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, Parallel-Group Study

Zoe D. Draelos, MD,[1] Steven E. Kempers, MD,[2] Stacy R. Smith, MD,[3] David C. Wilson, MD,[4] Christopher V. Powala,[5] Mark Bradshaw, PhD,[6] Esther Estes, MD, MPH,[5] Stuart D. Shanler, MD, FAAD, FACMS[5]

[1]Dermatology Consulting Services, High Point, NC; [2]Minnesota Clinical Study Center, Fridley, MN; [3]California Dermatology & Clinical Research Institute, Encinitas, CA; [4]The Education and Research Foundation, Inc., Lynchburg, VA; [5]Aclaris Therapeutics, Malvern, PA; [6]Global Consulting Partners in Medical Biometrics, New York, NY

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 SK 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.
- Currently, there is no US FDA-approved drug for the treatment of SKs. However, ablative/destructive procedures (eg, cryosurgery, electrodessication/curettage, etc) are available, but their efficacy and safety have not been rigorously evaluated in well-controlled clinical trials.
- A noninvasive, well-tolerated, topical agent for the removal of SK lesions is an important unmet need.
- A-101, a patented investigational new drug, is a 40% hydrogen peroxide topical solution, with a surface tension-reducing agent formulated for the treatment of SK lesions.[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 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, parallel-group study. Patients were randomized 1:1 to receive A-101 or matching vehicle.
- Eligible patients: aged ≥ 18 years with 4 eligible SK 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 lesion on the trunk or extremities and ≥ 1 lesion on the face.
  - Target lesions could not be on the eyelid, within 5 mm of the orbital rim, in an intertriginous area, or pedunculated.

Table 1: Validated PLA[3] Scale

Grade	Descriptor
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 (≤ 1 mm)
3	Thick: A visible SK lesion (> 1 mm)

- All treatments were performed by a nonphysician subinvestigator to maintain blinding. After initial treatment on Day 1, SK lesions with a PLA score > 0 were retreated on Day 22. At Day 106, the investigator assessed the lesions using the validated PLA scale.
- Efficacy analyses were based on the intent-to-treat (ITT) population; any subject with missing PLA data on Day 106 was considered a nonresponder.

End Points

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

Results

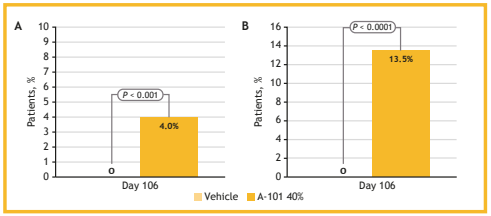
- A total of 450 patients were enrolled—220 of 223 and 226 of 227 patients randomized to A-101 and vehicle, respectively, completed the study.
- Demographic characteristics were similar across all treatment groups.
- Mean age of patients was 69 years (range, 42-90). 59% of subjects were women, and 97.8% (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 lesions (4.0% vs 0%, $P < 0.002$) and 3 of 4 lesions (13.5% vs 0%, $P < 0.0001$) versus vehicle in the primary and secondary endpoints, respectively, at Day 106 (**Figure 1**).

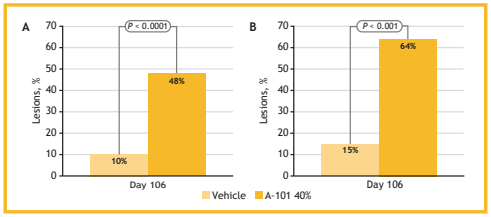
Figure 1: Clearance of all 4 SK Lesions (A) and Clearance of at Least 3 of 4 SK Lesions (B)



Exploratory Endpoints

- Significantly higher mean per-patient percentage of lesions achieving clear/near clear (PLA ≤ 1) was observed in the A-101 arm (48% vs 10% at Day 106; $P < 0.0001$) (**Figure 2A**).
- Significantly higher mean per-patient percentage of facial lesions achieving clear/near clear (PLA ≤ 1) was also observed in the A-101 arm (64% vs 15% at Day 106; $P < 0.0001$) (**Figure 2B**).

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



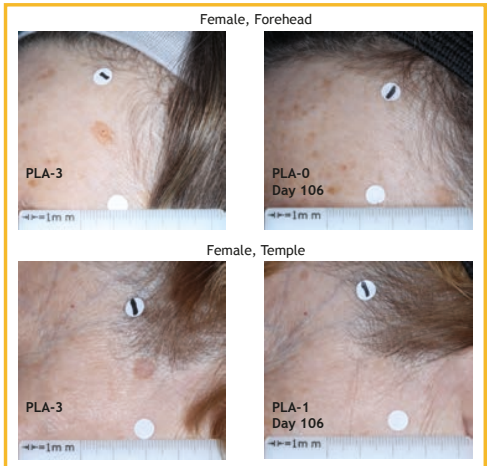
Safety

- 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 lesions.

Table 2: > 90% of Patients Experience No Local Skin 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 Target SK Before and After A-101 Treatment



Conclusions

- A-101 (**Figure 3**), a 40% hydrogen peroxide topical solution, is a safe, effective, and well-tolerated treatment for seborrheic keratoses.
- For SKs on the face and cosmetically sensitive locations, A-101 was highly effective, with very low occurrence of hypopigmentation and/or scarring.
- If approved, A-101 would be the first US FDA-approved topical treatment for seborrheic keratosis.

References

1. Bickers DR, et al. *J Am Acad Dermatol*. 2006;55:490-500.
2. Simionescu O, et al. *J Cell Mol Med*. 2012;16:1223-1231.
3. DuBois JC, et al. *Dermatol Surg*, in press.
4. Data on file. Aclaris Therapeutics Inc., 2014, Malvern, PA, USA.

Acknowledgments

This study was funded by Aclaris Therapeutics, Inc. Editorial support for this poster was provided by PAREXEL and funded by Aclaris Therapeutics, Inc.