A-101 (Hydrogen Peroxide) Topical Solution Safety and Efficacy in Patients With Seborrheic Keratoses: Results From Two Identical Randomized, Double-Blind, Placebo-Controlled, Phase 3 Studies

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Introduction

Seborrheic keratosis (SK) is a common cutaneous lesion that affects more than 83 million Americans, 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, electrodesiccation/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.

(Hydrogen peroxide) topical solution, 40% (w/w) (ESKATA®), Aclaris Therapeutics, Inc., Wayne, PA; HP40® is a proprietary formulation of a stabilized, high concentration of hydrogen peroxide for asymptomatic SKs.

Phase 2 studies showed that a numerically greater percentage of subjects achieved lesion clearance when treated with HP40 versus 22.5% (w/w) formulation; both concentrations achieved significantly greater clearance than placebo.1

The purpose of this study was to evaluate the safety and efficacy of HP40 versus its matching vehicle for the treatment of SK.

Materials and Methods

Patients and Study Design

A multicenter, phase 3, randomized, double-blind, vehicle-controlled study (NCT02667275; Study A) was performed; a second, identical phase 3 study (NCT02667236; Study B) was also performed. Patients were randomized 1:1 to receive HP40 or matching vehicle.

Eligible patients: aged ≥ 18 years with 4 eligible SKs, 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). 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.

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.

Table 1: Validated Physician’s Lesion Assessment (PLA)1 Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Descriptor</th>
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<tbody>
<tr>
<td>0</td>
<td>Clear: No visible SK</td>
</tr>
<tr>
<td>1</td>
<td>Near Clear: A visible SK with a surface appearance different from the surrounding skin (not elevated)</td>
</tr>
<tr>
<td>2</td>
<td>Thin: A visible SK (≤ 1 mm)</td>
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<tr>
<td>3</td>
<td>Thick: A visible SK (&gt; 1 mm)</td>
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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

In Study A, 487 patients were randomized (vehicle: 243; HP40: 244), while in Study B, 450 patients were randomized (vehicle: 227; HP40: 223).

Demographic characteristics were similar across all treatment groups in both studies.

Across the 2 studies, 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 6 were represented: Type 1: 0.4%; Type 2: 0.9%; Type 3: 11.2%; Type 4: 23.7%; Type 5: 30.3%; Type 6: 14.1%; Type 7: 9.9%.

Exploratory Endpoints

Significantly higher mean per-patient percentage of SKs achieving Clear/Near Clear (PLA ≤ 1) was observed in the HP40 arm (Figure 2A).

Significantly higher mean per-patient percentage of facial SKs achieving Clear/Near Clear (PLA ≤ 1) was also observed in the HP40 arm (Figure 2B).

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

Local skin reactions were predominantly mild and had generally resolved by Day 106 in both studies (Table 2).

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>A</td>
<td>96.4%</td>
<td>0.0%</td>
<td>3.4%</td>
</tr>
<tr>
<td>B</td>
<td>97.7%</td>
<td>0.0%</td>
<td>0.0%</td>
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At all visits, atrophy, hypopigmentation, scarrring, or ulceration were reported for ≤ 4% of SKs in both studies.

Figure 3: Patient Photos of SKs Before and After HP40 Treatment

Conclusions

- (Hydrogen peroxide) topical solution, 40% (w/w) (HP40) is a safe, effective, and well-tolerated treatment for seborrheic keratoses (Figure 3).
- For SKs on the face and cosmetically sensitive locations, HP40 was highly effective, with low occurrence of hypopigmentation and/or scarring.
- On December 14, 2017, HP40 was approved by the FDA as the first and only topical treatment for raised seborrheic keratoses.

References


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