Dimebon Improves Cognition, Function, and Behavior in Mild and Moderate Alzheimer's Disease: Results by Severity of a One-Year, Double-Blind, Placebo-Controlled Study

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BACKGROUND

- Dimebon is an orally available investigational drug shown to have neuroprotective effects in models relevant to Alzheimer's disease (AD) and Huntington's disease.
- Dimebon improved cognition, functional ability, and behavior as compared to placebo in a 1-year, double-blind, placebo-controlled study of patients with mild-to-moderate AD.[1]
- The most potent mechanism of action for Dimebon identified to date is enhancement of mitochondrial function in the setting of cellular stress.

METHODS

- The study design and methods have been previously published.[1]
- 183 patients with mild-to-moderate AD (MMSE of 10-24) were randomized to receive Dimebon 20 mg TID or matching placebo for 26 weeks. After the initial 26 weeks, patients were offered the opportunity to remain on their blinded study drug for an additional 26 weeks (1-year double-blind total treatment period).
- Standard inclusion and exclusion criteria were utilized, although patients enrolled were not on any background anti-dementia therapy.
- Efficacy endpoints included the Alzheimer's Disease Assessment Scale—cognitive subscale (ADAS-cog); Clinician's Interview-Based Impression of Change, plus Care-giver Input (CIBIC-plus); Alzheimer's Disease Cooperative Study—Activities of Daily Living (ADCS-ADL); Mini-Mental State Examination (MMSE); and Neuropsychiatric Inventory (NPI).
- For the mild and moderate subgroup analyses, patients with mild AD were defined as those with a baseline MMSE > 18 (n = 94) and patients with moderate AD as those with a baseline MMSE ≤ 18 (n = 89).
- The data are presented using an observed-case analysis for the patient population that initially enrolled into the trial (n = 183) and also for the population of patients who consented for the entire 1-year treatment period (1-year cohort, n = 134).

Figure 2. ADAS-cog: Dimebon Significantly Improved Cognition at 1 Year in Patients With Mild and With Moderate AD

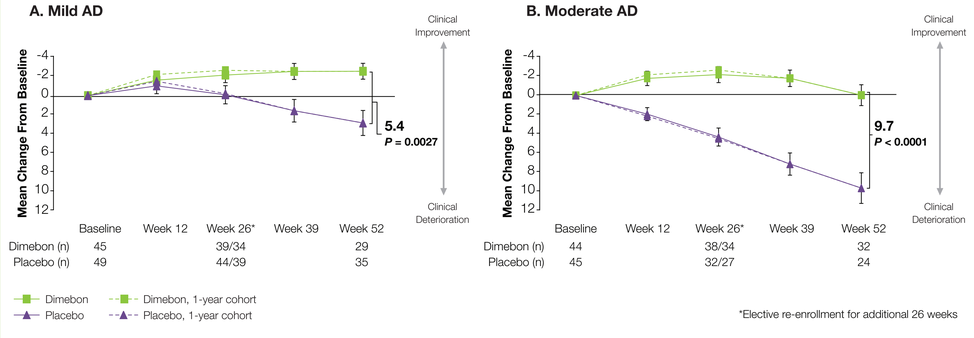

Figure 4. ADLs: Dimebon Improved Activities of Daily Living in Patients With Mild and With Moderate AD

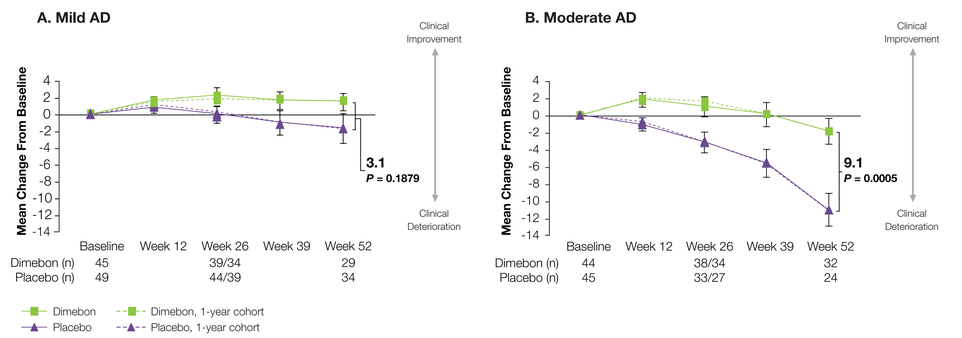

Figure 1. CIBIC-plus: Dimebon Improved Overall Function at 1 Year in Patients With Mild and With Moderate AD

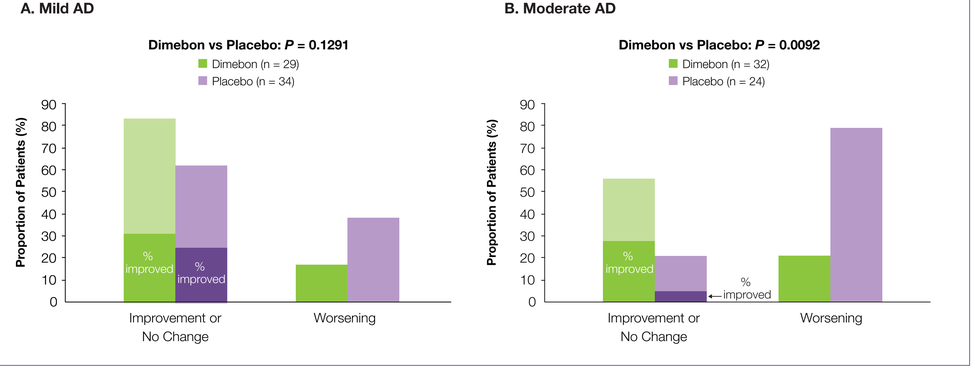

Figure 3. NPI: Dimebon Significantly Improved Neuropsychiatric Symptoms in Patients With Moderate AD

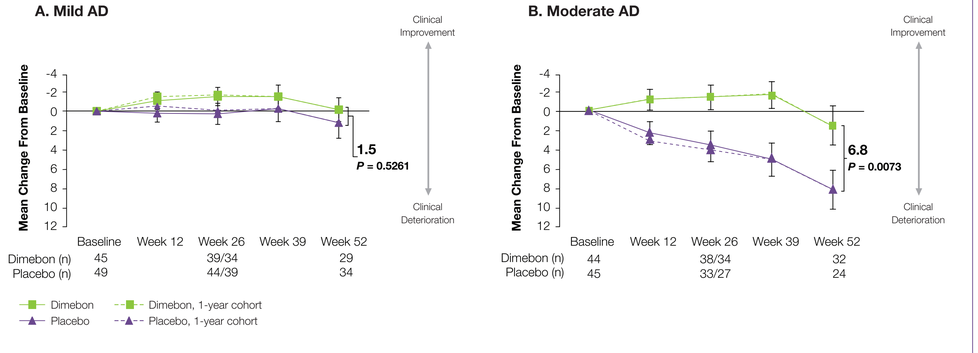

Table 1. Dimebon Treatment Was Well Tolerated

Week 52	Dimebon (n = 89)	Placebo (n = 94)
Number of patients reporting at least 1 adverse event, no. (%)	70 (79%)	70 (75%)
Number of subjects reporting at least 1 serious adverse event, no. (%)	3 (3%)	11 (12%)

CONCLUSIONS

- Patients with both mild and with moderate AD demonstrated benefit from treatment with Dimebon on cognition and memory, activities of daily living, behavior, and global function.
- Patients with mild AD were at or above baseline on all 5 outcome measures studied after 1 year of treatment.
  - Mild AD patients treated with Dimebon remained above baseline for 1 year on the ADAS-cog.
- Patients with moderate AD demonstrated substantial and sustained benefit over placebo on all 5 outcome measures at 1 year.
  - Moderate AD patients treated with Dimebon were improved 9.7 points over placebo on the ADAS-cog.
- Dimebon was safe and well tolerated.
- Dimebon improves the clinical course of patients with both mild and with moderate AD.

REFERENCE

1. Doody RS, Gavrilova SI, Sano M, et al; Dimebon investigators. Effect of dimebon on cognition, activities of daily living, behaviour, and global function in patients with mild-to-moderate Alzheimer's disease: a randomised, double-blind, placebo-controlled study. *Lancet*. 2008;372:207-215.

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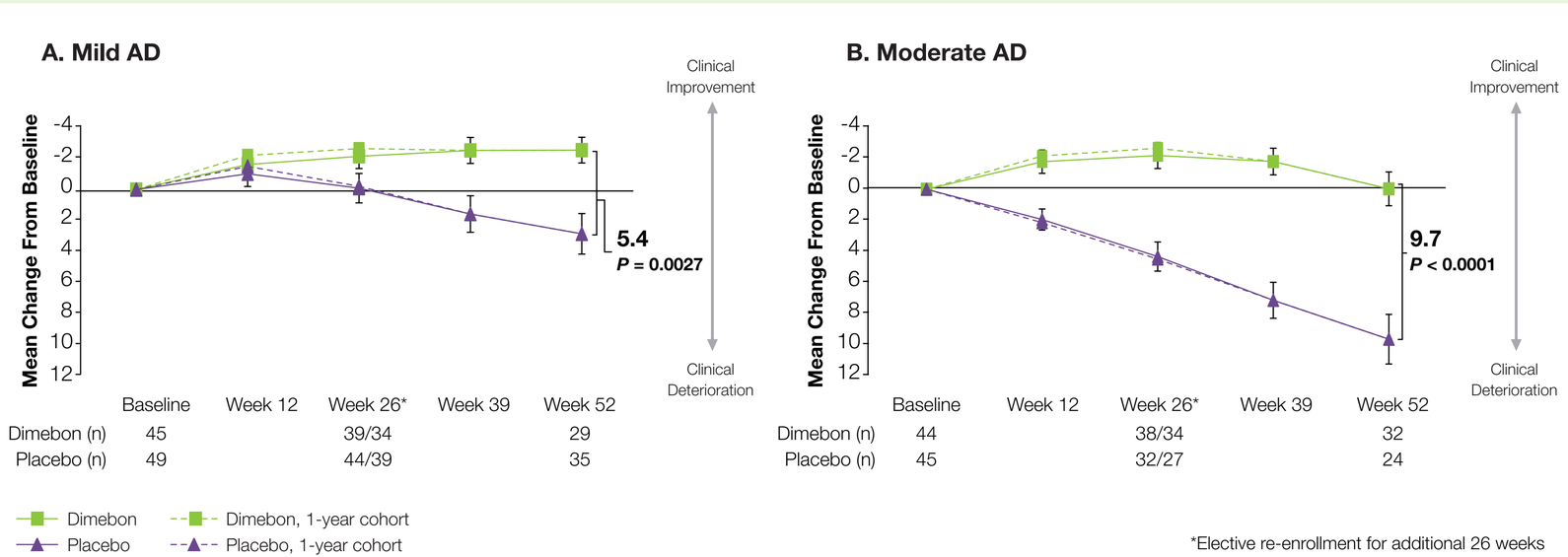

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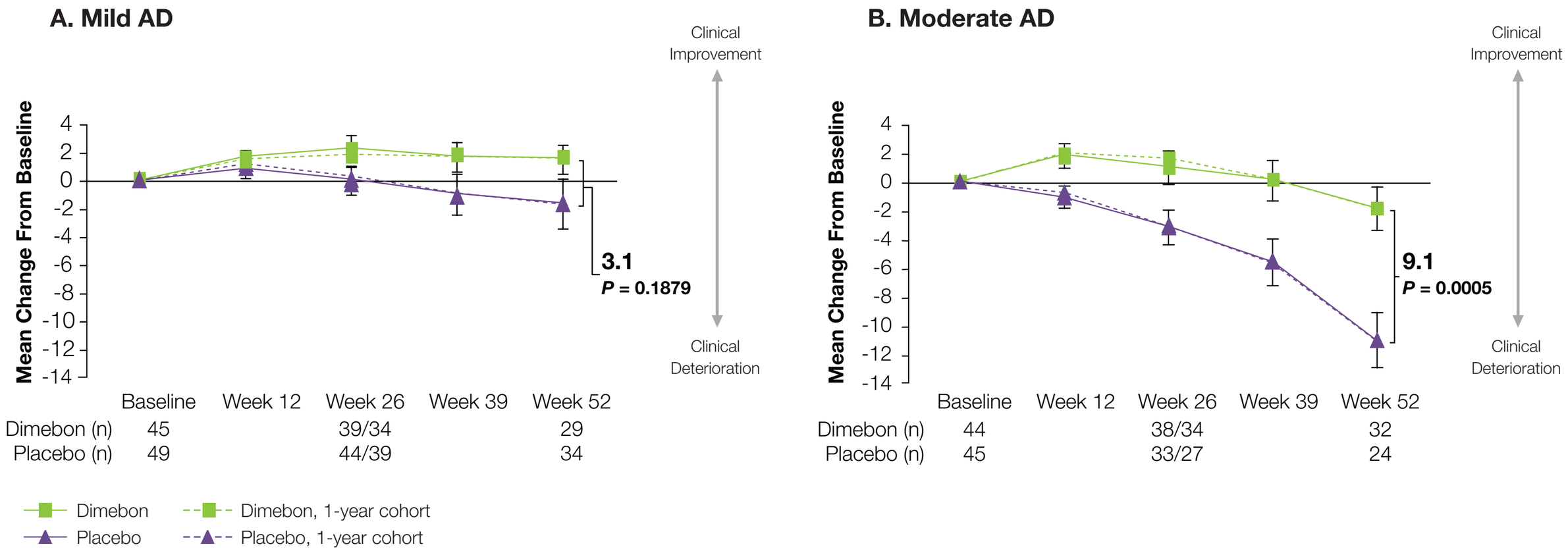

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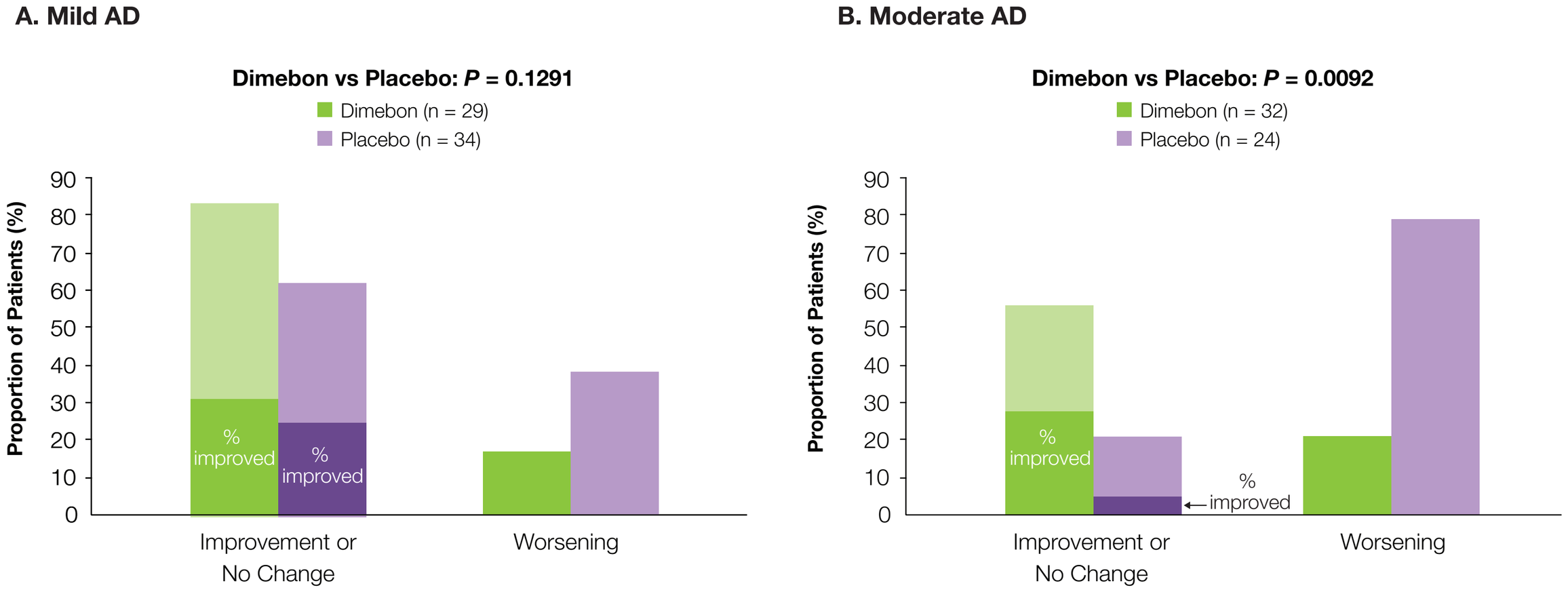

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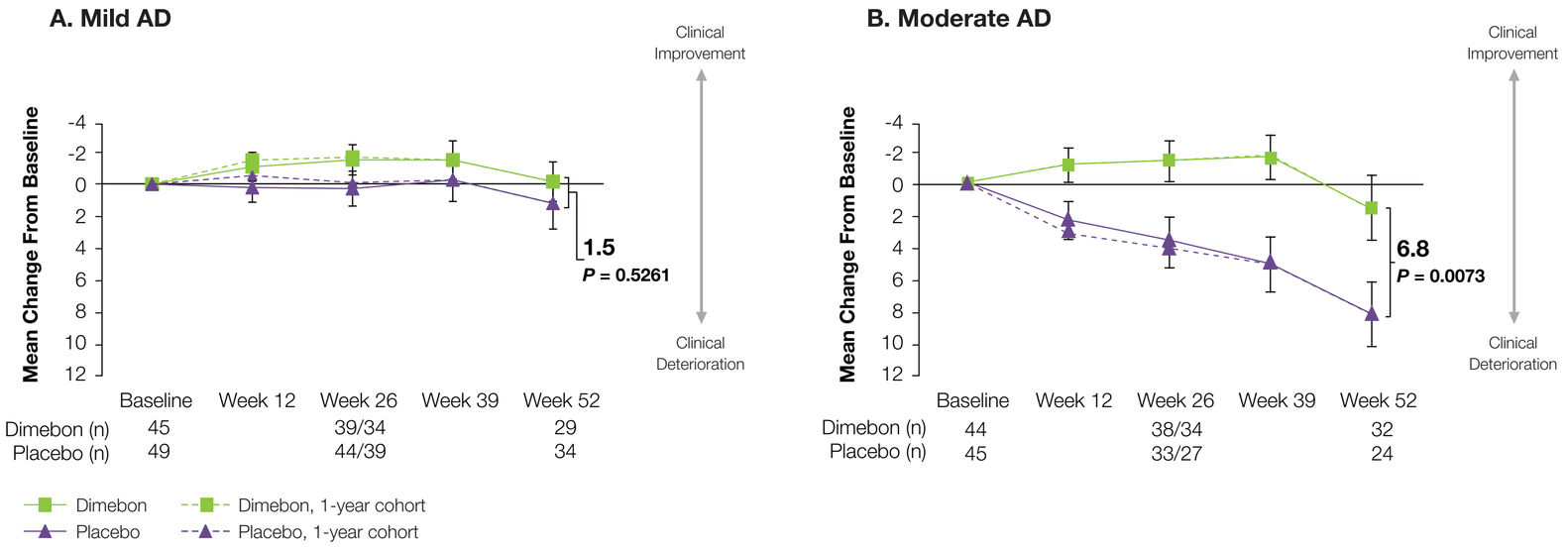

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