Consecutive Headache-Free Days With OnabotulinumtoxinA Treatment in Patients With Chronic Migraine: A Pooled PREEMPT Analysis

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Additional Information

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Background

- Chronic migraine (CM) impairs quality of life and is associated with substantial personal, societal, and familial burden[1,2]
- Consecutive days without headache is associated with health-related quality of life[3,4]
- The Phase 3 REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) studies demonstrated that onabotulinumtoxinA treatment is safe, well tolerated, and improves quality of life in individuals with CM[5,6]

Objective

- To evaluate the effect of onabotulinumtoxinA versus placebo on the number of consecutive headache-free days and days without moderate/severe headache in adults with CM

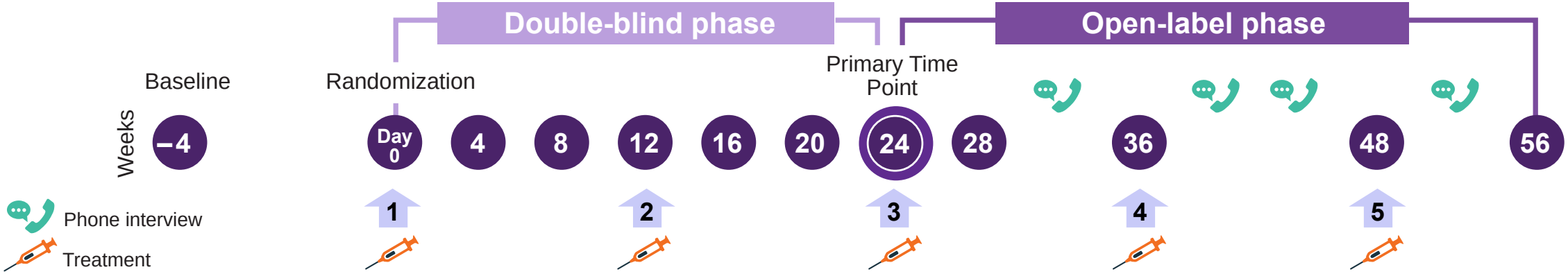
Methods

- This was a post hoc analysis of the phase 3, 24-week PREEMPT clinical trials (NCT00156910, NCT00168428)[1]
- The intent-to-treat population (all participants with ≥1 baseline value) was used in efficacy analyses[1]
- Participant diaries documented each headache day (defined as a day with ≥4 continuous hours of headache),[1] and headache severity was rated as mild, moderate, or severe
- Percentages of participants experiencing either ≥7, ≥14, or ≥21 consecutive headache-free days were compared between the onabotulinumtoxinA and placebo groups according to the following:
  - Without headache and without acute medication use, double-blind (DB) phase
  - Without moderate/severe headache and without acute medication use, DB phase
  - Without moderate/severe headache regardless of acute medication use, DB phase
  - Without moderate/severe headache and without acute medication use, entire study
  - Without moderate/severe headache regardless of acute medication use, entire study
- Only diary data after the first dose were used to calculate consecutive days without headache
- Data were pooled across studies to improve precision
- Comparisons between onabotulinumtoxinA and placebo treatment groups were made using a 2-tailed Fisher’s exact test

Study Design

- The full methodology for the PREEMPT trials has been published[1]
- The PREEMPT trials are a pair of randomized, double-blind, placebo-controlled, 24-week trials followed by 32-week open-label phases (**Figure 1**)
- Individuals were randomized (1:1) to injections of onabotulinumtoxinA (155 U to 195 U) or placebo every 12 weeks for 2 cycles
- All individuals then received 3 open-label cycles of onabotulinumtoxinA (155 U to 195 U)

Figure 1. Study Design



Results

- The PREEMPT pooled analysis population comprised 1384 participants randomized to onabotulinumtoxinA (n=688) or placebo (n=696) in the DB phase[1]
- Baseline demographics and headache characteristics were similar between groups (**Table 1**)[1]
  - The mean number of headache days per month was not significantly different between groups[1]

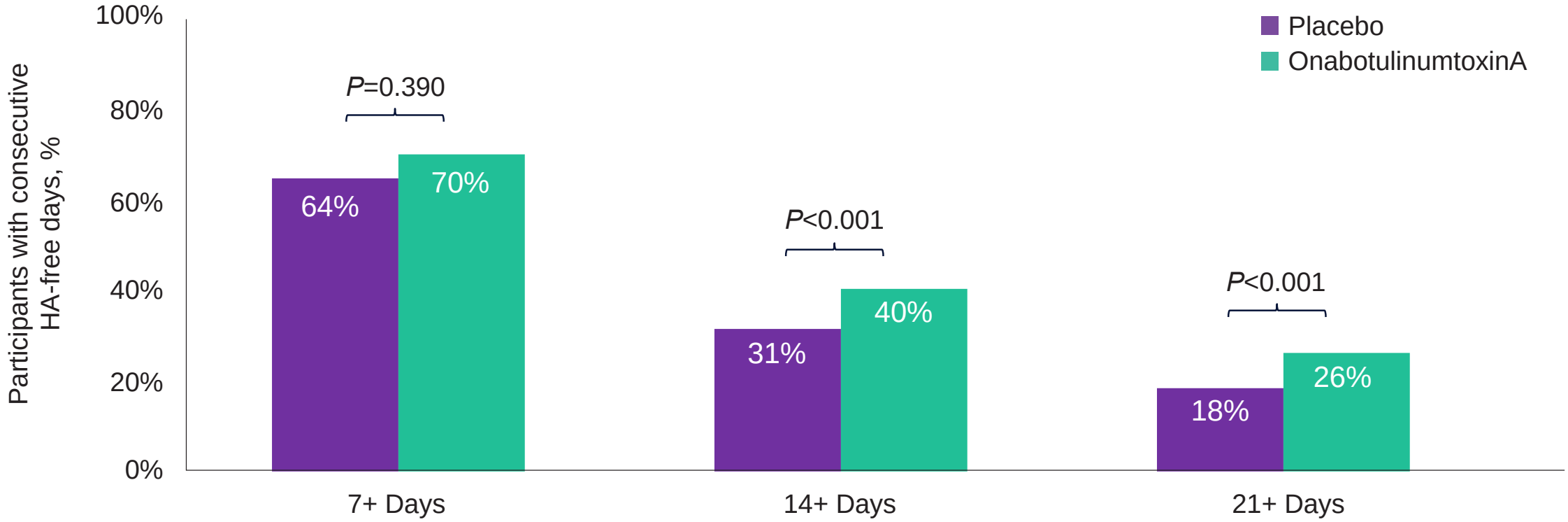
Table 1. Baseline Demographics and Headache Characteristics[1]

	OnabotulinumtoxinA (n=688)	Placebo (n=696)	*P* Value
Age, years, mean (SD)	41.1 (10.4)	41.5 (10.7)	0.579
Female, %	87.6	85.2	0.185
White, %	89.7	90.5	0.602
Headache days/month,[a] mean (SD)	19.9 (3.7)	19.8 (3.7)	0.498
HIT-6 score, mean (SD)	65.5 (4.1)	65.4 (4.3)	0.638
MSQ score, mean (SD)			
Role restrictive	38.5 (16.6)	38.7 (17.3)	0.974
Role preventive	56.0 (21.2)	56.1 (21.7)	0.825
Emotional function	42.1 (24.1)	42.4 (25.0)	0.806

HIT-6, 6-item Headache Impact Test; MSQ, Migraine-Specific Quality of Life Questionnaire; n, number of participants; SD, standard deviation.
[a]Headache days per 28-day period.

- During the DB treatment phase, a significantly higher percentage of participants treated with onabotulinumtoxinA versus placebo experienced ≥7, ≥14, and ≥21 consecutive headache-free days without acute medication use (**Figure 2**)

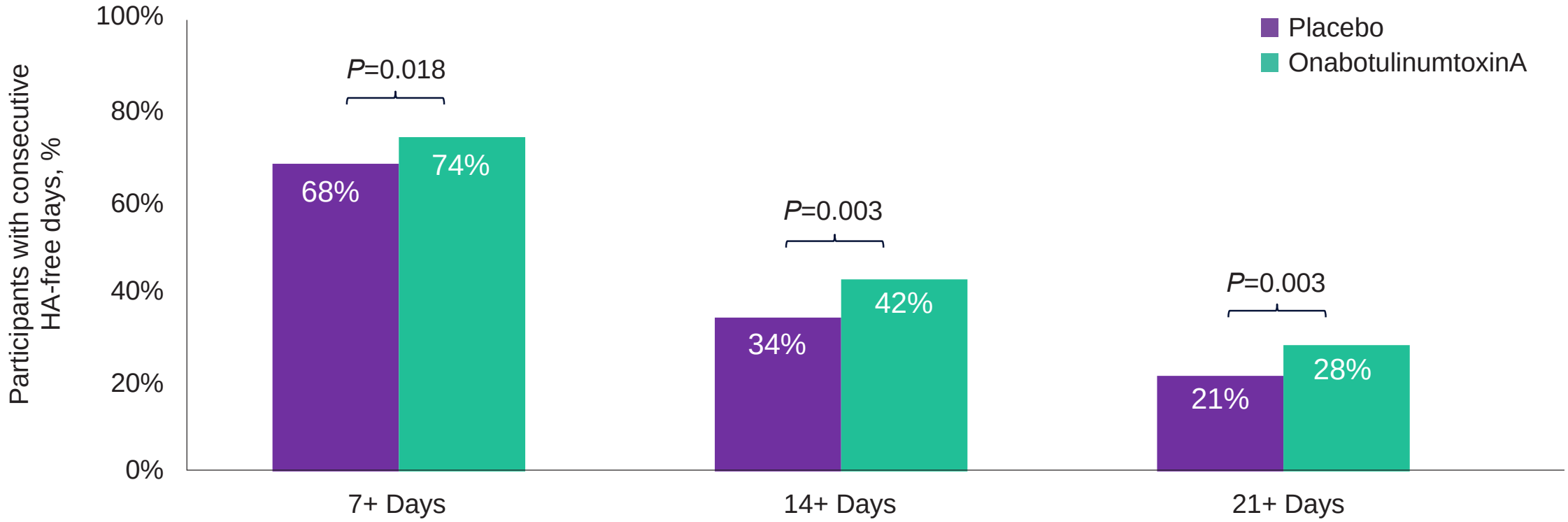
Figure 2. Headache-Free Days Without Acute Medication[a]: Double-blind Phase



HA, headache.
[a]Participants with consecutive days without a headache and without acute medication use during the entire 24-week double-blind phase.

- Significant differences with onabotulinumtoxinA treatment remained when the analysis was restricted to participants who experienced ≥7, ≥14, and ≥21 consecutive moderate/severe headache-free days without acute medication use (**Figure 3**)

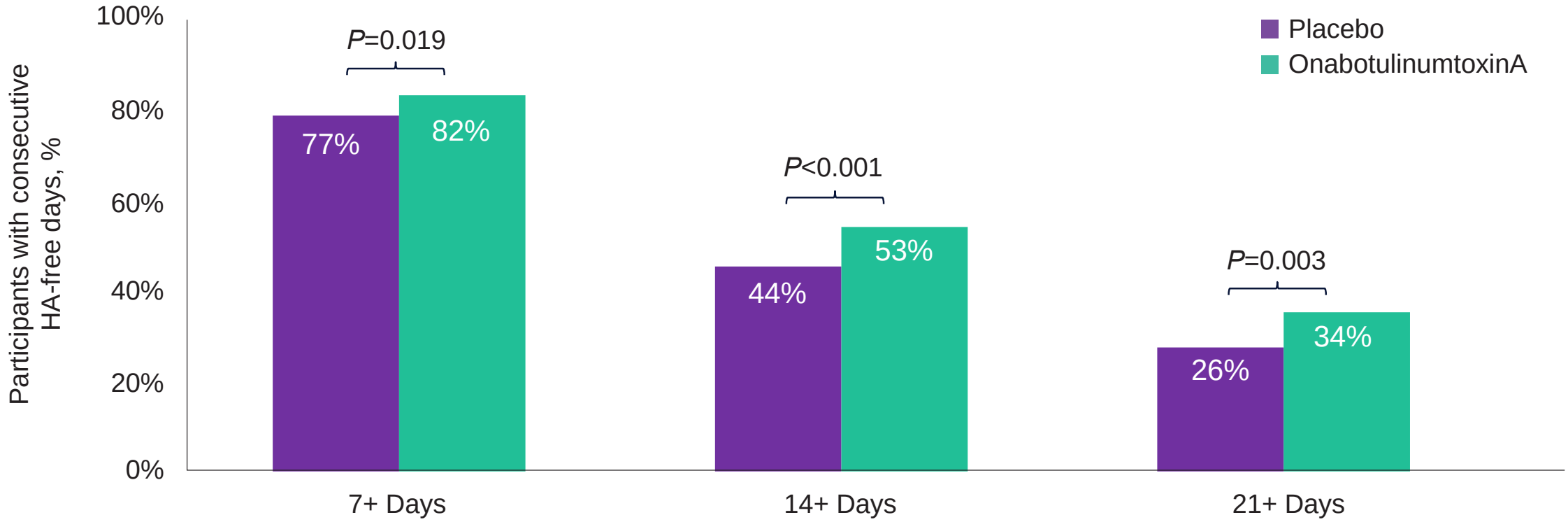
Figure 3. Moderate/Severe Headache-free Days Without Acute Medication[a]: Double-blind Phase



HA, headache.
[a]Participants with consecutive days without a moderate/severe headache and without acute medication use during the entire 24-week double-blind phase.

- A significantly higher percentage of participants treated with onabotulinumtoxinA versus placebo experienced ≥7, ≥14, and ≥21 consecutive moderate/severe headache-free days regardless of acute medication use (**Figure 4**)

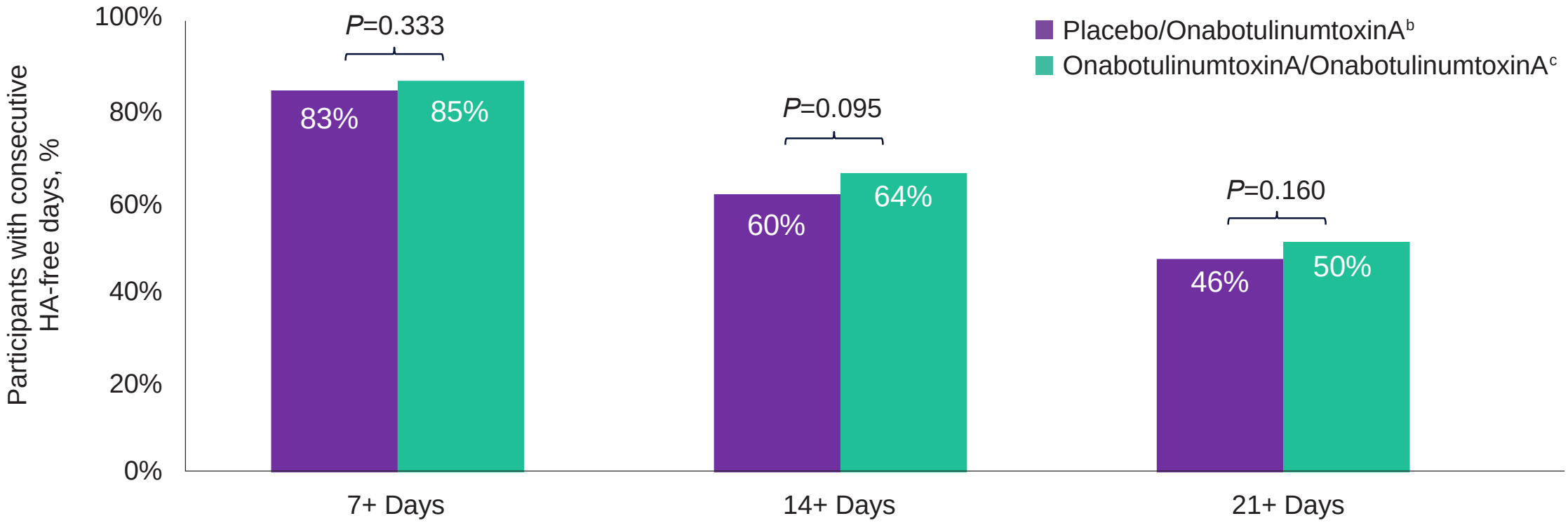
Figure 4. Moderate/Severe Headache-Free Days[a]: Double-blind Phase



HA, headache.
[a]Participants with consecutive days without a moderate/severe headache during the entire 24-week double-blind phase.

- During the entire study, the percentages remained similar between groups for participants who experienced ≥7, ≥14, and ≥21 consecutive moderate/severe headache-free days without acute medication use (**Figure 5**)

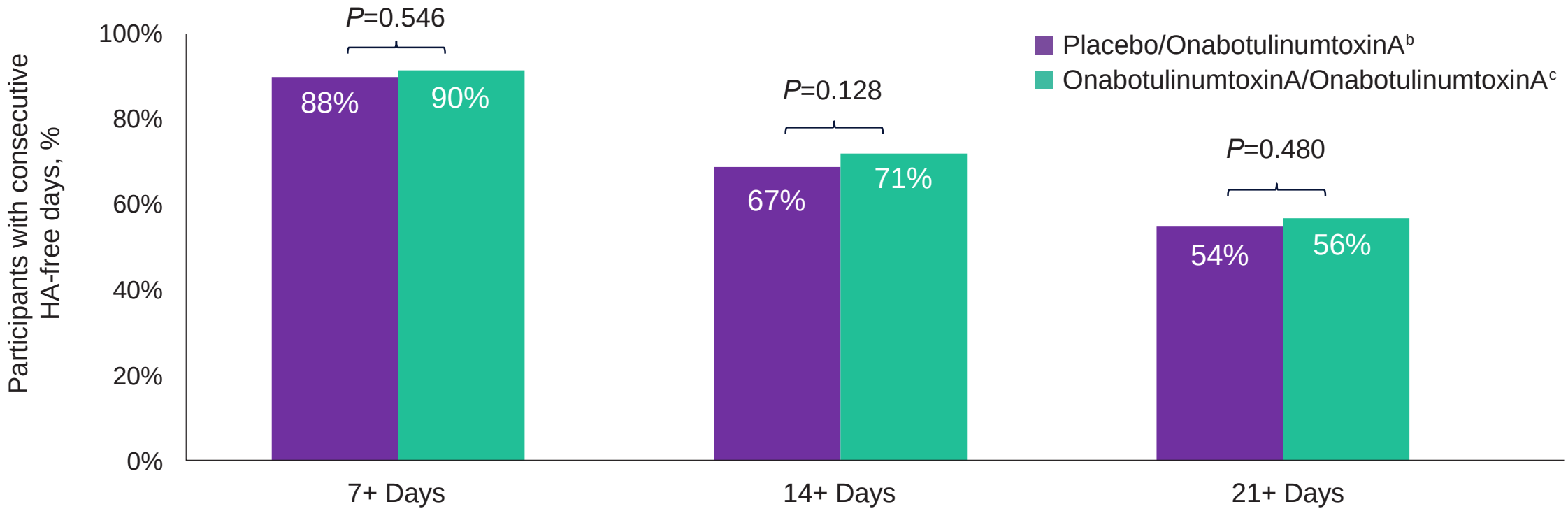
Figure 5. Moderate/Severe Headache-Free Days[a] Without Acute Medication: Entire Study



HA, headache.
[a]Participants with consecutive days without a moderate/severe headache and without acute medication use during the entire study. [b]Participants were randomized to placebo during the double-blind phase and received onabotulinumtoxinA during the open-label phase. [c]Participants were randomized to onabotulinumtoxinA during the double-blind phase and continued to receive onabotulinumtoxinA during the open-label phase.

- During the entire study, the placebo/onabotulinumtoxinA and onabotulinumtoxinA/onabotulinumtoxinA groups were similar in the percentages of participants who experienced ≥7, ≥14, and ≥21 consecutive moderate/severe headache-free days regardless of acute medication use (**Figure 6**)

Figure 6. Moderate/Severe Headache-Free Days[a]: Entire Study



HA, headache.
[a]Participants with consecutive days without a moderate/severe headache during the entire study. [b]Participants were randomized to placebo during the double-blind phase and received onabotulinumtoxinA during the open-label phase. [c]Participants were randomized to onabotulinumtoxinA during the double-blind phase and continued to receive onabotulinumtoxinA during the open-label phase.

Conclusions

OnabotulinumtoxinA treatment resulted in significantly more consecutive headache-free days and moderate/severe headache-free days, compared with placebo, in participants with CM

Participants receiving onabotulinumtoxinA experienced significantly more consecutive weeks without a moderate/severe headache, regardless of acute medication use status, compared with placebo

Regardless of onabotulinumtoxinA or placebo treatment during the double-blind phase, similar percentages of participants treated with onabotulinumtoxinA during the entire study had ≥1, ≥2, and ≥3 consecutive moderate/severe headache-free weeks

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