi-centre, Randomized, Double-Blind, Placebo-Controlled
- 207 Subjects in 3 treatment groups (1:1:1)
  - 400 mg BID
  - 800 mg BID
  - Placebo BID
- 12 months treatment / stable ChEI allowed
- ADAS-cog; ADCS-ADL;CDR Sum of Boxes
- 31 sites in Canada and the United Kingdom

Prospective Statistical Analysis Plan



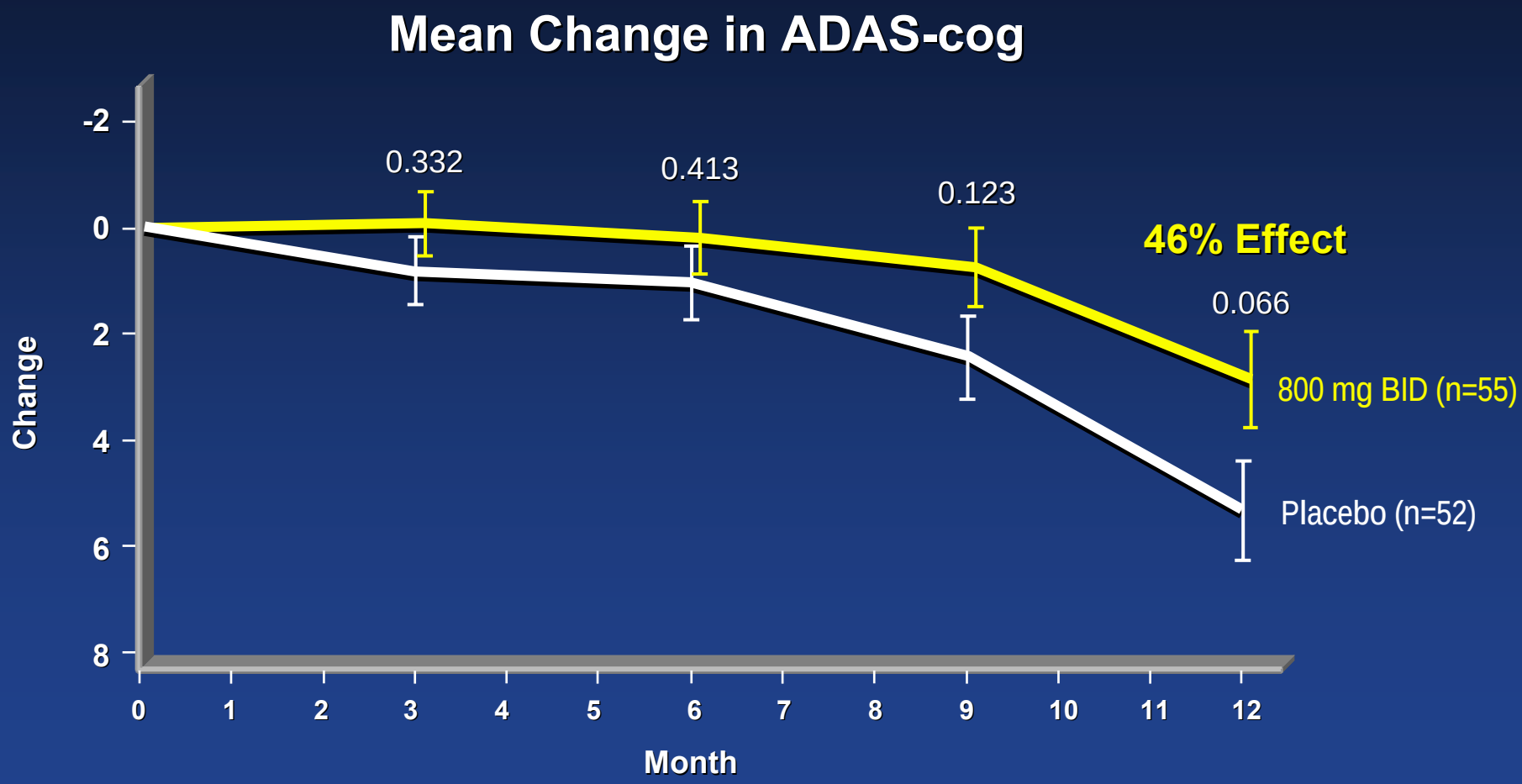
Cognition—Mild Subjects*

(800mg BID group, n=48, 73% of total)



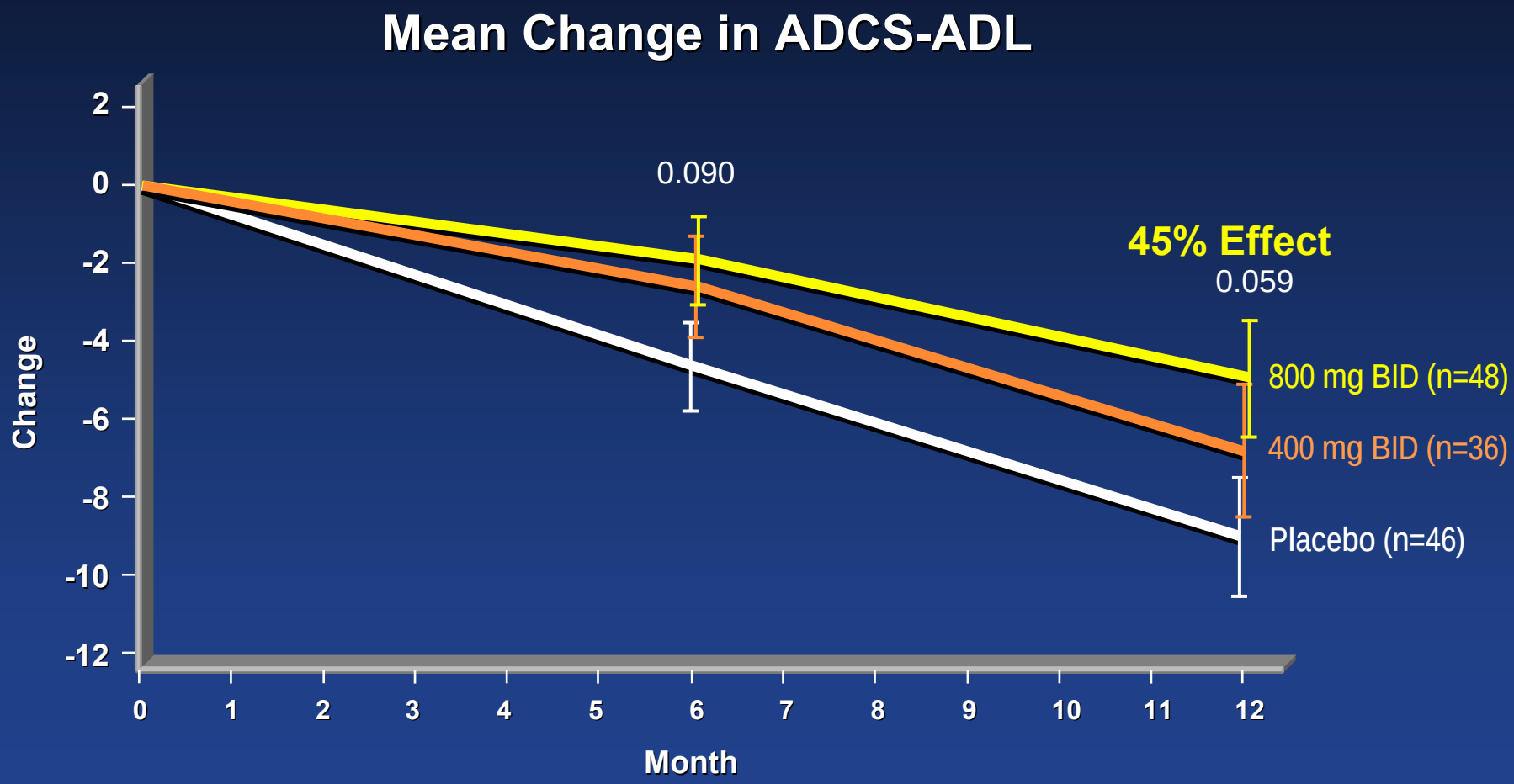
*MMSE ≥ 20 Score Patients Over Time, LOCF

Cognition—Mild Subjects (ADAS-cog <40)
(800mg BID group, n=55, 83% of total)



MPC-7869

Activities of Daily Living—Mild Subjects*



*MMSE ≥ 20 Score Patients Over Time, LOCF

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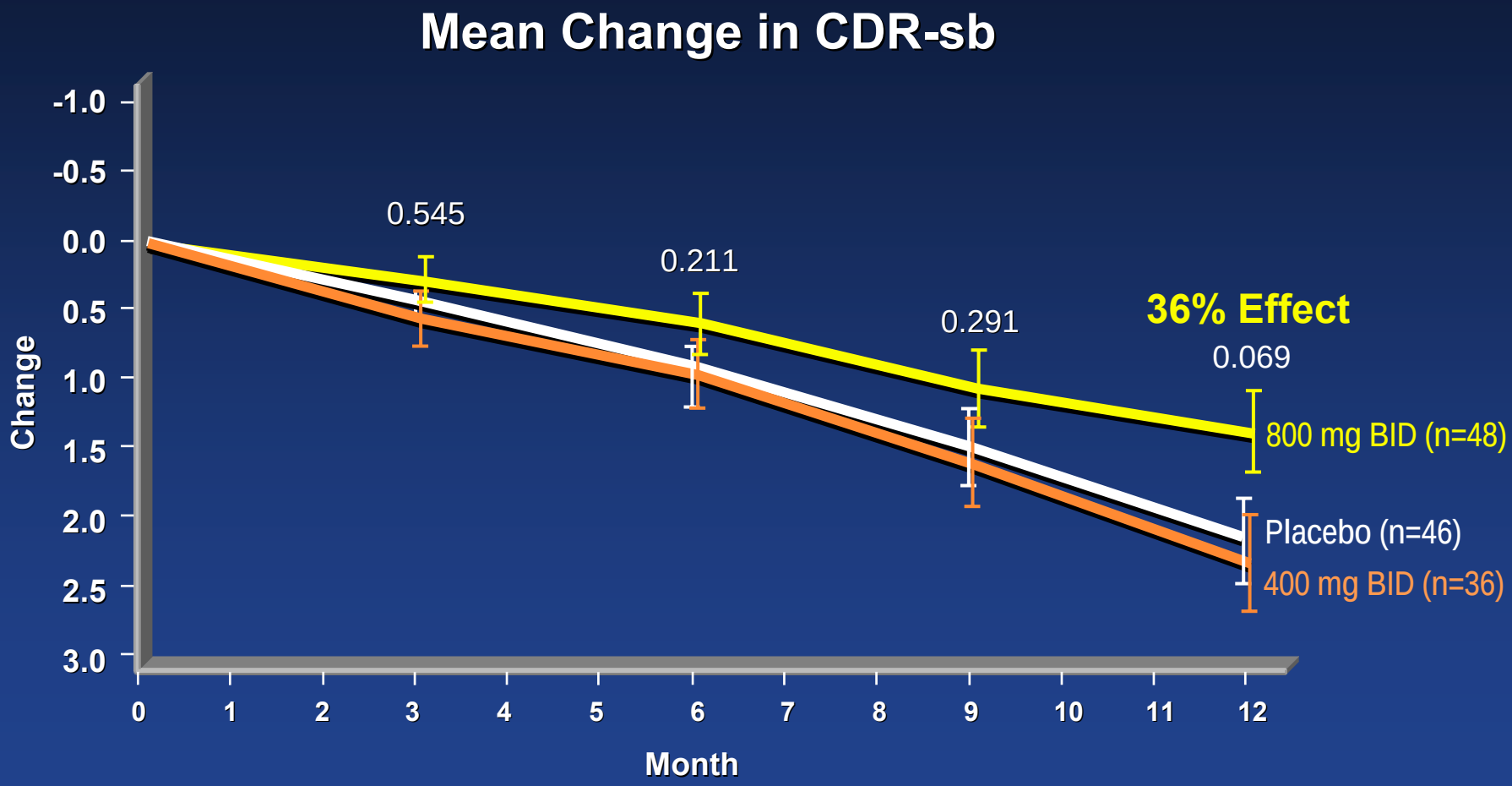
Global Function—Mild Subjects*



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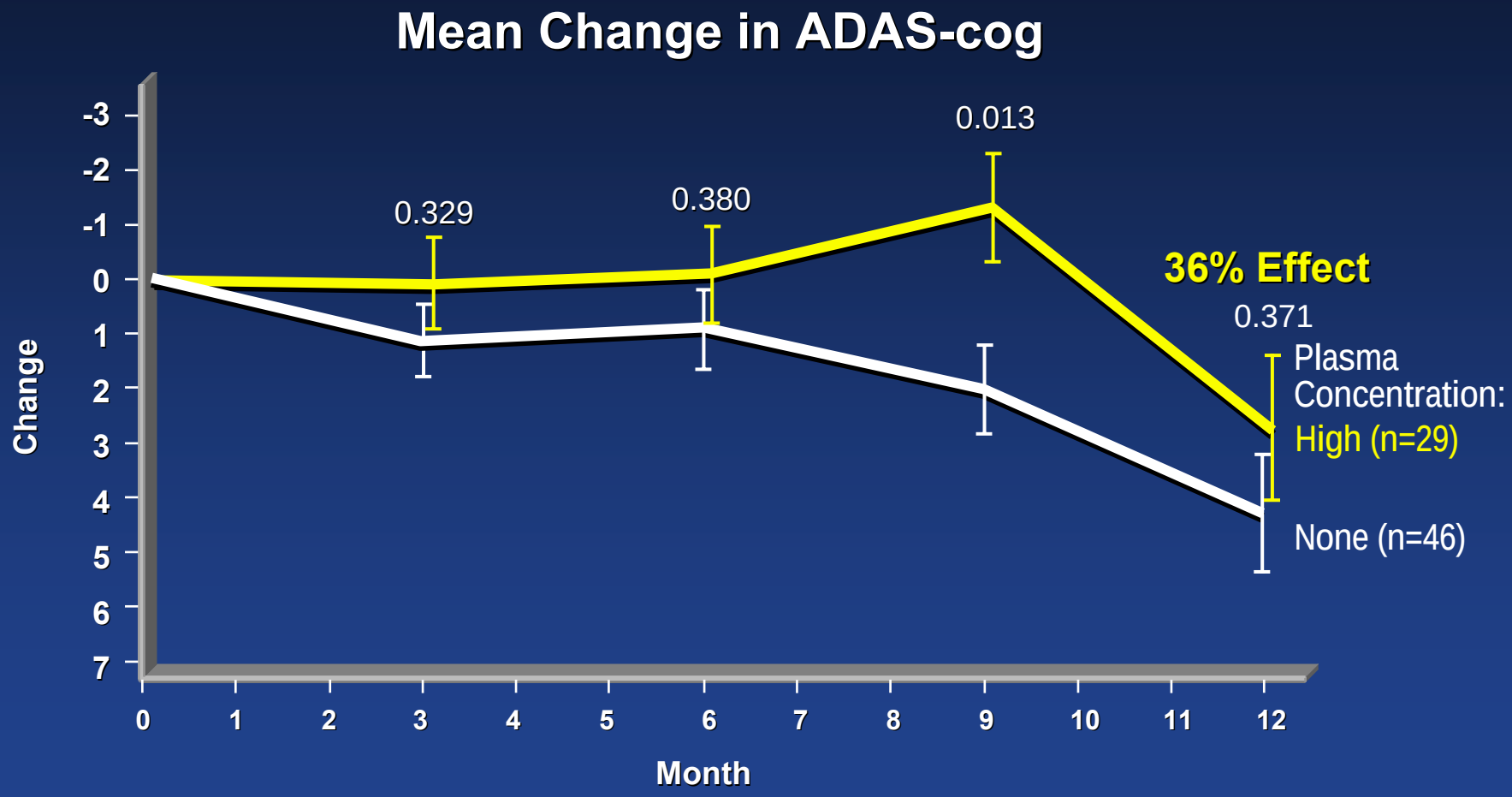
Exploratory: Drug Concentration Effect

- There was a significant plasma concentration response relationship (p= 0.038)
- High concentration was defined as plasma drug concentration above 75 µg/ml
- 29 mild patients had high drug concentrations (60% of 800 mg BID group)

Cognition—Mild Patients*, High Plasma Drug Group



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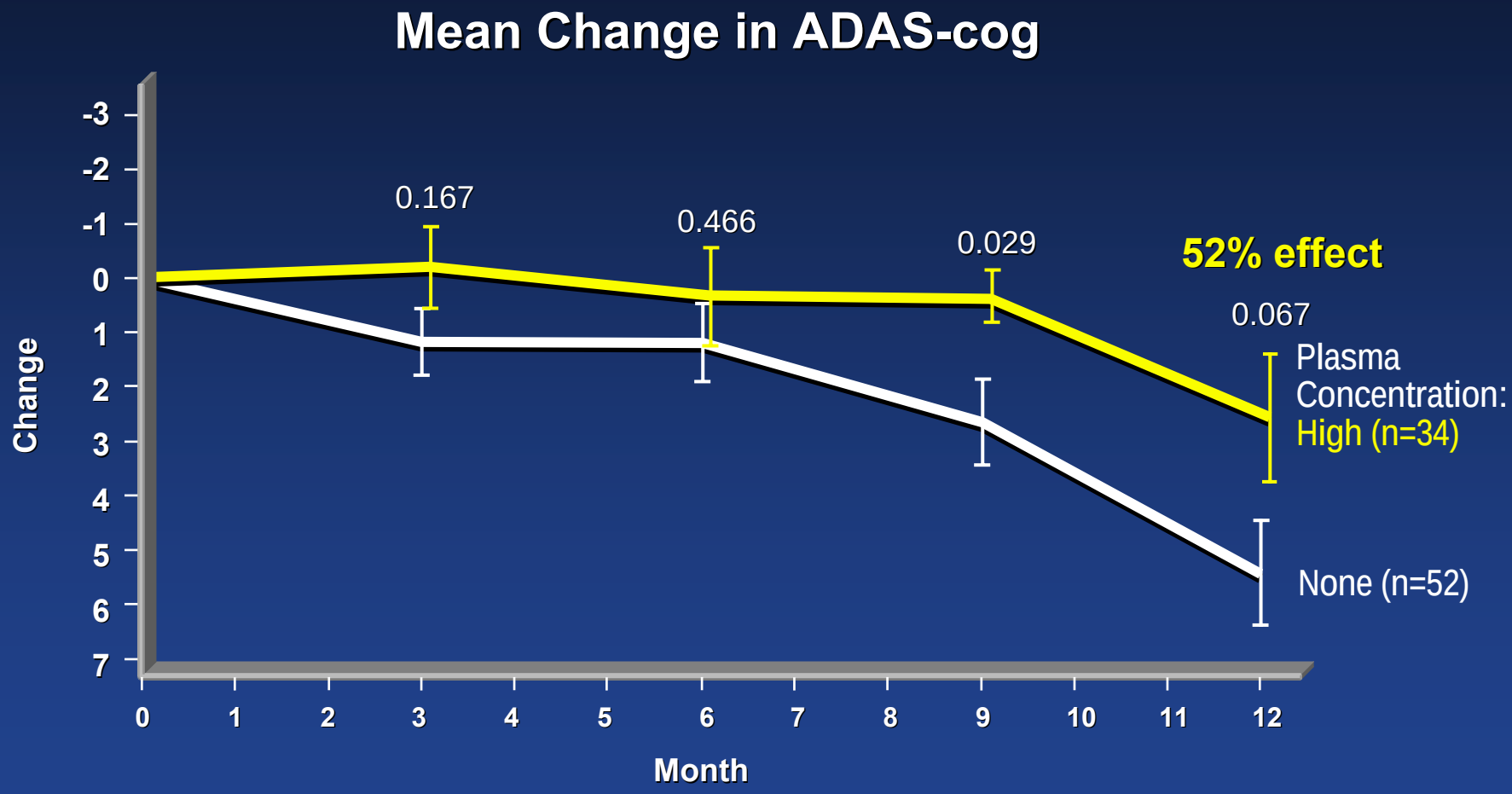
Cognition—Mild (ADAS-cog < 40), High Plasma Drug Group



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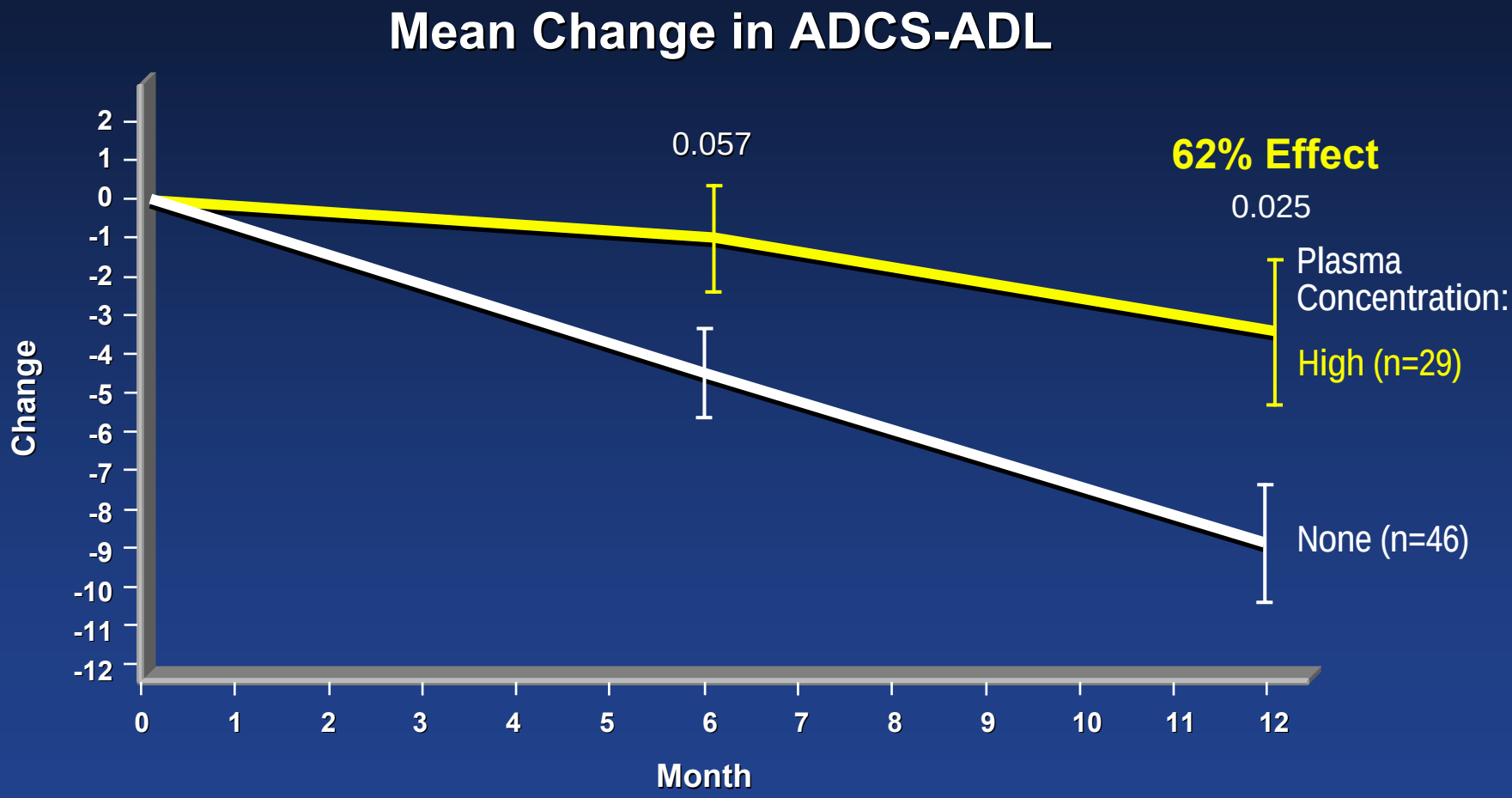
Activities of Daily Living— Mild Patients*, High Plasma Drug Group



*MMSE ≥ 20 Score Patients Over Time, LOCF

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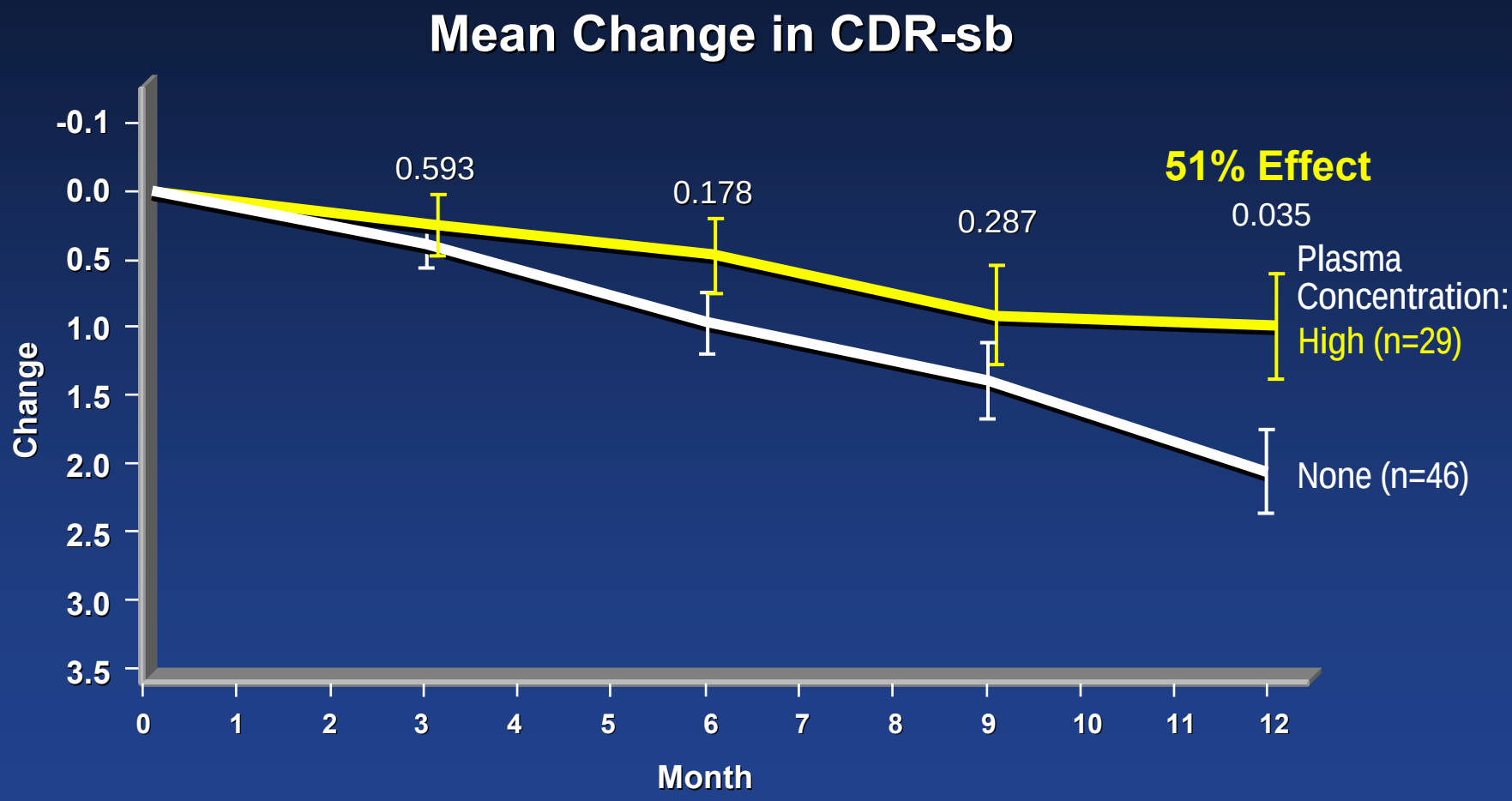
Global Function—Mild Patients*, High Plasma Drug Group



*MMSE ≥ 20 Score Patients Over Time, LOCF

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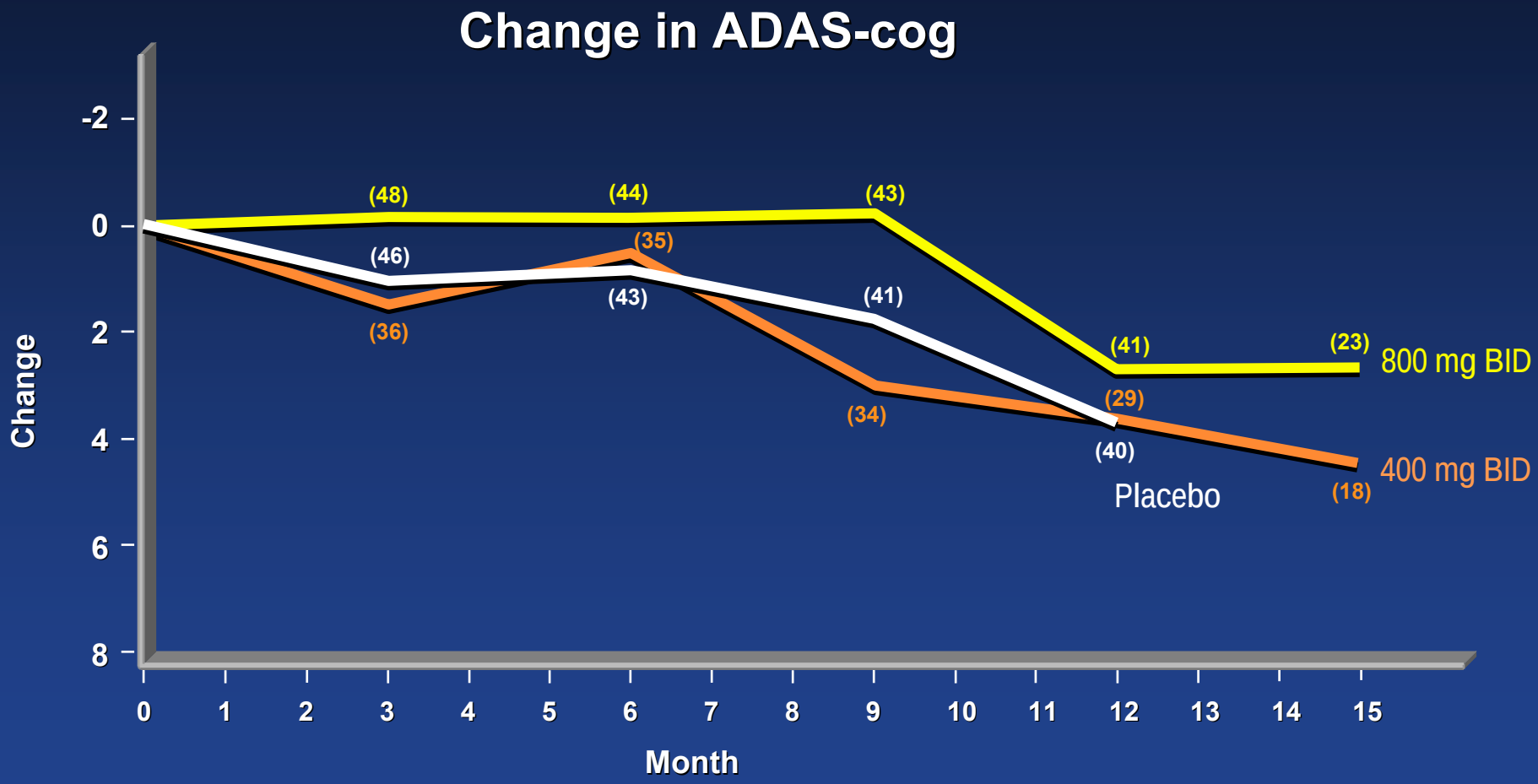
Optional Follow-on Study

- Optional follow-on study available to subjects in Canada
- 86 of 106 eligible subjects enrolled for additional 12 months treatment
  - Placebo subjects randomized to 400mg or 800mg BID
  - 400mg and 800mg BID subjects continue treatment
- Treatment groups remain blinded to subject/investigator
- 15 month ADAS-cog data available

Cognition—Mild Subjects*

Observed Cases (Including 15 month follow-on)



*MMSE ≥ 20 at Baseline

MPC-7869

Effect of MPC-7869 in Subjects with Mild to Moderate AD Over 12 Months

Phase 2 Summary:

- Mild subjects responded; moderate subjects did not
- Mild AD subjects on 800 mg twice daily showed positive trends in all 3 outcome measures (not statistically significant)
- Mild AD subjects with the highest blood levels of MPC-7869 :
  - showed statistically significant benefits in Activities of Daily Living and Global Function
  - Positive trends, not statistically significant, in Cognition
- No significant safety concerns (transient eosinophilia)