18-Month Data From an Open-Label Extension of a 1-Year Controlled Trial of Dimebon in Patients With Mild-to-Moderate Alzheimer's Disease

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BACKGROUND

- Dimebon is an investigational drug with a mechanism of action that is distinct from currently marketed drugs for Alzheimer's disease (AD).
- Dimebon enhances mitochondrial function, which is impaired in AD and other neurodegenerative disorders.
  - Mitochondrial impairment may play a significant role in the loss of brain cell function in these diseases.
- In a 12-month, randomized, double-blind, placebo-controlled study of patients with mild-to-moderate AD, Dimebon treatment preserved function for 1 year on all 5 key aspects of AD (memory, thinking, overall function, activities of daily living, and behavior).[1]
  - Benefits increased over time compared with placebo-treated patients, who significantly worsened over the 1-year trial period.

OBJECTIVE

- The objective of this analysis was to evaluate the longer-term effectiveness of Dimebon in patients with mild-to-moderate AD in an open-label 6-month extension (OLE) of the pivotal 12-month study, and to evaluate the response of placebo patients when crossed over to treatment with Dimebon.

METHODS

- The study design and methods have been previously published.[1]
- In the initial, double-blind 12-month study, 183 patients with mild-to-moderate AD were randomized to receive Dimebon 20 mg TID or matching placebo for 26 weeks. They were then offered the opportunity to remain on their blinded study drug for an additional 26 weeks.
- At the end of 52 weeks, patients in the placebo group were allowed to switch to Dimebon, while all patients originally on Dimebon continued to receive the drug.
  - The patients were followed and assessed for the next 6 months in an unblinded, open-label extension phase.
- Efficacy endpoints included the Alzheimer's Disease Assessment Scale—cognitive subscale (ADAS-cog); Clinician's Interview-Based Impression of Change, plus Caregiver Input (CIBIC-plus); Alzheimer's Disease Cooperative Study—Activities of Daily Living (ADCS-ADL); Mini-Mental State Examination (MMSE); and Neuropsychiatric Inventory (NPI).
- For all efficacy endpoints, change from baseline in the Dimebon group was compared with the placebo group using an observed case (OC) analysis.

RESULTS

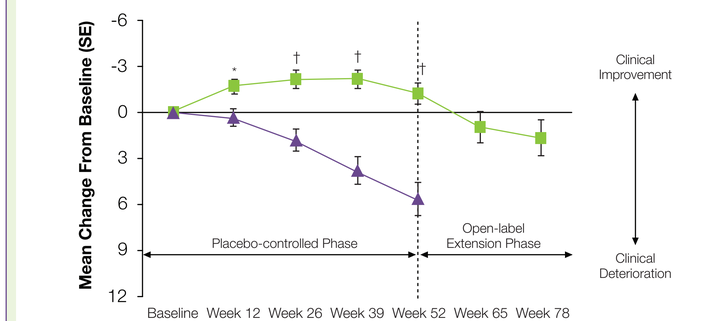
- 120 patients completed the 52 weeks of treatment in the double-blind study (61 Dimebon, 59 placebo), and 104 re-enrolled in the open-label extension phase (54 Dimebon and 50 placebo).

Table 1. Baseline Characteristics of Patients Enrolled in the OLE

	Dimebon (n = 89)	Placebo (n = 94)	Dimebon OLE (n = 54)	Placebo to Dimebon (n = 50)
Age, years	68 ± 9.3	68 ± 8.7	69 ± 8.7	69 ± 9.4
Female, no. (%)	64 (71.9%)	58 (61.7%)	40 (74%)	30 (60%)
Screening MMSE	18 ± 3.2	18 ± 3.5	19 ± 5.4	17 ± 6.8
< 10	0 (0.0%)	0 (0.0%)	3 (5.6%)	6 (12%)
10-19	61 (68.5%)	58 (61.7%)	24 (44.4%)	24 (48%)
> 19	28 (31.5%)	36 (38.3%)	27 (50%)	20 (40%)

MMSE, Mini-Mental State Examination

Figure 1. ADAS-cog: Dimebon treatment preserves cognition for 18 months.



*P < 0.01; †P < 0.0001 versus placebo

Figure 2. NPI: Dimebon treatment stabilizes neuropsychiatric symptoms for 18 months.

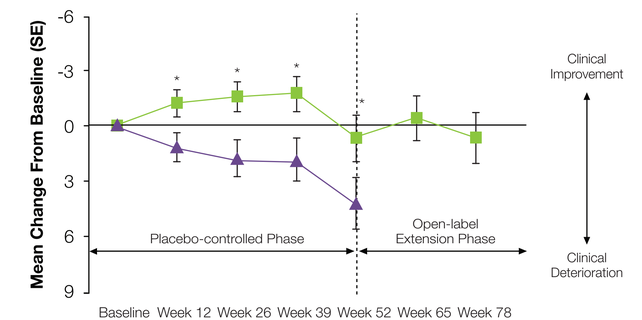


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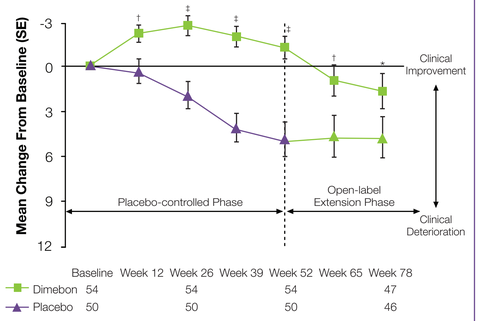
Figure 4. ADAS-cog: placebo-crossover; Dimebon stabilizes cognition.



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- Dimebon was well tolerated over the 18-month study period with no safety or tolerability issues identified.

Table 2. Effect of Treatment With Dimebon and Placebo on ADCS-ADL, MMSE, and CIBIC-plus

	Week 12	Week 26	Week 39	Week 52	Week 65	Week 78
ADCS-ADL (mean change from baseline)						
Dimebon	1.67*	1.55†	0.83*	-0.28†	-2.04	-2.40
Placebo	-0.09	-1.39	-2.83	-5.52		
MMSE (mean change from baseline)						
Dimebon	1.15	1.86§	1.52§	0.67‡	0.08	-0.02
Placebo	0.78	-0.34	-0.90	-1.66		
CIBIC-plus (percentage of patients showing improvement or no change)						
Dimebon	86.6†	80.3‡	81.0§	68.9†	52.0	57.4
Placebo	63.5	61.0	50.8	44.8		

*P < 0.05; †P < 0.01; ‡P < 0.001; §P < 0.0001 Dimebon-placebo difference

Table 3. Effect of Treatment With Dimebon and Placebo on ADCS-ADL, NPI, and CIBIC-plus: Observed Case OLE Subjects Only

	Week 12	Week 26	Week 39	Week 52	Week 65	Week 78
ADCS-ADL (mean change from baseline)						
Dimebon	1.67	1.93*	0.80	-0.11*	-2.04	-2.40
Placebo	0.33	-0.50	-1.74	-3.40	-3.83	-4.30
NPI (mean change from baseline)						
Dimebon	-1.65	-1.59	-1.85*	0.72	-0.38	0.68
Placebo	0.57	1.30	1.66	2.50	1.76	3.20
CIBIC-plus (percentage of patients showing improvement or no change)						
Dimebon	81.5	81.5†	79.6‡	68.5*	52.0	57.4*
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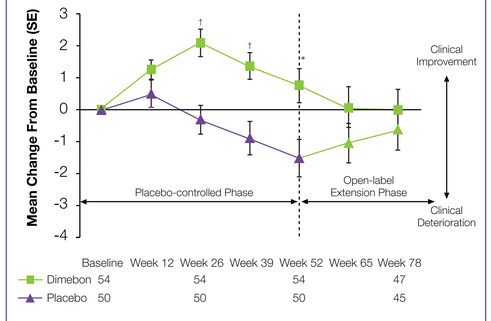

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CONCLUSIONS

- Dimebon improved the clinical course of patients with mild-to-moderate AD and demonstrated enduring benefit through 18 months of treatment.
- Dimebon preserved cognition and memory, function, and behavior through 18 months of treatment, as compared with placebo-treated patients who declined steadily through 12 months.
- Patients initially treated with placebo for 12 months, but then crossed over to Dimebon for 6 months were stabilized on all 5 endpoints, but at a lower level of function than those originally randomized to Dimebon.
  - Earlier treatment may provide a benefit.
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REFERENCES

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18-Month Data

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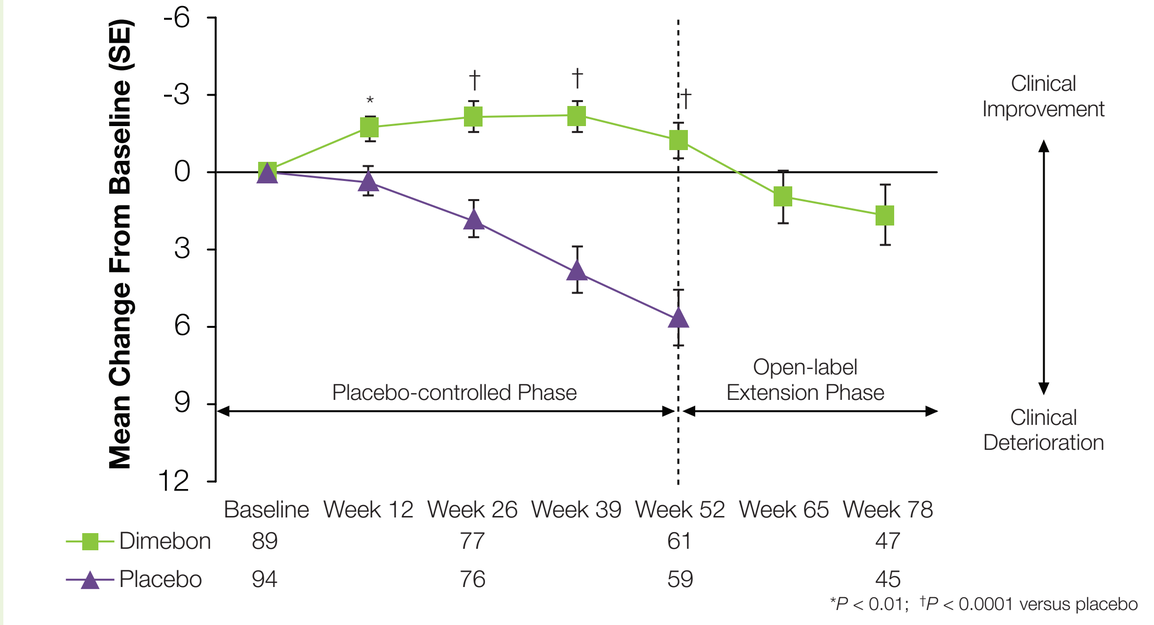

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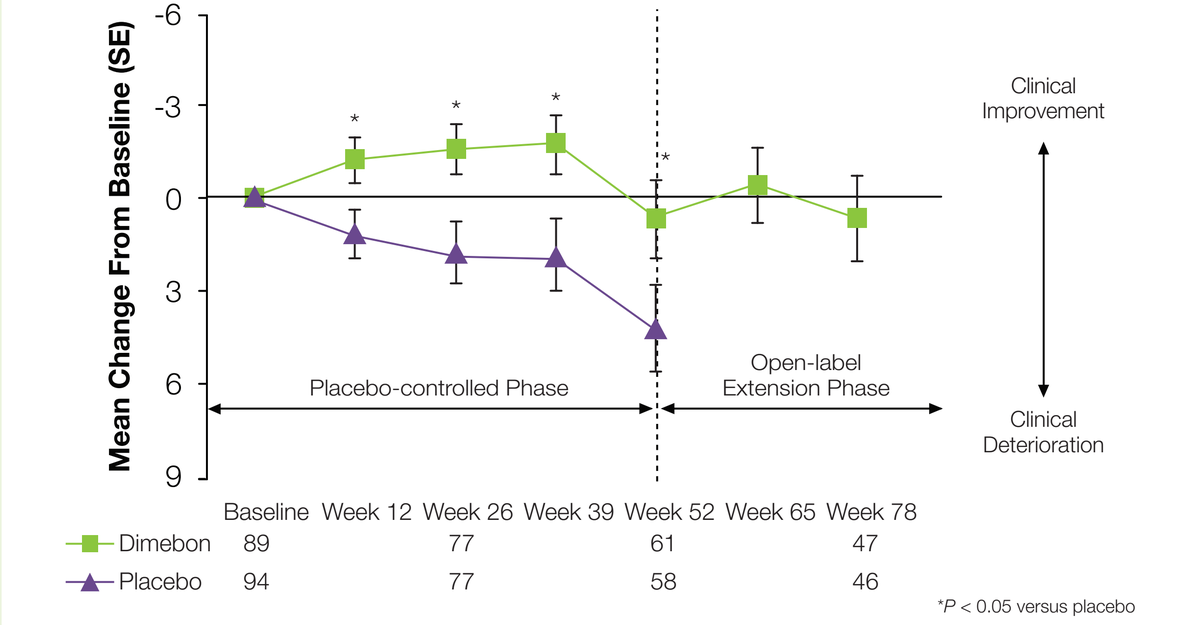

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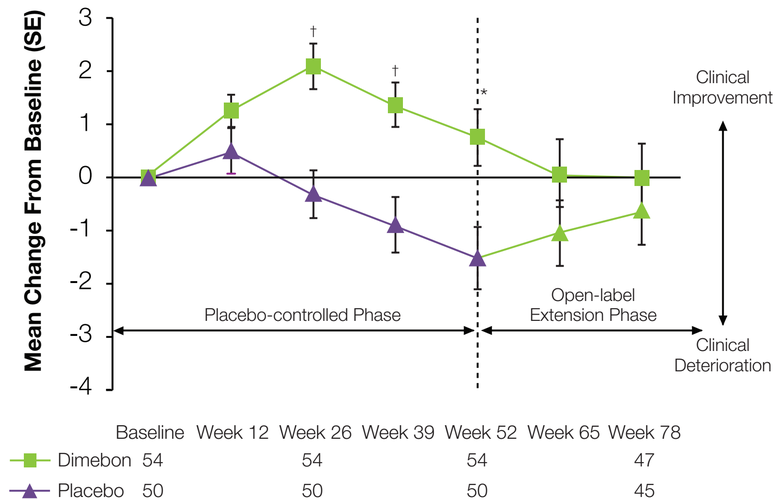

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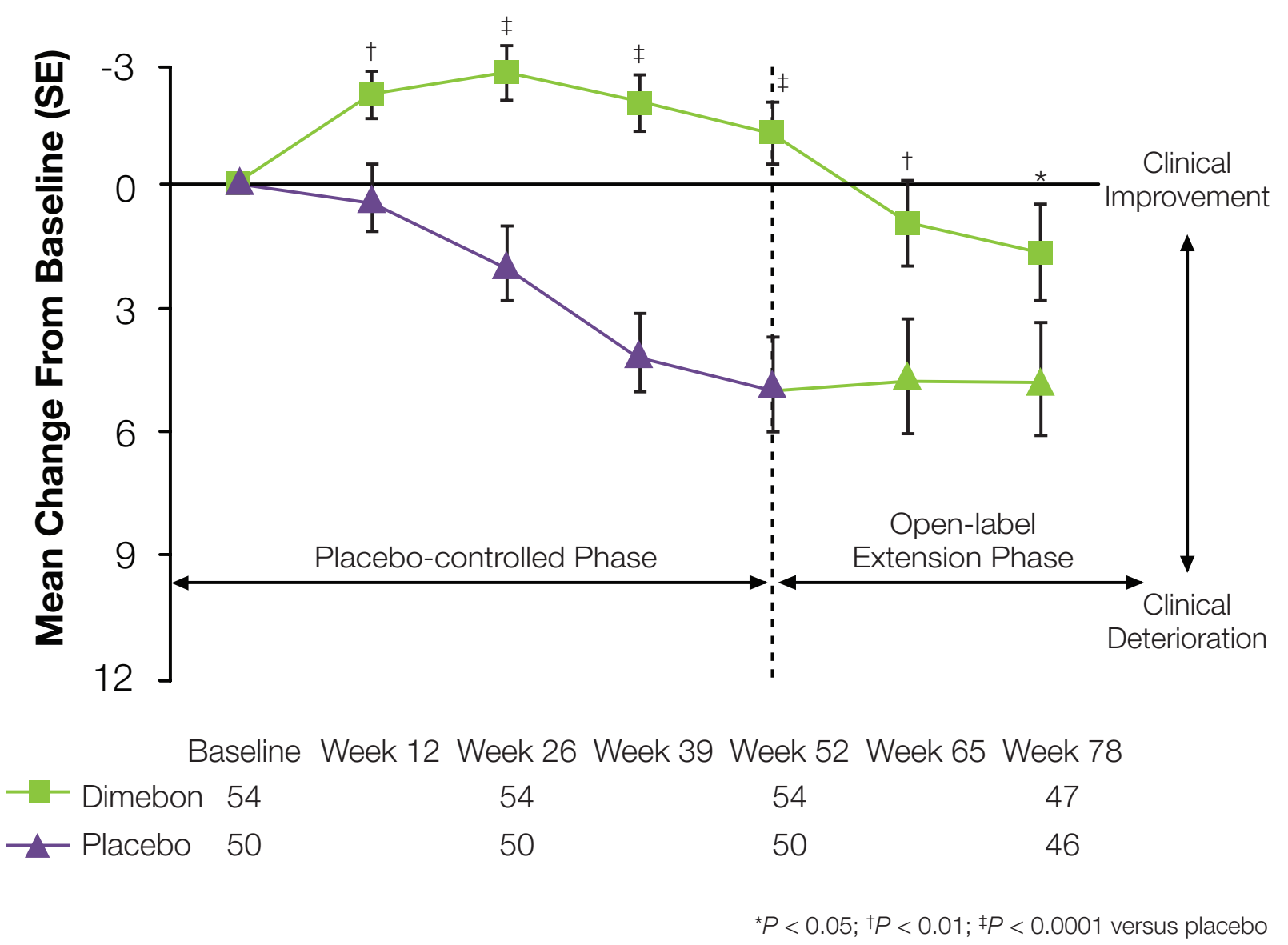

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