Safety of Hydrogen Peroxide Topical Solution, 45% (w/w) for Treatment of Common Warts: Results From Pediatric Patients in the Phase 2 WART-203 Trial

Kimberly K. Grande, MD[1]; Joel Schlessinger, MD[2]; Howard L. Sofen, MD[3]; Leonard Swinyer, MD[4]; Judith C. Schnyder, MBA[5]; Stuart D. Shanler, MD, FAAD, FACMS[5]

[1]The Skin Wellness Center, Knoxville, TN; [2]Skin Specialists, PC, Omaha, NE; [3]David Geffen UCLA School of Medicine, Los Angeles, CA; [4]Dermatology Research Center, Salt Lake City, UT; [5]Aclaris Therapeutics, Inc., Wayne, PA

CONCLUSIONS

1. The results of these post hoc analyses suggest that treatment with HP45 is well tolerated in pediatric patients with common warts
2. No serious, severe, or treatment-related TEAEs were reported during the study
3. Most LSRs were mild in severity, few LSRs were reported by the end of the treatment period (week 8), and all patient- and investigator-reported LSRs had resolved by the end of the study (week 20)
4. Phase 3 studies evaluating HP45 in patients aged ≥1 year with common warts are underway (NCT03687372, NCT03691831) and will provide further evidence regarding the safety and efficacy of HP45 in pediatric patients with common warts

SYNOPSIS

- Verruca vulgaris (the common wart) is a cutaneous manifestation of human papillomavirus infection,[1-3] with an estimated prevalence of approximately 10% in the global population and up to 20% in children[4]
- Common warts can occur at virtually any anatomic location, but are most commonly located on the fingers, hands, and sites prone to trauma (eg, knees, elbows)[5]
- No prescription therapies have received approval from the US Food and Drug Administration for the treatment of common warts, and the most commonly used therapies have very little rigorous clinical evidence for their efficacy in the treatment of warts[6]
- A proprietary, stabilized high-concentration hydrogen peroxide topical solution, 45% (w/w) (HP45), delivered via a proprietary delivery device, is currently in clinical development for the treatment of common warts and was evaluated in patients aged ≥8 years in the WART-203 study

OBJECTIVE

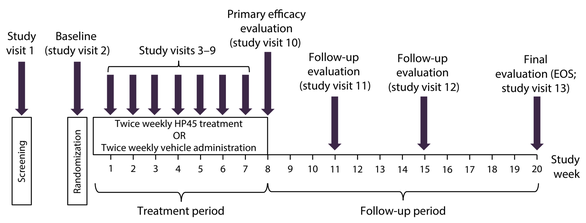
- The objective of this presentation is to describe the results of post hoc analyses evaluating the safety of HP45 for the treatment of common warts in the non-prespecified subset of patients aged ≥8 to <18 years who participated in the WART-203 study

METHODS

Study Design

- The WART-203 trial was a Phase 2, randomized, multicenter, double-blind, vehicle-controlled study designed to evaluate the efficacy and safety of HP45 compared with vehicle for the treatment of common warts (NCT03278028)
- Patients were required to complete a total of 13 study visits (**Figure 1**)
  - These included screening; randomization/first treatment; 7 additional weekly visits; primary efficacy evaluation at week 8; follow-up evaluations at weeks 11 and 15; and an end-of-study evaluation at week 20
- Patients received HP45 or vehicle twice weekly for 8 weeks during the treatment period of the study
  - The patient self-administered the first of the twice weekly treatments at the study center under the supervision of the investigator and the second of the twice weekly treatments at home
  - The parent/legal guardian administered treatment if the patient was a minor

Figure 1. Phase 2 WART-203 Study Design



Arrows indicate study visits.
EOS, end of study; HP45, hydrogen peroxide topical solution, 45% (w/w).

Study Patients

- Eligible patients had a clinical diagnosis of common warts and 1 to 6 eligible warts (1 designated by the investigator as the target wart) on the trunk or extremities
  - Eligible warts were discrete lesions present for ≥4 weeks with a grade ≥2 on the validated Physician's Wart Assessment™ (PWA; **Table 1**)
  - Clinically atypical, periungual, subungual, genital, anal, mosaic, plantar, flat, and filiform warts were not eligible for treatment in this study

Table 1. Physician's Wart Assessment™ (PWA) Grading

Grade	Description
0	Clear: no visible wart; no further treatment indicated
1	Near clear: a visible wart <3 mm in maximal diameter (or length)
2	A visible wart ≥3 mm and <6 mm in maximal diameter (or length)
3	A visible wart ≥6 mm in maximal diameter (or length)

- For enrollment in the WART 203 trial, eligible patients were ≥8 years of age; the post hoc analyses described in this presentation include pediatric patients ≥8 to <18 years of age
- In these post hoc analyses, only the non-prespecified pediatric patients aged ≥8 to <18 years who participated in the WART-203 study were included

Efficacy and Safety Assessments

- The primary and secondary efficacy analyses were performed on the per-protocol population which included all randomized patients who missed ≤3 treatment visits, completed study visit 10 (week 8; end of treatment period) and study visit 13 (week 20; end of study), and had no major protocol violations
- Efficacy was evaluated based on PWA assessments of target and nontarget warts
  - The primary efficacy endpoint was the mean change from baseline in target wart PWA grade at the end of the treatment period (week 8) for HP45 vs vehicle
- For all efficacy analyses, statistical significance was defined as α=0.05
- Safety analyses were performed on the safety population which included all randomized patients and included assessment of adverse events (AEs), local skin reactions (LSRs), clinical laboratory studies, and vital signs
  - LSR assessments included patients' assessments of symptoms of irritation (pruritus, stinging/burning) and investigators' assessments of signs of irritation (erythema, edema, erosion, ulceration, vesicles/bullae, excoriations, scabbing) associated with treated warts and the surrounding skin exposed to study treatment
  - LSR assessments were conducted at study visits 2 to 13; for visits in which study medication was applied, LSR assessments were performed pretreatment and 10 ± 4 or 20 ± 4 minutes after application for patient or investigator assessments, respectively
  - LSR severity was reported using a 4-integer scale as follows: 0 = none; 1 = mild; 2 = moderate; 3 = severe

RESULTS

Study Patients

- 20 pediatric patients (mean age, 12.1 years) were included and randomly assigned to treatment with HP45 or vehicle in the WART-203 study; 19 completed the study (HP45, n=13; vehicle, n=6), and 1 withdrew consent
- Baseline demographics and disease characteristics were similar in the 2 treatment groups (**Table 2**)

Table 2. Baseline Demographics and Disease Characteristics of the Pediatric Per-Protocol Population

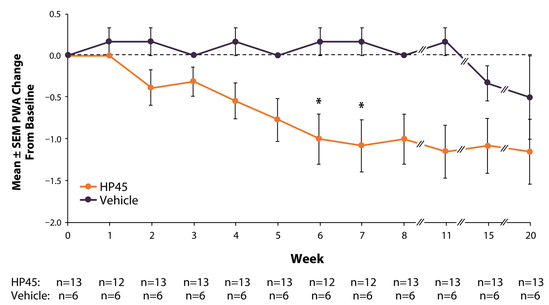
Characteristic	HP45 n=13	Vehicle n=6	Total N=19[a]
Mean (SD) age, y	12.5 (2.6)	11.0 (2.5)	12.1 (2.6)
Gender, n (%)			
Male	8 (61.5)	4 (66.7)	12 (63.2)
Female	5 (38.5)	2 (33.3)	7 (36.8)
Race, n (%)			
White	13 (100)	6 (100)	19 (100)
Ethnicity, n (%)			
Hispanic or Latino	3 (23.1)	2 (33.3)	5 (26.3)
Not Hispanic or Latino	10 (76.9)	4 (66.7)	14 (73.7)
Fitzpatrick Skin Type, n (%)			
I	1 (7.7)	0 (0)	1 (5.3)
II	5 (38.5)	1 (16.7)	6 (31.6)
III	4 (30.8)	4 (66.7)	8 (42.1)
IV	3 (23.1)	1 (16.7)	4 (21.1)
Median PWA grade (range)	2.0 (2–3)	2.5 (2–3)	2.0 (2–3)

HP45, hydrogen peroxide topical solution, 45% (w/w); PWA, Physician's Wart Assessment™.
[a]Of 20 patients who were enrolled and randomized to HP45 or vehicle, 1 patient withdrew consent.

Efficacy

- The 19 pediatric patients who completed the WART-203 study were included in the efficacy analyses (per-protocol population: HP45, n=13; vehicle, n=6)
- Greater reductions in mean target wart PWA grade from baseline were observed with HP45 vs vehicle at the end of the treatment period (week 8; −1.0 vs 0; *P*=0.05) and at the end of the study (week 20; −1.2 vs −0.5; *P*=0.24) (**Figure 2**)

Figure 2. Mean Change From Baseline in PWA Grade by Study Week (Primary Efficacy Variable), Pediatric Per-Protocol Population (N=19)



Between-treatment comparisons were performed using analysis of covariance with baseline PWA as the covariate.
HP45, hydrogen peroxide topical solution, 45% (w/w); PWA, Physician's Wart Assessment™.
*$P<0.05$.

- Detailed efficacy data are presented in the Fall CDC 2019 poster presentation by Grande et al, Efficacy of Hydrogen Peroxide Topical Solution, 45% (w/w) for Treatment of Common Warts: Results From Pediatric Patients in the Phase 2 WART-203 Trial

Safety

- All 20 pediatric patients who were randomized in the WART-203 study were included in the safety analyses (safety population: HP45, n=14; vehicle, n=6)
- Overall incidences of treatment-emergent AEs (TEAEs) were similar in the 2 treatment groups (safety population: HP45, 14.3%; vehicle, 16.7%) (**Table 3**)
  - All TEAEs were mild or moderate in severity and none were considered related to study treatment
- No pediatric patients discontinued study drug treatment due to TEAEs (**Table 3**)

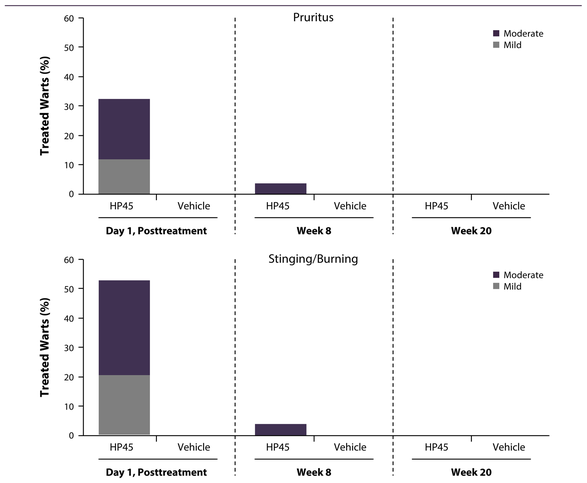
Table 3. Overall Summary of Safety, Pediatric Safety Population

Characteristic	HP45 (n=14)	Vehicle (n=6)	Total (N=20)
Number of TEAEs	3	1	4
TEAEs, n (%)	2 (14.3)	1 (16.7)	3 (15.0)
TEAEs by preferred term, n (%)			
Nasopharyngitis	2 (14.3)	1 (16.7)	3 (15.0)
Viral gastroenteritis	1 (7.1)	0 (0)	1 (5.0)
TEAEs by severity, n (%)			
Mild	1 (7.1)	1 (16.7)	2 (10.0)
Moderate	1 (7.1)	0	1 (5.0)
Severe	0	0	0
Treatment-related TEAEs, n	0	0	0
Discontinuations due to TEAEs, n	0	0	0
Number of SAEs	0	0	0

HP45, hydrogen peroxide topical solution, 45% (w/w); SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- In the patient- and investigator-rated LSR assessments at weeks 8 and 20, a total of 28 treated warts were evaluated in the HP45 group and 17 treated warts were evaluated in the vehicle group
- Incidences of patient-reported LSRs are shown in **Figure 3**
  - At week 8, moderate pruritus was reported for 1 of 28 warts (3.6%) treated with HP45 vs none of 17 warts treated with vehicle
  - Moderate stinging/burning was reported for 1 of the 28 warts (3.6%) treated with HP45 vs none of the 17 warts treated with vehicle at week 8

Figure 3. Frequencies of Patient-Reported LSRs by Study Week, Intensity, and Treatment Group, Pediatric Safety Population (N=20)[a]



[a]HP45, n=14; vehicle, n=6.

- Incidences of investigator-reported LSRs at weeks 8 and 20 are shown in **Figure 4**
  - Mild erythema was reported for 3 of 28 warts (10.7%) in the HP45 group vs 1 of 17 warts (5.9%) in the vehicle group at week 8
  - No events of erosion, excoriation, ulceration, or vesicles/bullae were reported for either treatment group at any study visit
- All patient- and investigator-reported LSRs in the HP45 group were mild or moderate and resolved by the end of the study (week 20) (**Figures 3 and 4**)
- No treatment-related changes in clinical laboratory values or vital signs were observed at the end of the study (week 20)

Figure 4. Frequencies of Investigator-Reported LSRs by Study Week, Intensity, and Treatment Group, Pediatric Safety Population (N=20)[a]

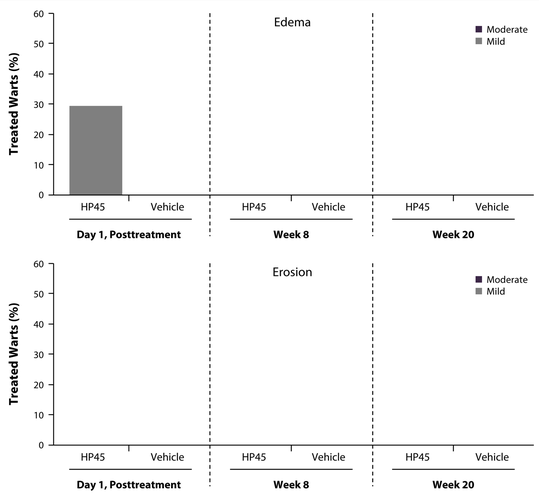
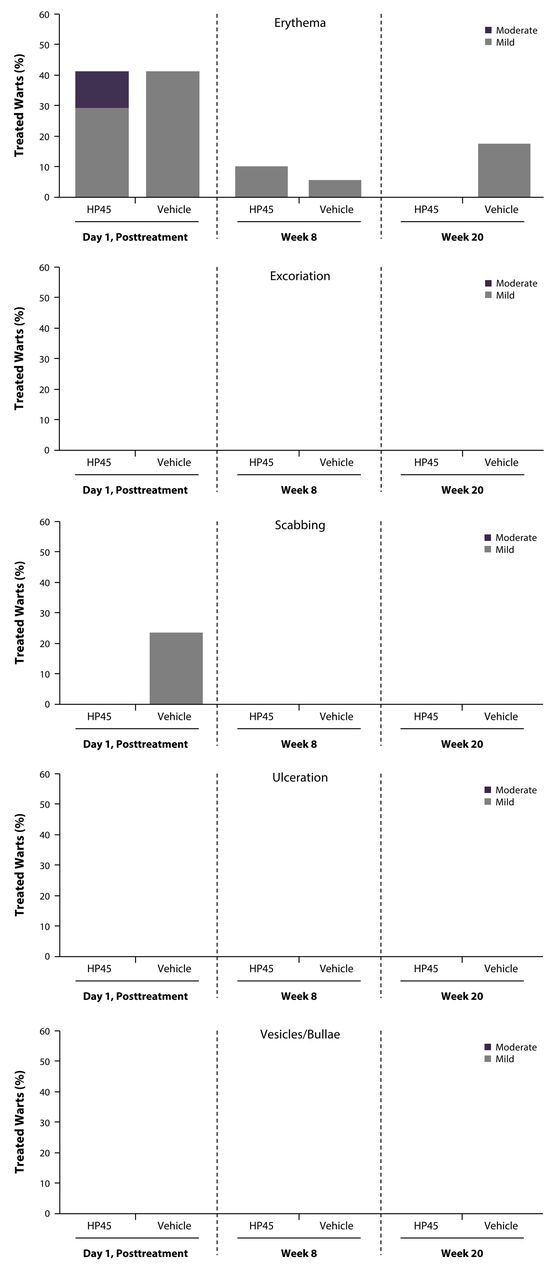


Figure 4. Frequencies of Investigator-Reported LSRs by Study Week, Intensity, and Treatment Group, Pediatric Safety Population (N=20)[a] (cont'd)



[a]HP45, n=14; vehicle, n=6.

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Email address for questions or comments: kgrande.swc@gmail.com

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