

Anatomic Site–Specific Treatment Response With 40% Hydrogen Peroxide (w/w) Topical Formulation for Raised Seborrheic Keratoses: Pooled Analysis of Data from Two Phase 3 Studies

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ABSTRACT

Objective: Seborrheic keratoses (SKs) may present in any non-glabrous skin, but data are limited on the response to treatment as based on the SK location. We aimed to understand the relationship between SK location and clearance with up to 2 treatments of 40% (w/w) hydrogen peroxide topical solution (HP40).

Methods: We conducted a sub-analysis of data pooled from two randomized, double-blind, vehicle (VEH)-controlled clinical trials, including 937 patients, each with 4 target SKs (N=3,748 SKs), with at least 1 on the face and 1 on the trunk or extremities. Treatment response was defined as 0 or 1 on a 4-point Physician's Lesion Assessment (PLA) scale (0=clear; 1=near-clear) after up to 2 applications, 3 weeks apart, and was assessed by SK location (face, trunk, and extremity). Local skin reactions were stratified by anatomic location and categorized based on immediate and delayed post-treatment reactions. Sensitivity analysis was conducted using the mean-per-patient (MPP) percent of SKs that are clear or near-clear at day 106.

Results: Treatment response was greater with HP40 versus VEH regardless of anatomic location of the SK. Clear or near-clear SKs with HP40 was observed in 65% of facial SKs (vs 10% VEH), 46% of truncal SKs (vs 5% VEH), and 38% of extremity SKs (vs 9% VEH). Facial SKs were more likely to be clear or near clear after a single treatment (43%), versus SKs on the trunk (31%) or extremities (14%). Most common immediate reactions with HP40 were erythema, stinging, and edema, which resolved to none or mostly mild within a week. Delayed reactions such as dyspigmentation and scarring occurred at low rates and were least reported for the facial SKs.

Conclusions: SK clearance with HP40 was highest among SKs on the face and lowest among SKs on the extremities. Dyspigmentation rates were lowest among SKs treated on the face. Anatomic location of SK was a predictor of both treatment response and risk of dyspigmentation with HP40 application.

ClinicalTrials.gov listings: NCT02667236 and NCT02667275

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INTRODUCTION

Seborrheic keratoses (SKs) are benign epidermal tumors that exhibit somatic mutations in the fibroblast growth factor receptor 3 protein (FGFR3) and the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA),[1,2] but maintain overall genetic stability without malignant potential.[1-4] SKs are one of the most common benign skin tumors in humans, a category of dermatologic disease that accounts for over $7 billion in medical costs and $1.57 billion in lost work and other activities in the US annually.[5] The prevalence of SKs increases with age, ranging from 38% in people aged 24 to 49 years to more than 90% in those 70 years and older.[6] Given the high prevalence of SKs, patients frequently present to dermatologists seeking treatment for physical (eg, itching) or psychosocial reasons (eg, embarrassment), as well as for concerns about malignancy. While SKs can present in any non-glabrous skin, patient motivations for the removal of SKs can be location dependent. For instance, SKs on the face may more likely cause cosmetic distress.

Nonspecific destructive methods such as cryosurgery, electrosurgery, or curettage are commonly used methods for SK removal. In December 2017, the US Food and Drug Administration approved the first topical treatment of a proprietary formulation of 40% (w/w) hydrogen peroxide (HP40; ESKATA®; Aclaris Therapeutics, Inc., Wayne, PA) solution for raised SKs, on the basis of 2 identical, vehicle-controlled, double-blind

clinical trials.[7] Here, we report on the safety and treatment effect of HP40 based on the anatomic location of the SKs.

METHODS

A detailed explanation of the study design has been previously reported.[7] Briefly, two identical, randomized, double-blind, vehicle-controlled, phase 3 trials (NCT02667236 and NCT02667275) enrolled adults aged ≥18 years with 4 stable, clinically typical, raised SKs (> 0-2 mm thick and 5-15 mm in diameter) with at least 1 SK on the face and at least 1 on the trunk or extremity. A physician investigator identified the 4 target SKs to be treated on each patient, and a non-physician sub-investigator applied the HP40 or vehicle in order to maintain blinding, to address the temporary peroxide whitening effect that could be seen immediately in the active treatment arm. Treatment was applied sequentially to the 4 SKs for 20 seconds per SK at each pass for a total of 4 passes, 1 minute apart.

Efficacy was measured at day 106 using the validated Physician's Lesion Assessment (PLA) scale, in which 0=clear (no visible SK); 1=near-clear (visible SK, not raised); 2=thin SK (≤1 mm); and 3=thick SK (1 mm).[7] If any SK was not clear 3 weeks after the first treatment, a second treatment was administered. Sub-analysis of the treatment effect based on the anatomic location of the SK was then conducted. Sensitivity analysis was also conducted using the mean-per-patient (MPP) percent of SKs, defined as the sum of the intra-patient efficacy (ie, percent of target SKs that are PLA=0 in each patient) divided by the number of patients with target SKs for that body area at day 106.

Treatment-related adverse reactions were localized skin reactions (LSRs), stratified first by the location of the SKs (face, trunk, and extremity) and then categorized by immediate or delayed post-treatment reactions.

RESULTS

The pooled analysis included 467 patients in the HP40 arm with a total of 1,868 SKs and 470 patients in the vehicle arm with a total of 1,880 SKs. Baseline characteristics of the study population are shown in Table 1. All patients had at least 1 SK on the face; most had 1 or more SKs on the trunk; however, only 30% had an SK on the extremity. Of all target SKs, the majority (59%) were on the trunk, 30% on the face, and 11% on the extremities.

The highest treatment effect of HP40, defined as percentage of SKs clear or near-clear (PLA≤1) versus vehicle, was seen on the face (65% vs 10%), followed by the trunk (46% vs 5%), and then the extremities, (38% vs 9%; Figure 1). Findings were consistent in the sensitivity analysis evaluating treatment effect based on the MPP percent of SKs: a higher proportion of clear or near-clear (PLA ≤1) SKs was observed with HP40 in facial SKs compared to vehicle (64% vs 10%) trunk SKs (48% vs 6%) or extremity SKs (35% vs 10%) at day 106. Facial SKs also exhibited the highest likelihood of clearance or near-clearance with a single treatment (43%) followed by the trunk (31%) and extremities (14%). Select photos of SKs before and after treatment with HP40 are shown in Figure 2.

Following the first treatment, the most common immediate LSRs after HP40 treatment were erythema stinging and edema (in descending order of frequency by anatomic location). All acute LSRs improved within 1 week, occurred at similar rates regardless of anatomic location, and resolved to none or mostly mild by day 106 (Table 2). Vesiculation (a clinically relevant but less common LSR), occurred at the lowest rate in the extremi-

TABLE 1.

Patient Baseline Characteristics

Characteristic	HP40 (N = 467)	Vehicle (N = 470)	Total (N = 937)
Age, years			
Mean (SD)	68.3 (8.68)	69.1 (8.67)	68.7 (8.68)
Range	45-91	42-90	42-91
Age group, n (%)			
18-55 years	34 (7.3)	30 (6.4)	64 (6.8)
56-70 years	244 (52.2)	238 (50.6)	482 (51.4)
71+ years	189 (40.5)	202 (43.0)	391 (41.7)
Sex, n (%)			
Male	181 (38.8)	208 (44.3)	389 (41.5)
Female	286 (61.2)	262 (55.7)	548 (58.5)
Race, n (%)			
White	460 (98.5)	457 (97.2)	917 (97.9)
African American	4 (0.9)	4 (0.9)	8 (0.9)
Asian	2 (0.4)	6 (1.3)	8 (0.9)
Other	1 (0.2)	3 (0.6)	4 (0.4)
Ethnicity, n (%)			
Hispanic or Latino	17 (3.6)	19 (4.0)	36 (3.8)
Not Hispanic or Latino	443 (94.9)	438 (93.2)	881 (94.0)
Missing	7 (1.5)	13 (2.8)	20 (2.1)
Fitzpatrick Type, n (%)			
1	58 (12.4)	60 (12.8)	118 (12.6)
2	225 (48.2)	213 (45.3)	438 (46.7)
3	145 (31.0)	139 (29.6)	284 (30.3)
4	34 (7.3)	52 (11.1)	86 (9.2)
5	5 (1.1)	5 (1.1)	10 (1.1)
6	0 (0)	1 (0.2)	1 (0.1)

HP40, hydrogen peroxide topical solution 40% (w/w); N, number of patients; n, number of patients in subset; SD, standard deviation.

FIGURE 1. SKs graded as clear or near-clear at day 106: HP40 compared with vehicle. n, number of patients; PLA, Physician's Lesion Assessment Scale.

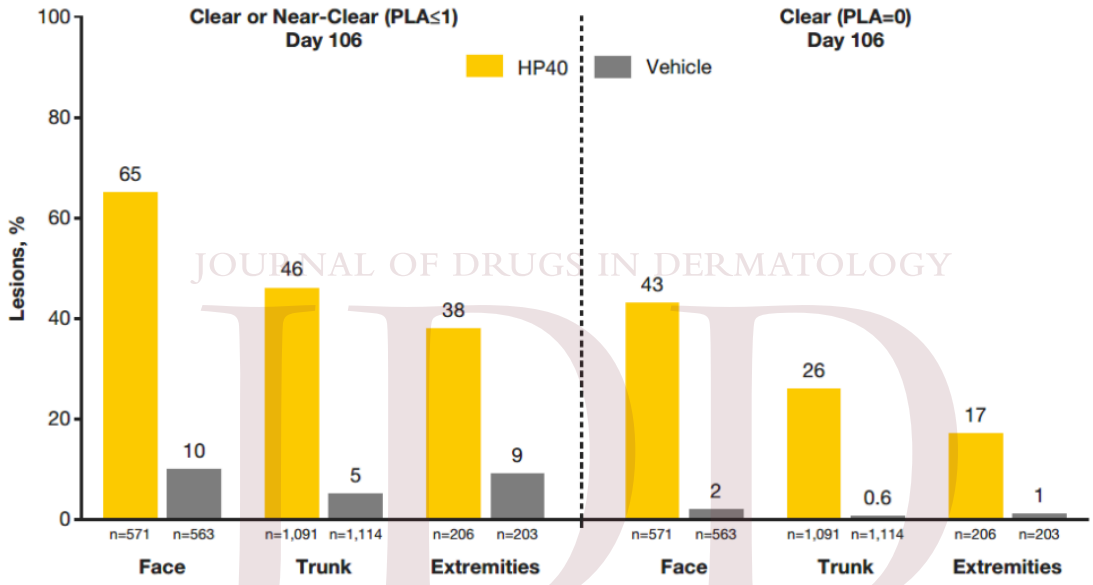
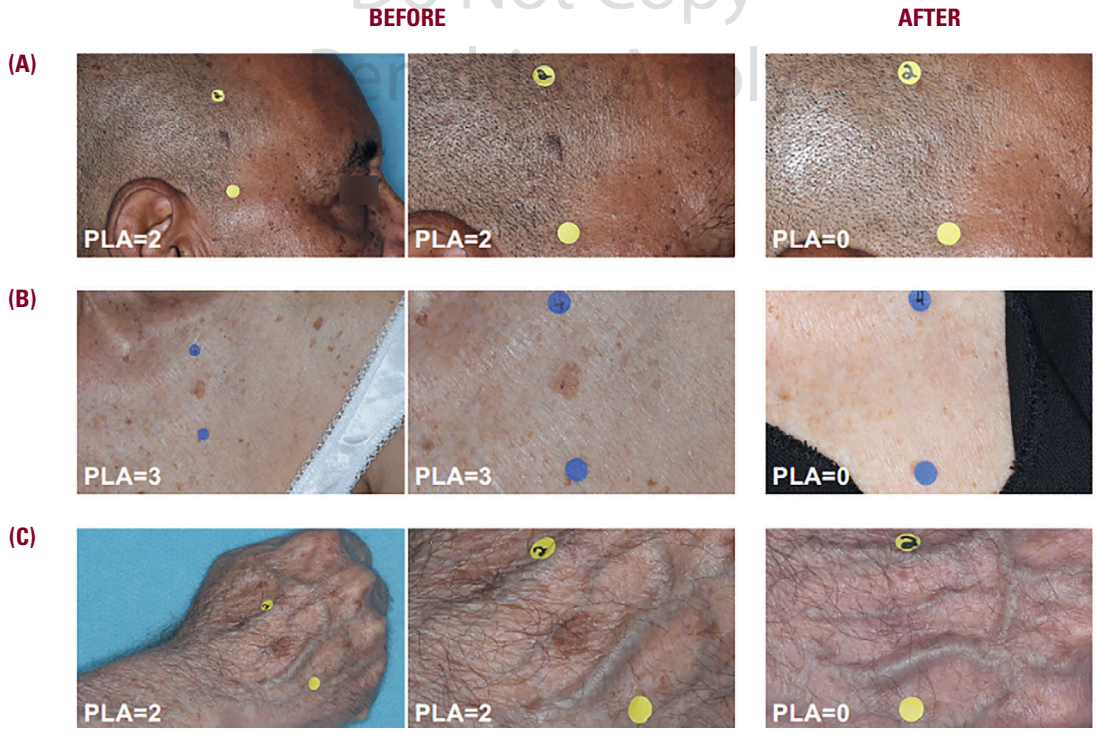


FIGURE 2. Target SKs at baseline (zoomed out and in) and day 106 after HP40 treatment. (A) face; (B) trunk/décolletage; (C) extremity/hand. PLA, Physician's Lesion Assessment Scale.



ties, and all vesiculations completely resolved within a week. Longer-term concerns—hyperpigmentation, hypopigmentation, and scarring—occurred at low rates at day 106 regardless of anatomic location, with the lowest rates observed on the facial SKs (2.3%, 1.9%, and 0%, respectively (Table 3).

DISCUSSION

SKs can be disturbing to patients, particularly when present on aesthetically sensitive areas such as the face.[9,10] Currently, there are several physical methods for removing SKs that include surgical excision, curettage, electrosurgery, ablative lasers, and cryosurgery.[6] However, these modalities may require specialized training and lack well-controlled clinical trials demonstrating overall efficacy and complication rates.[9,10] These destructive techniques may cause pain lasting beyond the treatment, require anesthesia, or pose risk of post-procedural adverse reactions. Cryosurgery with liquid nitrogen is the most popular method, but the efficacy of this modality depends on specialized training such as balancing adequate freeze time and

TABLE 2.

Percentage of SKs With Acute (Immediate) Local Skin Reactions by Anatomic Location

LSR	Location	HP40			Vehicle
		Day 1[a]	Day 8	Day 106	Day 106
Erythema	Face n (%)	519 (90.9)	246 (43.2)	36 (6.4)	7 (1.3)
	Trunk n (%)	1011 (92.7)	433 (39.7)	134 (12.4)	7 (0.6)
	Extremities n (%)	171 (83.0)	63 (30.6)	18 (8.9)	0 (0)
Stinging	Face n (%)	497 (87.0)	10 (1.8)	0 (0)	1 (0.2)
	Trunk n (%)	678 (62.1)	18 (1.7)	0 (0)	0 (0)
	Extremities n (%)	151 (73.3)	1 (0.5)	1 (0.5)	0 (0)
Edema	Face n (%)	432 (75.7)	7 (1.2)	0 (0)	0 (0)
	Trunk n (%)	845 (77.5)	21 (1.9)	0 (0)	0 (0)
	Extremities n (%)	132 (64.1)	0 (0)	0 (0)	0 (0)
Vesicles	Face n (%)	57 (10.0)	0 (0)	0 (0)	0 (0)
	Trunk n (%)	150 (13.8)	0 (0)	0 (0)	0 (0)
	Extremities n (%)	10 (4.9)	0 (0)	0 (0)	0 (0)
Crusting	Face n (%)	0 (0)	204 (35.8)	13 (2.3)	17 (3.1)
	Trunk n (%)	0 (0)	539 (49.4)	83 (7.7)	57 (5.2)
	Extremities n (%)	0 (0)	98 (47.6)	4 (2.0)	8 (4.0)
Erosion	Face n (%)	0 (0)	18 (3.2)	0 (0)	0 (0)
	Trunk n (%)	0 (0)	22 (2.0)	1 (0.1)	0 (0)
	Extremities n (%)	0 (0)	3.4 (7)	0 (0)	0 (0)
Pruritis	Face n (%)	98 (17.2)	37 (6.5)	2 (0.4)	3 (0.5)
	Trunk n (%)	204 (18.7)	117 (10.8)	6 (0.6)	10 (0.9)
	Extremities n (%)	37 (18.0)	7 (3.4)	1 (0.5)	1 (0.5)
Scaling	Face n (%)	178 (31.2)	258 (45.3)	22 (3.9)	31 (5.6)
	Trunk n (%)	347 (31.8)	554 (50.8)	110 (10.1)	78 (7.1)
	Extremities n (%)	53 (25.7)	110 (53.4)	16 (7.9)	19 (9.6)
Ulceration	Face n (%)	0 (0)	4 (0.7)	0 (0)	0 (0)
	Trunk n (%)	0 (0)	13 (1.2)	0 (0)	1 (0.1)
	Extremities n (%)	0 (0)	2 (1.0)	0 (0)	0 (0)

[a]10 minutes after first treatment. LSR, localized skin reaction; n, number of lesions in subset

freeze-thaw cycles to achieve destruction while avoiding damage to the underlying dermis and the surrounding skin that may lead to scarring and dyspigmentation.[11,12] In one study of Asian patients, electrocautery for SKs caused post-inflammatory hyperpigmentation in 20% of cases.[10]

Despite the significant limitations of procedural techniques, attempts to use topical agents for the management of SKs have been limited.[8,13] In a non-randomized, open-label study of 15 patients, applications of topical calcipotriene 0.005% ointment, imiquimod 5% cream, and tazarotene 0.1% cream were ineffective or impractical. Tazarotene led to clearance in 47% of SKs but required 6 months of therapy and caused significant skin irritation and burning in patients.[11] In a double-blind, paired comparison study of 58 volunteers, ammonium lactate 12% lotion (Lac-Hydrin®) was no better than vehicle for the treatment of SK. Thus, a topical treatment that allows for consistent application by any healthcare provider, and with a favorable safety profile, would represent an important therapeutic modality in the management of non-irritated SKs.

Past analysis of data from two phase 3 trials with HP40 versus vehicle based the measurement of primary efficacy on proportion of patients with complete clearance of all 4 target SKs versus vehicle at day 106.[7] In this paper, we wanted to understand the treatment effect measured as a percentage of SK lesions cleared, and stratified by anatomic location. This is relevant because one-third of patients present with 15 or more SKs,[9] and understanding the anticipated treatment effect based on each SK's anatomic location would allow the clinician to better counsel patients on the likelihood of treatment success. Consistent with the data from phase 2 trials, this analysis showed treatment response was highest for facial SKs (65% of SKs clear/near-clear and 43% of SKs clear).[8] In addition, SKs on the face were more likely to be clear or near-clear 21 days after initial treatment (43%) compared with the trunk (31%) or extremities (14%).

In previous reports, analysis of safety data for HP40 was presented with a listing of LSRs based on severity at day 106. Here, we sought to understand the LSR data in clinical context of anatomic location and timing of the post-treatment reactions. The most common acute LSRs were erythema, stinging, and edema, which occurred at similar rates regardless of anatomic location of the SKs. These acute LSRs generally resolved or lessened within 1 week of HP40 application, although mild erythema persisted in 6-12% of the SKs at day 106. The proportions of SKs reported to have hyperpigmentation, hypopigmentation, or scarring were low and mostly mild at 106 days after treatment, regardless of anatomic location. Facial SKs, which may be of greater concern to patients, consistently had the lowest reporting of these delayed treatment reactions (Table 3).

There are several possible explanations for the higher treatment effect of HP40 on facial SKs. One possible explanation is variations in skin topology (histology and physiology), such as water or lipid composition differences across different anatomic sites. Facial skin has higher trans-epidermal water loss compared with the skin on the trunk and extremities[15] and the stratum corneum on the face is significantly thinner compared

TABLE 3.

Percentage of SKs With Delayed Local Skin Reactions at Day 106 by Severity and Anatomic Location

LSR	Location	HP40				Vehicle
		Mild	Moderate	Severe	Total	Total
Hyperpigmentation	Face n (%)	10 (1.8)	3 (0.5)	0 (0)	13 (2.3)	1 (0.2)
	Trunk n (%)	108 (10.0)	9 (0.8)	0 (0)	117 (10.8)	2 (0.2)
	Extremities n (%)	11 (5.5)	3 (1.5)	0 (0)	14 (6.9)	0 (0)
Hypopigmentation	Face n (%)	10 (1.8)	1 (0.2)	0 (0)	11 (1.9)	0 (0)
	Trunk n (%)	37 (3.4)	1 (0.1)	0 (0)	38 (3.5)	1 (0.1)
	Extremities n (%)	6 (3.0)	0 (0)	0 (0)	6 (3.0)	0 (0)
Scarring	Face n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Trunk n (%)	5 (0.5)	1 (0.1)	0 (0)	6 (0.6)	0 (0)
	Extremities n (%)	2 (1.0)	0 (0)	0 (0)	2 (1.0)	0 (0)
Atrophy	Face n (%)	2 (0.4)	0 (0)	0 (0)	2 (0.4)	0 (0)
	Trunk n (%)	1 (0.1)	0 (0)	0 (0)	1 (0.1)	0 (0)
	Extremities n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

LSR, localized skin reaction; n, number of lesions in subset.

to the chest and abdomen,[16] suggesting that a reduced barrier function may augment the penetration of HP40 on the face. In addition, the lipid content from sebum production on the face[17,18] may also enhance the treatment effect of HP40. Another explanation is that because SKs on the face are exposed more often to ultraviolet radiation; their ultraviolet damage signatures may have impaired salvage pathways when subjected to oxidation induced by HP40.[1,19,20] The differential benefit of HP40 on facial SKs is relevant, given that smaller and thinner lesions on cosmetically sensitive locations are the most challenging to manage with cryosurgery. Finally, facial SKs tend to be smaller and thinner compared with lesions on the trunk or extremities, although baseline lesion size stratified by length x width of SKs (25-100 mm^2 vs >100 mm^2) in this study was similar, regardless of anatomic location. In addition, baseline thickness by PLA (≤1 mm vs >1 mm) was similar for SKs on the face and extremities.[21]

While the exact mechanism of action of HP40 topical solution in the removal of SKs has not been characterized, the chemical and physical properties of hydrogen peroxide have been studied extensively since it was first described by the French chemist Louis-Jacques Thénard in 1818.[22] We hypothesize that the high concentration of hydrogen peroxide solution, upon penetration into an SK lesion, generates reactive oxygen species leading to lipid and membrane peroxidation with membrane lysis; protein oxidation, which tends to favor necrotic cell damage/death; and ultimately, DNA damage via site-specific hydroxyl formation, thiol oxidation, and mitochondrial membrane damage, which tend to favor apoptosis.

There are several limitations that must be noted in this analysis. First, a sub-stratification of extremity locations (eg, dorsum of the hand versus forearm) and trunk (eg, neck vs back) was not conducted. SKs also present as various histologic subtypes, which are not reliably predictable from clinical appearance. All SKs in this trial were required to be raised but subtyping of SK variants was not performed (ie, no biopsies were obtained) and the size limitation to a minimum of 5 mm diameter and raised thickness excluded common variants such as dermatosis papulosa nigra and macular SKs, respectively. Further work will evaluate patient satisfaction with HP40 treatment and will be correlated with treatment outcomes including the physician-graded PLA score.[23]

CONCLUSION

The recent FDA-approved 40% (w/w) hydrogen peroxide topical solution in a single-use applicator represents a novel SK treatment option for providers to offer to their patients. The highest treatment effect and the lowest risk of dyspigmentation with HP40 versus vehicle was observed on facial SKs, which also cleared at the highest rate after a single treatment. Most common immediate reactions with HP40 were erythema, stinging, and edema, which resolved to none or mostly mild within a week.

DISCLOSURES

Dr. Smith has served on advisory boards for Aclaris Therapeutics. Dr. Xu is a consultant to Aclaris Therapeutics. Dr. Estes and Shanler are employed by Aclaris Therapeutics. Funding/Support: This study was supported by Aclaris Therapeutics, Inc.

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REFERENCES

1. Heidenreich B, Denisova E, Rachakonda S, et al. Genetic alterations in seborrheic keratoses. *Oncotarget.* 2017;8:36639-36649.
2. Neel VA, Todorova K, Wang J, et al. Sustained Akt activity is required to maintain cell viability in seborrheic keratosis, a benign epithelial tumor. *J Invest Dermatol.* 2016;136:696-705.
3. Hafner C, Lopez-Knowles E, Luis NM, et al. Oncogenic PIK3CA mutations occur in epidermal nevi and seborrheic keratoses with a characteristic mutation pattern. *Proc Natl Acad Sci U S A.* 2007;104:13450-13454.
4. Logie A, Dunois-Larde C, Rosty C, et al. Activating mutations of the tyrosine kinase receptor FGFR3 are associated with benign skin tumors in mice and humans. *Hum Mol Genet.* 2005;14:1153-1160.
5. Lim HW, Collins SAB, Resneck JS, Jr., et al. The burden of skin disease in the United States. *J Am Acad Dermatol.* 2017;76:958-972 e952.
6. Hafner C, Vogt T. Seborrheic keratosis. *J Dtsch Dermatol Ges.* 2008;6:664-677.
7. Baumann L, Blauvelt A, Draelos Z, et al. Safety and efficacy of hydrogen peroxide topical solution, 40% (w/w) in patients with seborrheic keratoses: results from two identical, randomized, double-blind, placebo-controlled, phase 3 studies (A-101-SEBK-301/302). *J Am Acad Dermatol.* 2018. doi: 10.1016/j.jaad.2018.05.044.
8. DuBois JC, Jarratt M, Beger BB, et al. A-101, a proprietary topical formulation of high-concentration hydrogen peroxide solution: A randomized, double-blind, vehicle-controlled, parallel group study of the dose-response profile in subjects with seborrheic keratosis of the face. *Dermatol Surg.* 2018;44:330-340.
9. Jackson JM, Alexis A, Berman B, et al. Current understanding of seborrheic keratosis: Prevalence, etiology, clinical presentation, diagnosis, and management. *J Drugs Dermatol.* 2015;14:1119-1125.
10. Tay YK, Tan SK. A study comparing the efficacy and risk of adverse events using two techniques of electrocautery for the treatment of seborrheic keratoses. *Dermatol Surg.* 2013;39:810-813.
11. Herron MD, Bowen AR, Krueger GG. Seborrheic keratoses: a study comparing the standard cryosurgery with topical calcipotriene, topical tazarotene, and topical imiquimod. *Int J Dermatol.* 2004;43:300-302.
12. Kee CE. Liquid nitrogen cryotherapy. *Arch Dermatol.* 1967;96:198-203.
13. Burkhart CG. The search for topical treatments for seborrheic keratoses continues. *Int J Dermatol.* 2006;45:1110.
14. Klaus MV, Wehr RF, Rogers RS, 3rd, et al. Evaluation of ammonium lactate in the treatment of seborrheic keratoses. *J Am Acad Dermatol.* 1990;22:199-203.
15. Darlenski R, Fluhr JW. Influence of skin type, race, sex, and anatomic location on epidermal barrier function. *Clin Dermatol.* 2012;30:269-273.
16. Lee Y, Hwang K. Skin thickness of Korean adults. *Surg Radiol Anat.* 2002;24:183-189.
17. Sadowski T, Klose C, Gerl MJ, et al. Large-scale human skin lipidomics by quantitative, high-throughput shotgun mass spectrometry. *Sci Rep.* 2017;7:43761.
18. Greene RS, Downing DT, Pochi PE, et al. Anatomical variation in the amount and composition of human skin surface lipid. *J Invest Dermatol.* 1970;54:240-247.
19. Rebel H, Kram N, Westerman A, et al. Relationship between UV-induced mutant p53 patches and skin tumours, analysed by mutation spectra and by induction kinetics in various DNA-repair-deficient mice. *Carcinogenesis.*

2005;26:2123-2130.
20. de Gruijl FR, van der Leun JC. Development of skin tumors in hairless mice after discontinuation of ultraviolet irradiation. *Cancer Res.* 1991;51:979-984.
21. Data on file. Aclaris Therapeutics, Inc.
22. Thénard LJ. Observations sur des nouvelles combinaisons entre l'oxigène et divers acides. *Ann Chim Phys (Paris).* 1818;2:306-312.
23. Clinicaltrials.gov. A study assessing subject satisfaction with A-101 topical solution for seborrheic keratoses (SK-FAN). https://clinicaltrials.gov/ct2/show/NCT03487588. Accessed April 4, 2018.

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