Safety of Hydrogen Peroxide Topical Solution 40% and 45% (w/w) in Patients With Seborrheic Keratoses on the Trunk, Extremities, and Face: Results of a Phase 2, Randomized, Double-Blind, Vehicle-Controlled, Parallel-Group Study

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CONCLUSIONS

1. **Over the 15-week study, both HP40 and HP45 were well tolerated and associated with a favorable safety profile**
2. **Most patient- and investigator-reported LSRs that occurred during treatment with HP40 and HP45 had resolved by the end of the study**
3. **Only minimal changes in skin pigmentation were observed at the end of the study compared with earlier time points**

INTRODUCTION

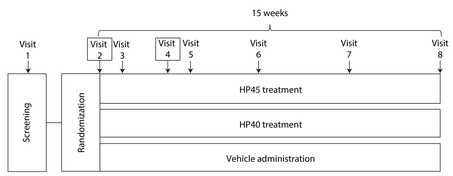
- Seborrheic keratoses (SKs) are benign epithelial skin lesions that affect approximately 84 million individuals in the United States, and are characterized by growths that vary in size and appearance[1,2]
- Existing treatment options often involve invasive procedures that may lead to adverse cosmetic effects such as pigmentation changes, scarring, and wound infection[3]
- The US Food and Drug Administration has approved a proprietary, stabilized hydrogen peroxide topical solution 40% (w/w) (HP40) for the treatment of raised SKs[4]
- The objective of this presentation is to describe the safety findings of a Phase 2 study designed to evaluate the efficacy and safety of HP40 compared with a proprietary hydrogen peroxide topical solution 45% (w/w) (HP45) and vehicle in patients with SKs on the trunk, extremities, and face

MATERIALS AND METHODS

Study Design

- This was a Phase 2, multicenter, randomized, double-blind, vehicle-controlled, parallel-group study with 3 treatment groups (NCT03148691)
- The duration of study participation was a maximum of 124 days per patient, comprising 8 study visits, with target lesions treated at 2 treatment visits (**Figure 1**)
  - During screening (visit 1), 4 eligible SK target lesions located on the trunk, extremities, and face were identified for each patient; ≥1 target lesion must have been on the face and ≥1 must have been on the trunk or extremities
  - At visit 2, patients were randomized in a 1:2:2 ratio to receive vehicle, HP40, or HP45, respectively, and received the first treatment; a second treatment was administered on day 22 (visit 4) if target lesions met retreatment criteria
  - Other visits were attended for follow-up and assessment

Figure 1. Study Design



All target SK lesions were treated during visit 2; SK lesions meeting the criteria for retreatment were treated at visit 4.
HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w); SK, seborrheic keratosis.

Study Patients

- Eligible patients were ≥18 years of age with a diagnosis of 4 clinically stable typical SK target lesions on the trunk, extremities, and face (≥1 target lesion on the face and ≥1 target lesion on the trunk or extremities)
  - Target lesions were required to be discrete with a clinically typical appearance; have a grade of ≥2 on the validated Physician Lesion Assessment™ (PLA; **Table 1**); length and width 5 to 15 mm, thickness ≤2 mm; and not be obstructed or within 5 mm of the orbital rim

Study Assessments

- Lesion severity (primary effectiveness parameter) was assessed using the PLA (**Table 1**)

Table 1. PLA Scoring

Grade	Description
0	Clear: no visible SK lesion
1	Near clear: a visible SK lesion with a surface appearance different from the surrounding skin (not elevated)
2	Thin: a visible SK lesion (thickness ≤1 mm)
3	Thick: a visible SK lesion (thickness >1 mm)

PLA, Physician Lesion Assessment; SK, seborrheic keratosis.

- Safety was assessed in the intent-to-treat (ITT) population by treatment-emergent adverse events (TEAEs), local skin reactions (LSRs), clinical laboratory evaluations, and vital signs
  - The ITT population included all patients who were randomized to receive treatment with HP40, HP45, or vehicle
- LSRs were assessed both by patients and investigators
  - For each target lesion, patients reported the average severity of stinging/burning and pruritus (itching) over the previous 24 hours at visits 2 and 4 prior to treatment, 10 minutes after treatment completion, and at visit 3 and visits 5 through 8
  - Investigators assessed the occurrence and severity of erythema, edema, scaling/dryness, vesicles/bullae, crusting, erosion, ulceration, post-inflammatory hyperpigmentation, post-inflammatory hypopigmentation (did not include the superficial transient skin blanching/whitening related to the action of the study medication), atrophy, and scarring prior to the start of treatment applications at visits 2 and 4; the average severity of all signs was reported for each target lesion at visit 3 and visits 5 through 8
  - Patients and investigators scored the average overall severity of each LSR sign/symptom for each target lesion using a 4-point scale (0 = none; 1 = mild; 2 = moderate; and 3 = severe)
  - Worsening of any target lesion was reported as a TEAE only if the use of study treatment was interrupted or discontinued, or if other treatment was required to manage the TEAE

RESULTS

Study Patients

- A total of 253 patients were enrolled in the ITT population and randomized to treatment with HP40 (n=103), HP45 (n=100), or vehicle (n=50)
- Baseline demographics and clinical characteristics were similar across groups (**Table 2**)

Table 2. Baseline Demographics and Clinical Characteristics, Intent-to-Treat Population

Characteristic	HP40 (n=103)	HP45 (n=100)	Vehicle (n=50)
Age, y			
Mean ± SD	69.1 ± 8.8	70.0 ± 8.1	69.0 ± 8.3
Range	49–87	45–89	53–89
Age group			
18–55 y	7 (6.8)	4 (4.0)	2 (4.0)
56–70 y	53 (51.5)	54 (54.0)	30 (60.0)
≥71 y	43 (41.7)	42 (42.0)	18 (36.0)
Gender			
Female	59 (57.3)	67 (67.0)	31 (62.0)
Race			
White	98 (95.1)	92 (92.0)	46 (92.0)
African American	4 (3.9)	8 (8.0)	4 (8.0)
Asian	1 (1.0)	0	0
Fitzpatrick skin type			
I	10 (9.7)	9 (9.0)	6 (12.0)
II	45 (43.7)	40 (40.0)	24 (48.0)
III	36 (35.0)	35 (35.0)	14 (28.0)
IV	8 (7.8)	7 (7.0)	2 (4.0)
V	4 (3.9)	8 (8.0)	4 (8.0)
VI	0	1 (1.0)	0

Data are n (%) unless otherwise indicated.
HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w).

Safety

- In the HP40, HP45, and vehicle groups, TEAEs were reported by 17.5%, 26.0%, and 22.0% of patients, respectively; most were mild or moderate in intensity (**Table 3**)

Table 3. Overall Summary of Safety

Characteristic	HP40 (n=103)	HP45 (n=100)	Vehicle (n=50)
No. of TEAEs	32	36	14
TEAEs[a]	18 (17.5)	26 (26.0)	11 (22.0)
No. of SAEs	2	1	1
SAEs[a]	2 (1.9)	1 (1.0)	1 (2.0)
TEAEs by severity[b]			
Mild	15 (14.6)	10 (10.0)	7 (14.0)
Moderate	2 (1.9)	15 (15.0)	4 (8.0)
Severe	1 (1.0)	1 (1.0)	0
SAEs by severity[b]			
Mild	0	0	0
Moderate	1 (1.0)	0	1 (2.0)
Severe	1 (1.0)	1 (1.0)	0
Discontinuations due to TEAE	0	1 (1.0)	0
Discontinuations due to SAE	0	1 (1.0)	0
Treatment-related TEAEs	2 (1.9)	2 (2.0)	1 (2.0)
TEAEs by preferred term			
Nasopharyngitis	2 (1.9)	2 (2.0)	1 (2.0)
Bronchitis	0	3 (3.0)	1 (2.0)
Basal cell carcinoma	1 (1.0)	1 (1.0)	0
Dermatitis contact	0	1 (1.0)	1 (2.0)
Drug eruption	0	2 (2.0)	0
Eyelid edema	1 (1.0)	1 (1.0)	0
Headache	0	2 (2.0)	0
Hypertension	2 (1.9)	0	0
Hyponatremia	1 (1.0)	0	1 (2.0)
Upper respiratory tract infection	1 (1.0)	0	1 (2.0)
Viral gastroenteritis	1 (1.0)	1 (1.0)	0

Data are n (%) unless otherwise indicated. HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w); SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a] Patients who had >1 TEAE for a treatment are counted once for that treatment.
[b] If a patient experienced >1 TEAE or SAE for a treatment, the patient is counted only once for the worst severity.

- Among TEAEs related to study treatment, malaise and eyelid edema were related to HP40 treatment and cellulitis and eyelid edema were related to HP45 treatment (**Table 4**)

Table 4. Summary of Treatment-Related TEAEs

	HP40 (n=103)	HP45 (n=100)	Vehicle (n=50)
Number of patients with treatment-related TEAEs	2 (1.9)	2 (2.0)	1 (2.0)
Treatment-related TEAEs by preferred term			
Eyelid edema	1 (1.0)	1 (1.0)	0
Malaise	1 (1.0)	0	0
Cellulitis	0	1 (1.0)	0
Seborrheic dermatitis	0	0	1 (1.0)

HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w); TEAEs, treatment-emergent adverse events.

- 4 serious TEAEs occurred across the 3 groups; these were not considered related to treatment (**Table 5**)

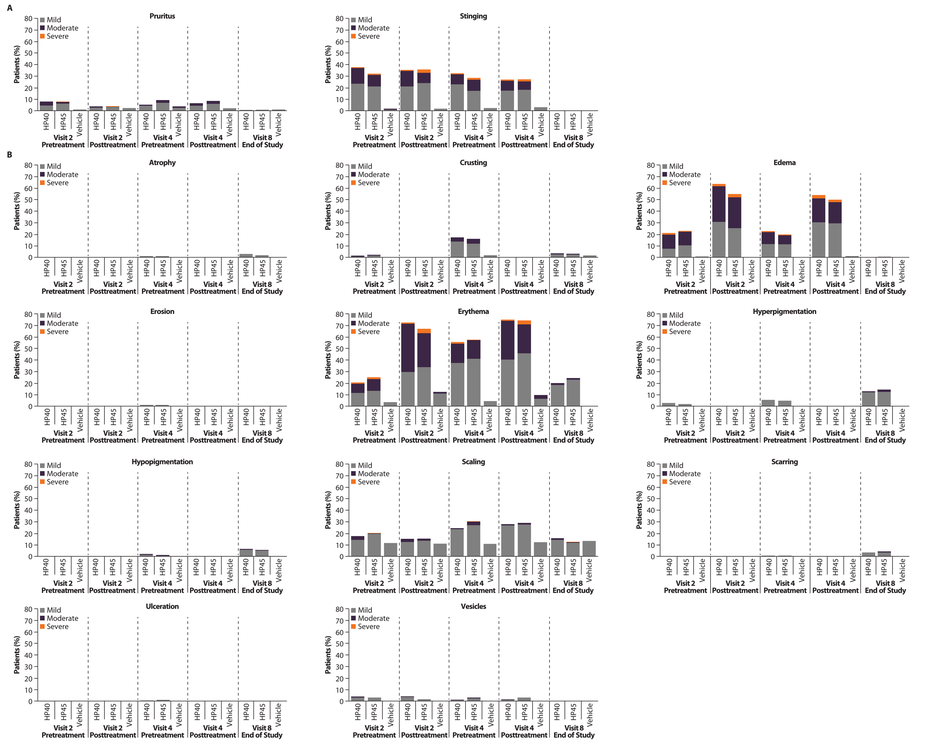
Table 5. Summary of SAEs

	HP40 (n=103)	HP45 (n=100)	Vehicle (n=50)
Patients with SAEs[a]	2 (1.9)	1 (1.0)	1 (2.0)
SAEs by preferred term			
Atrial fibrillation	0	0	1 (2.0)
Deep vein thrombosis	1 (1.0)	0	0
Pancreatic carcinoma	0	1 (1.0)	0
Syncope	1 (1.0)	0	0

HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w); SAEs, serious adverse events.
[a] Patients who had >1 SAE for a treatment are counted once for that treatment.

- The only study discontinuation resulting from a TEAE occurred with 1 patient treated with HP45 who had an SAE of pancreatic carcinoma
- Incidences of LSRs were similar between groups and most were of mild intensity (**Figure 2**)
  - By visit 8, <1% of patients reported an LSR of pruritus and no patients reported an LSR of stinging; no events of erosion, ulceration, or vesicles were reported by the investigator
  - At visit 8, investigators reported low percentages of moderate erythema in both treatment groups (<2%); similar results were observed for investigator-rated scaling

Figure 2. Frequencies of LSRs by Visit, Intensity, and Treatment Condition: (A) Patient-Reported LSRs and (B) Investigator-Reported LSRs



HP40, hydrogen peroxide topical solution, 40% (w/w); HP45, hydrogen peroxide topical solution, 45% (w/w); LSRs, local skin reactions.

- No treatment-related variances in clinical laboratory values or vital signs were observed

References

1. Del Rosso JQ. *J Clin Aesthet Dermatol*. 2017;10:16-25.
2. Ranasinghe GC, Friedman AJ. *J Drugs Dermatol*. 2017;16:1064-8.
3. Baumann LS, et al. *J Am Acad Dermatol*. 2018;79:869-77.
4. Eskata [package insert]. Malvern, PA: Aclaris Therapeutics, Inc; 2017.

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Disclosures

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