Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel for Acne: Association of Efficacy With Cutaneous Safety/Tolerability Events

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SYNOPSIS

- Topical treatment of acne—particularly with retinoids—often incurs a transient period of dermal irritation characterized by erythema, scaling, and other dermal changes[1]
- These events may reflect the same mechanisms of action by which retinoids address acne pathophysiology, suggesting that cutaneous safety/tolerability symptoms early in treatment may be associated with later treatment efficacy
- In acne clinical trials, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel demonstrated efficacy with 12 weeks of once-daily treatment, with some participants experiencing an early, transient period of dermal irritation[2-4]

OBJECTIVE

- To determine whether efficacy of CAB gel is associated with occurrence of cutaneous safety/tolerability events

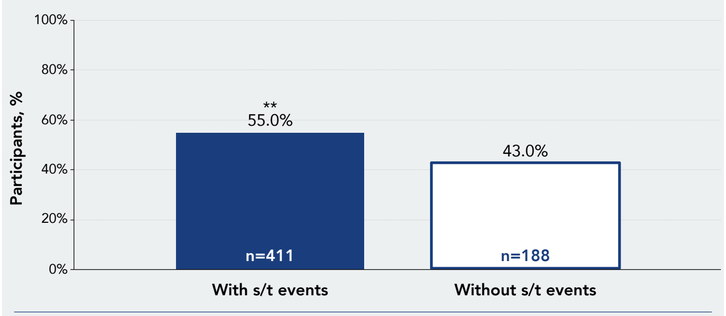
METHODS

- Data were pooled from two phase 2 (NCT03170388, NCT04892706) and two phase 3 (NCT04214639, NCT04214652) double-blind, 12-week studies of participants with moderate to severe acne
- Efficacy endpoints included treatment success (percentage of participants achieving ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 [clear] or 1 [almost clear]) and least squares mean percent change from baseline in inflammatory (IL) and noninflammatory lesions (NIL) at week 12
- Cutaneous safety/tolerability assessments of erythema and scaling (investigator-assessed) and itching, burning, and stinging (participant-assessed) were graded on a 4-point scale (0=none, 1=mild, 2=moderate, 3=severe)
  - Assessments of hypopigmentation and hyperpigmentation were excluded from this analysis as there were no notable post-baseline increases
- Treatment compliance, defined as participants missing ≤5 consecutive days of dosing and applying 80–120% of expected applications, was summarized using descriptive statistics
- Efficacy endpoints at week 12 were compared for CAB-treated participants who did not experience any safety/tolerability event at weeks 2, 4, or 8 (ie, no increase from baseline in any score) vs those who experienced any safety/tolerability event (≥1 point increase from baseline in any score)

RESULTS

- The pooled population included 599 CAB-treated participants, of whom 411 experienced any safety/tolerability event and 188 experienced no safety/tolerability events
- At week 12, over half of CAB-treated participants experiencing any safety/tolerability event achieved treatment success compared with 43% of those without safety/tolerability events (*P*<0.01; **Figure 1**)

FIGURE 1. **Treatment Success[a] at Week 12 in Participants With or Without Any Safety/Tolerability Events (ITT Population, Pooled)**

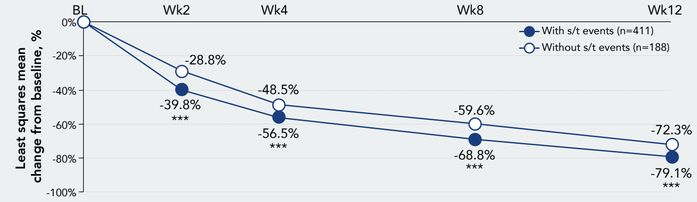


**P<0.01.
[a]Defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
ITT, intent to treat; s/t, safety/tolerability.

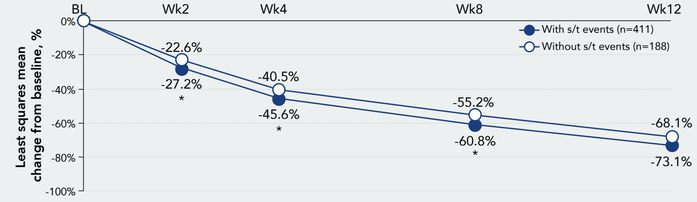
- CAB-treated participants who experienced any safety/tolerability event had significantly greater IL reductions at week 12 (79.1% vs 72.3%; *P*<0.001) and numerically greater NIL reductions (73.1% vs 68.1%) than those without events (**Figure 2**)
  - At weeks 2, 4, and 8, IL/NIL reductions were significantly greater among participants experiencing any cutaneous event than those without events (*P*<0.05, all)

FIGURE 2. **Lesion Count Reductions Through Week 12 in Participants With or Without Safety/Tolerability Events (ITT Population, Pooled)**

A) Inflammatory lesions



B) Noninflammatory lesions

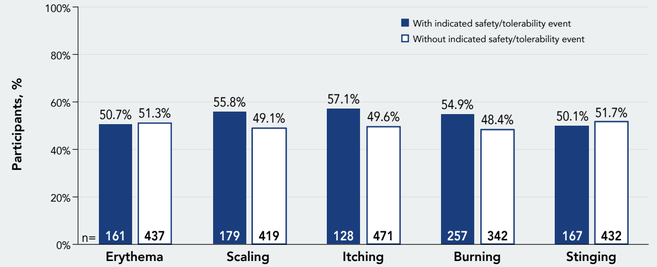


*P<0.05, ***P<0.001.
BL, baseline; ITT, intent to treat; s/t, safety/tolerability; Wk, week.

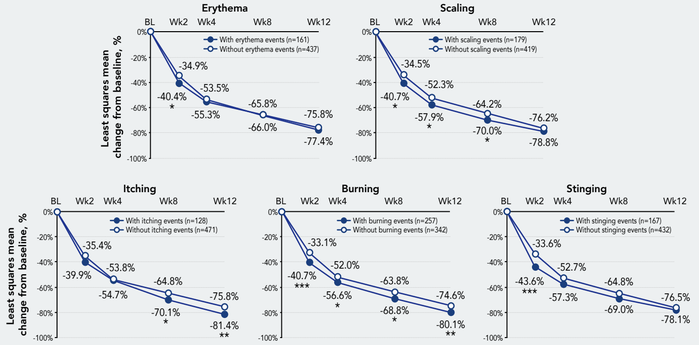
- Improved efficacy at week 12 was most associated with events of scaling, itching, and burning
  - Treatment success was higher for participants with scaling, itching, or burning events than for those without events (**Figure 3A**)
  - Participants with itching and burning events had significantly greater reductions from baseline in inflammatory lesions compared to those without (**Figure 3B**)
- Participants who experienced safety/tolerability events also experienced significantly greater IL reductions at weeks 2, 4, or 8, though the pattern differed across safety events (**Figure 3B**)
- Efficacy differences between the 2 groups did not appear to be driven by differences in treatment compliance
  - Compliance was slightly higher among participants with vs without any safety/tolerability events (93.5% vs 90.4%)
  - However, compliance rates were lower in participants with itching, burning, or stinging events (90.6–91.7%) than participants without these events (93.0–93.2%)

FIGURE 3. **Efficacy in Participants With or Without Specific Safety/Tolerability Events[a] (ITT Population, Pooled)**

A) Treatment success[b] at week 12



B) Reductions in inflammatory lesion counts through week 12 in participants with or without specific safety/tolerability events



*P<0.05, **P<0.01, ***P≤0.001.
[a]Safety/tolerability events are not mutually exclusive; participants may have experienced more than one event.
[b]Defined as percentage of participants with ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
BL, baseline; ITT, intent to treat; Wk, week.

CONCLUSIONS

- Across 4 clinical studies, CAB-treated participants who experienced transient safety/tolerability events also experienced greater acne improvements at week 12 than those who did not experience safety/tolerability events
- Improved efficacy appeared to be most associated with events of itching and burning
  - Participants with these events had greater treatment success and IL reductions at week 12 than those without these events, despite reporting lower compliance rates
- These findings are consistent with the theory that early instances of cutaneous irritation during topical acne treatment may reflect therapeutic mechanisms of action[1]
- Given the importance of setting patient expectations of acne treatment, educating patients on the link between early, transient skin events and long-term acne improvements may help bolster treatment adherence and overall treatment effectiveness

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AUTHOR DISCLOSURES

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