Clinically Meaningful Benefits of OnabotulinumtoxinA Beyond Headache Days in Chronic Migraine: Analysis of the COMPEL and Pooled PREEMPT Studies

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CONCLUSIONS

- OnabotulinumtoxinA-treated patients were more likely than placebo-treated patients to meet responder criteria for headache impact, health-related quality of life, headache severity, and reduction in monthly headache days in PREEMPT
- Among onabotulinumtoxinA-treated patients, a clinically meaningful improvement on 1 or more outcome measures was met by 72.1% at 24 weeks in PREEMPT and 87% at year 2 in COMPEL
- Reduction in headache days failed to fully capture the treatment benefit associated with 24 weeks of onabotulinumtoxinA treatment in the pooled PREEMPT population and 108 weeks of treatment in COMPEL

RESULTS

Trial Population

- The PREEMPT pooled analysis population comprised 1384 patients randomized to onabotulinumtoxinA (n=688) or placebo (n=696)
- In COMPEL, 716 patients were enrolled to receive onabotulinumtoxinA treatment
- Baseline demographics and headache characteristics are shown in **Table 1**

Table 1. Baseline Demographics and Headache Characteristics

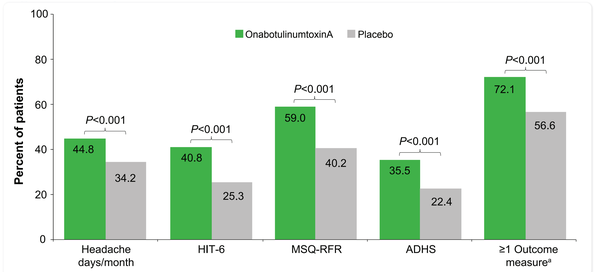
Characteristic	PREEMPT Pooled: OnabotulinumtoxinA (n=688)	PREEMPT Pooled: Placebo (n=696)	COMPEL: OnabotulinumtoxinA (n=716)
Age, mean, y	41.1	41.5	43.0
Female, %	87.6	85.2	84.8
White, %	89.7	90.5	81.3
Headache days/month[a], mean (SD)	19.9 (3.68)	19.8 (3.68)	22.0 (4.8)
Moderate/severe headache days/month, mean (SD)	18.1 (4.12)	18.0 (4.25)	18.0 (5.7)
HIT-6 score[b], mean (SD)	65.5 (4.1)	65.4 (4.3)	64.7 (4.8)

HIT-6, 6-item Headache Impact Test; SD, standard deviation.
[a]Headache days per 28-day period.
[b]Scores of 36-49 indicate little or no impact; 50-55, some impact; 56-59, substantial impact; ≥60, severe impact.

Responder Analysis (PREEMPT)

- Greater proportions of patients treated with onabotulinumtoxinA qualified as responders in each outcome measure (*P*<0.001, Fisher's Exact Test; **Figure 1**) vs those randomized to placebo
  - The MSQ-RFR showed the single-outcome greatest response rate and difference between groups
- More than 7 in 10 patients treated with onabotulinumtoxinA qualified as responders on 1 or more outcome measures
  - Comparatively, only 4.5 in 10 patients were considered treatment responders when only reduction in headache days was considered

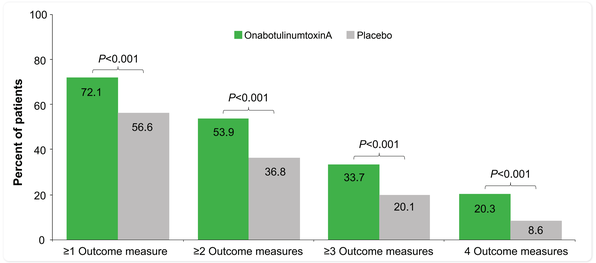
Figure 1. Responder Rates Across Outcome Measures (mLOCF)



ADHS, Average Daily Headache Severity, HIT-6, 6-item Headache Impact Test; mLOCF, modified last observation carried forward; MSQ-RFR, Migraine-Specific Quality-of-Life Questionnaire Role Function-Restrictive.
[a]Any patient who achieved ≥1 of the criteria—50% reduction in headache days, clinically meaningful change in HIT-6, MSQ-RFR, or headache severity—at week 24 was counted as a responder.

- The significant between-groups difference in rates of response on 1 or more outcome measures was maintained as the number of measures increased (*P*<0.001, Fisher's Exact Test; **Figure 2**)
- More than 1 in 3 patients treated with onabotulinumtoxinA qualified as responders on 3 or more outcomes and 1 in 5 qualified as responders on all outcomes

Figure 2. Percentage of PREEMPT Patients Who Achieved Response on 1 or More Outcome Measures[a]

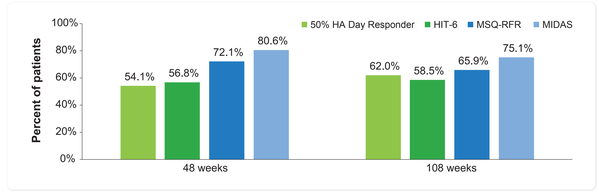


HIT-6, 6-item Headache Impact Test; MSQ-RFR, Migraine-Specific Quality-of-Life Questionnaire Role Function-Restrictive.
[a]Any patient who achieved ≥1 of these 4 outcome measures—50% reduction in headache days, or clinically meaningful change in HIT-6, MSQ-RFR, or headache severity—at week 24 was counted as a responder.

Clinically Meaningful Improvement (COMPEL)

- More than half of patients treated with onabotulinumtoxinA qualified as responders in each outcome measure (**Figure 3**)
  - MIDAS showed the greatest single-outcome response rate, followed by MSQ-RFR

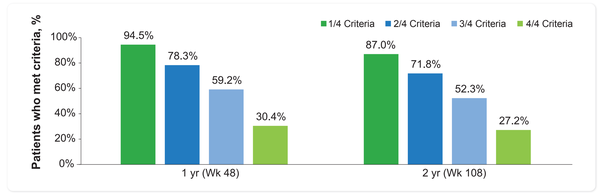
Figure 3. Rates of Clinically Meaningful Improvements at 48 and 108 Weeks Across Outcome Measures in COMPEL (mLOCF)



HA, headache; HIT-6, 6-item Headache Impact Test; mLOCF, modified last observation carried forward; MIDAS, Migraine Disability Assessment Scale; MSQ-RFR, Migraine-Specific Quality-of-Life Questionnaire Role Function-Restrictive.

- 8.7 in 10 patients treated with onabotulinumtoxinA qualified as responders on 1 or more outcome measures at year 2 (**Figure 4**)
  - Comparatively, only 6.2 in 10 patients were considered treatment responders when only reduction in headache days was considered
- More than 1 in 2 patients treated with onabotulinumtoxinA qualified as responders on 3 or more outcomes, and 1 in 4 qualified as responders on all outcomes

Figure 4. Percentage of COMPEL Patients Who Achieved Response on 1 or More Outcome Measure[a]



HIT-6, 6-item Headache Impact Test; MIDAS, Migraine Disability Assessment Scale; MSQ-RFR, Migraine-Specific Quality-of-Life Questionnaire Role Function-Restrictive.
[a]Any patient who achieved ≥1 of these 4 outcome measures—50% reduction in headache days, or clinically meaningful change in HIT-6, MSQ-RFR, or MIDAS—at week 48 or 108 was counted as a responder.

Adverse Events

- A summary of adverse events (AEs) for pooled onabotulinumtoxinA and placebo patients in PREEMPT and all patients in COMPEL is shown in **Table 2**
  - The only AEs reported with an incidence >5% in PREEMPT were neck pain (8.7%) and muscular weakness (5.5%) in the onabotulinumtoxinA group and upper respiratory tract infection (5.3%) in the placebo group
  - No AEs were reported with an incidence >5% in COMPEL

Table 2. Summary of Overall Adverse Events—PREEMPT Pooled and COMPEL Patients

	PREEMPT Pooled: OnabotulinumtoxinA (n=687) n (%)	PREEMPT Pooled: Placebo (n=692) n (%)	COMPEL: OnabotulinumtoxinA (n=716) n (%)
All adverse events	429 (62.4)	358 (51.7)	436 (60.9)
Treatment-related adverse events	202 (29.4)	88 (12.7)	131 (18.3)
Serious adverse events	33 (4.8)	16 (2.3)	75 (10.5)
Treatment-related, serious adverse events	1 (0.1)	0 (0.0)	1 (0.1)
Discontinuations related to adverse events	26 (3.8)	8 (1.2)	32 (4.5)
Deaths	0 (0.0)	0 (0.0)	0 (0.0)

INTRODUCTION

Background

- Chronic migraine (CM) is a complex, distinct neurological disease defined by ≥15 headache days/month and individualized presentation that may include prodromal symptoms, aura, photophobia, phonophobia, and nausea/vomiting[1]
- The Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) studies established the benefit of onabotulinumtoxinA treatment for a reduction of headache frequency[2-4]
- The Chronic Migraine OnabotulinuMtoxinA Prolonged Efficacy open Label (COMPEL) study provided additional evidence for the efficacy and long-term safety and tolerability of onabotulinumtoxinA treatment for the prevention of headache in those with CM over 2 years[5-6]
- Clinical trials of preventive treatments for CM generally classify response as ≥50% reduction from baseline in monthly headache days, but headache-day reduction may not fully capture the benefits of treatment[7]

Objective

- To evaluate the effect of onabotulinumtoxinA treatment on clinically meaningful changes in headache severity, headache-related impact, disability, and quality of life (QoL)

METHODS

- This was a post-hoc analysis of pooled data from the PREEMPT trials (NCT00156910, NCT00168428) and COMPEL (NCT01516892) study
- Full methodology for the PREEMPT trials has been published[2-4]
  - The PREEMPT trials are a pair of randomized, double-blind, placebo-controlled, 24-week trials followed by 32-week open-label phases
  - During randomized treatment, patients were randomized (1:1) to injections of onabotulinumtoxinA (155 U to 195 U) or placebo every 12 weeks for 2 cycles
- Full methodology for the COMPEL trial has also been published[5-6]
  - COMPEL was a single-arm, open-label, multicenter, prospective study that enrolled adults with CM receiving onabotulinumtoxinA 155 U every 12 weeks (9 treatments, 108 weeks)
- The percentages of patients achieving clinically meaningful responder status at 24, 48, or 108 weeks were calculated according to the following outcome measures:
  - Change in headache days: ≥50% reduction in monthly headache-day frequency
  - Headache Impact Test (HIT-6), assessing the impact of headaches on QoL: ≥5-point improvement
  - Migraine-Specific Quality-of-Life Questionnaire Role Function-Restrictive dimension (MSQ-RFR), assessing the impact of migraine on QoL: ≥10.9-point improvement
  - Average Daily Headache Severity (ADHS): ≥1-point improvement on a 4-point ordinal scale where 0=no pain and 3=severe pain (PREEMPT only)
  - Migraine Disability Assessment Scale (MIDAS) assessing the impact of headaches on disability: ≥5-point improvement (COMPEL only)
- Missing scores were estimated using modified last observation carried forward adjustment
- Percentages of patients achieving responder status for ≥1, ≥2, ≥3, and all 4 outcome measures were calculated

DISCLOSURES

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