Safety and Efficacy of A-101 Hydrogen Peroxide Topical Solution 40% in Adults With Seborrheic Keratosis: Results From the Phase 3, Randomized, Double-Blind, Vehicle-Controlled Study

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Introduction

- Seborrheic keratosis (SK) is a common cutaneous lesion that affects more than 83 million Americans,[1] particularly those who are middle-aged and older. While benign, these lesions are cosmetically unacceptable to many patients.
- Malignancy concerns following the appearance of lesions act as a primary driver for a patient to seek medical advice.
- Removal of SKs is often performed for cosmetic reasons, but it may be indicated for inflamed, pruritic, or painful lesions.
- Prior to December 2017, there was no US FDA-approved drug for the treatment of SKs. Ablative/destructive procedures (eg, cryosurgery, electrodessication/curettage, etc) had been available; however, their efficacy and safety have not been rigorously evaluated in well-controlled clinical trials, and they often involve burning, cutting, or freezing.
- A noninvasive, well-tolerated, topical agent for the removal of SKs is an important unmet need.
- A-101 is a patented topical formulation based on a high concentration of hydrogen peroxide (40% w/w) for asymptomatic SK.[2]
- Phase 2 studies showed that a numerically greater percentage of subjects achieved lesion clearance when treated with A-101 40% versus A-101 32.5%; both concentrations achieved significantly greater clearance than placebo.[3]
- The purpose of this study (A-101-SEBK-301; NCT02667236) was to evaluate the safety and efficacy of A-101 40% versus its matching vehicle for the treatment of SK.

Materials and Methods

Patients and Study Design

- Multicenter, phase 3, randomized, double-blind, vehicle-controlled study. Patients were randomized 1:1 to receive A-101 or matching vehicle.
- Eligible patients: aged ≥ 18 years with 4 eligible lesions, identified by study investigator.
- Eligible target lesions were stable, typical SKs, measuring 5-15 mm in both width and length, 1-2 mm in thickness, and Physician's Lesion Assessment (PLA) grade ≥ 2 (**Table 1**).[4] Patients were required to present with ≥ 1 SK on the trunk or extremities and ≥ 1 SK on the face.
  - Target SKs could not be on the eyelid, within 5 mm of the orbital rim, in an intertriginous area, or pedunculated.

Table 1: Validated Physician's Lesion Assessment (PLA)[3] Scale

Grade	Descriptor
0	Clear: No visible SK
1	Near Clear: A visible SK with a surface appearance different from the surrounding skin (not elevated)
2	Thin: A visible SK (≤ 1 mm)
3	Thick: A visible SK (> 1 mm)

- All treatments were performed by a nonphysician subinvestigator to maintain blinding. After initial treatment on Day 1, SKs with a PLA score > 0 were retreated on Day 22. At Day 106, the investigator assessed the SKs using the validated PLA scale.

Endpoints

- Primary efficacy endpoint: percent of patients with complete clearance (PLA = 0) of all 4 SKs at 106 days after first treatment.
- Secondary endpoint: percent of patients with complete clearance (PLA = 0) in at least 3 of 4 SKs.
- Exploratory endpoints:
  - Mean per-patient percent of SKs judged Clear/Near Clear (PLA ≤ 1).
  - Mean per-patient percent of SKs on the face judged Clear/Near Clear (PLA ≤ 1).
- Safety: adverse events (AEs), local skin reactions.

Results

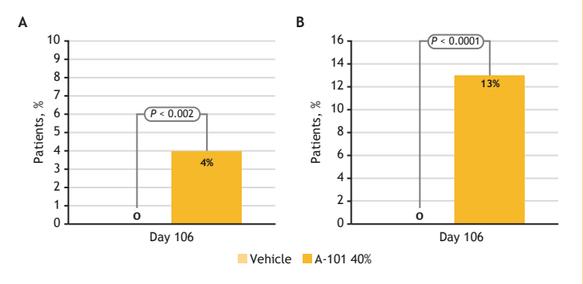
- A total of 450 patients were enrolled—220 of 223 and 226 of 227 patients randomized to A-101 and vehicle, respectively, completed the study.
- Demographic characteristics were similar across all treatment groups.
- Mean age of patients was 69 years (range, 42-90). 59% of subjects were women, and 97.8% (440) were Caucasian.
- Fitzpatrick types 1 to 5 were represented:
  - Type 1: 72 (16.0%); Type 2: 211 (46.9%); Type 3: 123 (27.3%); Type 4: 40 (8.9%); Type 5: 4 (0.9%).

Efficacy

Primary and Secondary Endpoints

- Significantly more patients receiving A-101 completely cleared (PLA = 0) all 4 of 4 SKs (4.0% vs 0%, $P < 0.002$) and 3 of 4 SKs (13.5% vs 0%, $P < 0.0001$) versus vehicle in the primary and secondary endpoints, respectively, at Day 106 (**Figure 1**).

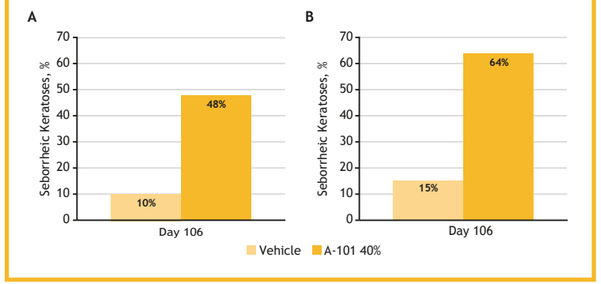
Figure 1: Percentage of Patients with Complete Clearance (PLA 0) of all 4 SKs (A) and at Least 3 of 4 SKs (B)



Exploratory Endpoints

- Significantly higher mean per-patient percentage of SKs achieving Clear/Near Clear (PLA ≤ 1) was observed in the A-101 arm (48% vs 10% at Day 106) (**Figure 2A**).
- Significantly higher mean per-patient percentage of facial SKs achieving Clear/Near Clear (PLA ≤ 1) was also observed in the A-101 arm (64% vs 15% at Day 106) (**Figure 2B**).

Figure 2: Mean Per-Patient Percent of SKs (A) or Facial SKs (B) Judged to be Clear/Near Clear (PLA ≤ 1)



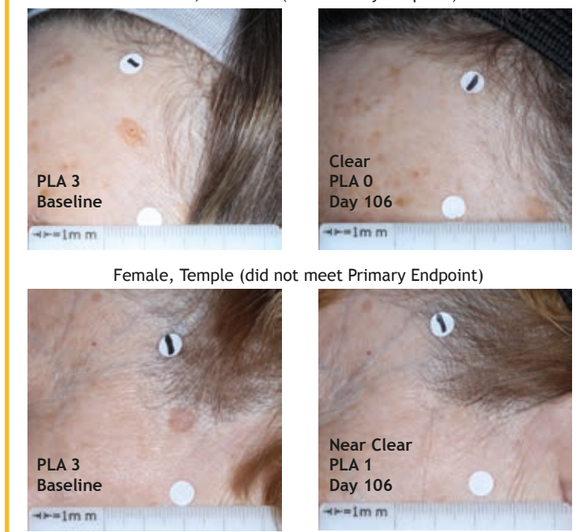
Safety

- AEs were comparable between groups: 54 (24.2%) patients in the A-101 group versus 45 (19.8%) patients in the vehicle group.
  - The most frequently reported treatment-emergent AEs were nasopharyngitis (1.3% A-101 vs 3.1% vehicle), bronchitis (1.3% A-101 vs 0.4% vehicle), and upper respiratory tract infection (0.4% A-101 vs 1.3% vehicle).
  - 4 (1.8%) patients in the A-101 group had 4 serious AEs (SAEs) versus 6 (2.6%) patients in the vehicle group who had 7 SAEs. All SAEs were considered not related to study medication.
- Local skin reactions were predominantly mild and had generally resolved by Day 106 (**Table 2**).
- At all visits, atrophy, erosion, hypopigmentation, scarring, or ulceration were reported for ≤ 4% of SKs.

Table 2: > 90% of SKs Without Local Dyspigmentation or Scarring

		No Reaction	Mild	Moderate	Severe
Hypopigmentation	A-101 40%	97.7%	2.3%	0.0%	0.0%
	Vehicle	99.9%	0.1%	0.0%	0.0%
Hyperpigmentation	A-101 40%	93.8%	5.6%	0.6%	0.0%
	Vehicle	99.8%	0.1%	0.1%	0.0%
Scarring	A-101 40%	99.3%	0.6%	0.1%	0.0%
	Vehicle	100.0%	0.0%	0.0%	0.0%

Figure 3: Patient Photos of SK, Before and After A-101 Treatment



Conclusions

- A-101 (hydrogen peroxide) topical solution, 40% (w/w) is a safe, effective, and well-tolerated treatment for seborrheic keratoses (**Figure 3**).
- For SKs on the face and cosmetically sensitive locations, A-101 was highly effective, with very low occurrence of hypopigmentation and/or scarring.
- On December 14, 2017, A-101 (hydrogen peroxide) topical solution, 40% (w/w) was approved by the FDA as the first and only topical treatment for raised seborrehic keratoses.

References

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Acknowledgments

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