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Tirbanibulin Ointment 1% as a Novel Treatment for Actinic Keratosis: Phase 1 and 2 Results

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ABSTRACT

Background: Current field-directed treatments of actinic keratosis (AK), a pre-malignant condition, are often limited by severe local reactions and/or complex treatment. Tirbanibulin, a novel potent anti-proliferative synthetic agent that inhibits tubulin polymerization and Src kinase signalling, is being developed as a convenient, safe, and effective field treatment of actinic keratosis.

Hypothesis: A short course of tirbanibulin ointment 1% safely reduces AK lesions.

Methods: In the Phase 1 study, 4 treatment cohorts with forearm lesions received tirbanibulin ointment 1% over 25 or 100 cm^2 once daily for 3 or 5 days and were evaluated through day 45. In the Phase 2 study, 2 treatment cohorts with face or scalp lesions received tirbanibulin ointment 1% once daily for 3 or 5 days over 25 cm^2 and were evaluated through day 57. Lesion reductions, clearance rates, safety, and pharmacokinetics were assessed.

Results: Forearm AK lesions were reduced by day 45 in all Phase 1 cohorts (N=30). Complete AK clearance at day 57 for face/scalp AK lesions in Phase 2 cohorts (N=168) was demonstrated in 43% and 32% of participants of the 5-day and 3-day cohorts, respectively. Adverse reactions were mainly transient mild local erythema and flaking/scaling, pruritus, and pain. Tirbanibulin plasma concentrations were low or undetectable.

Conclusion: Tirbanibulin ointment 1% was well tolerated and active in AK reduction. Based on activity, the 5-day regimen was selected for Phase 3 development.

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INTRODUCTION

Actinic keratosis (AK) is a pre-malignant condition, associated with prolonged ultraviolet damage predominantly on the face/scalp, trunk, and extremities.[1,2] AK affects ~58 million individuals in the US,[3] and typically occurs in males, fair-skinned individuals, and those of advancing age.[4,5] As the progression of AK to invasive squamous cell carcinoma (iSCC) is unpredictable, the generally accepted approach is to treat all AK.[6] Current treatments are lesion- or field-directed therapies.[1] Lesion-directed therapies are used when the lesion burden is low; but these modalities can cause scarring and long-term pigmentary changes.[1,7] Field-directed therapies are used to treat multiple lesions, large areas, and subclinical lesions.[1,7] Commonly used topical treatments, while effective, frequently cause moderate-to-severe application-site reactions and deleterious effects on uninvolved skin,[7-11] which are often considered unacceptable to patients. Moreover, many of these treatments have lengthy or cumbersome dosing regimens that may undermine treatment compliance and compromise efficacy.[12,13] Given the disadvantages of available topical therapies, there is a need to develop an agent that has low potential for severe local reactions, effective AK clearance, and convenient dosing.

Tirbanibulin is a synthetic, first-in-class, potent anti-proliferative agent that inhibits tubulin polymerization and disrupts Src kinase signaling[14] that are upregulated in AK and iSCC.[15-17] Tirbanibulin also promotes the induction of p53, G2/M arrest of proliferating cell populations, and subsequent apoptosis via stimulation of caspase-3 and poly (ADP-ribose) polymerase cleavage.[14] In vitro, tirbanibulin demonstrated potent inhibition of the growth of primary human keratinocytes and several melanoma cell lines (GI50 ≤50 nM).[14] Preclinical in vitro and in vivo toxicity and dermal irritation studies also supported the further development of tirbanibulin ointment 1% in clinical trials (unpublished data). We hypothesized that a short course of tirbanibulin ointment 1% would be locally safe and active in clearing AK through its mechanism of action that promotes anti-proliferative and pro-apoptotic effects on the actively dividing dysplastic keratinocytes. Here, we describe the results of two early-phase studies in testing this hypothesis.

METHODS

Study Designs and Participants

The Phase 1 study was an open-label, proof-of-concept, single-center study in adults (aged ≥18 years) with clinically typical AK on the forearm. Participants were enrolled into 4 sequential cohorts: Cohort 1 received tirbanibulin ointment 1% 50 mg/day once daily for 3 days over 25 cm^2 treatment area with 4–8 AK lesions; Cohort 2 received 200 mg/day once daily for 3 days over 100 cm^2 treatment area with 8–16 AK lesions; Cohort 3 and Cohort 4 were similar to Cohort 1 and Cohort 2, respectively, but treatment was for 5 days. The Follow-up period was through day 45.

The Phase 2 study was an open-label, uncontrolled, dose-regimen-finding, multicenter study in adults (aged ≥18 years) with clinically typical AK on the face or scalp. Participants were sequentially enrolled and received tirbanibulin ointment 1% once daily for 3 or 5 days over 25 cm^2 treatment area with 4–8 AK lesions; approximately 50 mg/day per application. Response assessment was through day 57 and the Recurrence Follow-up Period was up to 12 months after day 57 for participants who achieved complete (100%) AK clearance in the treatment area at day 57. In both studies, tirbanibulin ointment 1% was formulated in a base ointment containing propylene glycol and glycerol monostearate.

These studies were conducted in accordance with the Declaration of Helsinki, 2013, the US Code of Federal Regulation, and Good Clinical Practice guidelines. The protocols, informed consent forms, and all other appropriate related documents were submitted and approved by the central Institutional Review Board, Quorum Review IRB, Seattle, WA, USA.

Assessments and Statistical Analyses

To assess activity in the Phase 1 study, AK lesion numbers at baseline, days 10, 17, 31, and 45 were summarized by cohort. Complete (100%) and partial (≥75%) AK clearance rates (defined as the proportion of participants who had 100% and ≥75% reduction in AK lesion counts, respectively, in the treatment area at day 45 compared with baseline) were evaluated for each cohort. No statistical inference was made. Participants missing an AK lesion count at day 45 were considered non-responders.

In the Phase 2 study, AK lesions at days 1 (baseline), 8, 15, 29, and 57 were summarized by cohort at each visit. Based on the number of participants who achieved 100% clearance at day 57, the complete response rate and its corresponding 95% Clopper–Pearson Exact confidence interval (CI) were estimated. AK lesion numbers at each timepoint and change from baseline were summarized by cohort at each visit and in subgroups (age, sex, AK lesion count, weight, skin type, and treatment location). The proportion of participants with partial clearance (≥75%) at day 57 were also analyzed. No statistical inference was made.

Recurrence rates and associated 95% CIs were estimated with the Kaplan-Meier method at each post-day 57 visit (at 3, 6, 9, and 12 months post-day 57) and presented by cohort for participants who achieved 100% clearance at day 57.

For both studies, safety was assessed by recording treatment-emergent adverse events (TEAEs) and their relationship to study drug; serious AEs (SAEs); laboratory evaluation of blood chemistry, hematology, and urine analysis; vital signs and electrocardiograms; and physical examinations at predetermined visits according to study protocols.

For both studies, signs of local skin reactions (LSRs; erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, and erosion/ulceration) were assessed by investigators on a 5-point scale (0 [not present], 1 [minimal], 2 [mild], 3 [moderate], or 4 [severe]) at predetermined visits according to protocol.

Blood samples were collected to measure plasma concentrations of tirbanibulin pre-dose and at predetermined timepoints for both cohorts in the Phase 2 study. Plasma concentrations were analyzed using validated liquid chromatography/tandem mass spectrometry (LC-MS/MS, lower limit of detection of 0.1 ng/mL).

RESULTS

Participant Populations

In the Phase 1 study, 30 participants were enrolled in one US site. Twenty-nine completed the study and one participant (Cohort 2) withdrew consent on day 2. All 168 participants (n=84 in each cohort) enrolled in the Phase 2 study, from 16 sites across the US, completed the treatment (100% compliance) and follow-up until day 57. Baseline characteristics of all participants met with protocol requirements and were comparable across treatment cohorts, except there were more participants with face than scalp AK lesions in the 3-day vs 5-day cohort in the Phase 2 study. The majority of participants in both studies were White, mean age >60 years, and of non-Hispanic ethnicity with Fitzpatrick skin type I–III (Table 1).

Activity

In the Phase 1 study, reductions in lesion counts from day 1 to 45 were observed in all cohorts (Figure 1). By day 45, 25%, 0%, 50%, and 12.5% of participants demonstrated 100% AK clearance in the treatment area in Cohorts 1–4, respectively (Table 2).

In the Phase 2 study, substantial overall AK clearance on the face or scalp was demonstrated in both cohorts. More participants had 100% clearance at day 57 in the 5-day vs the 3-day cohort (43% vs 32%) (Table 2). Partial clearance rates were also slightly higher in the 5-day vs the 3-day cohort (56% vs 52%) (Table 2). There was a consistent decrease in lesion counts across all visits from baseline to day 57, for both cohorts. A substantial overall mean (standard deviation) decrease from baseline in lesion

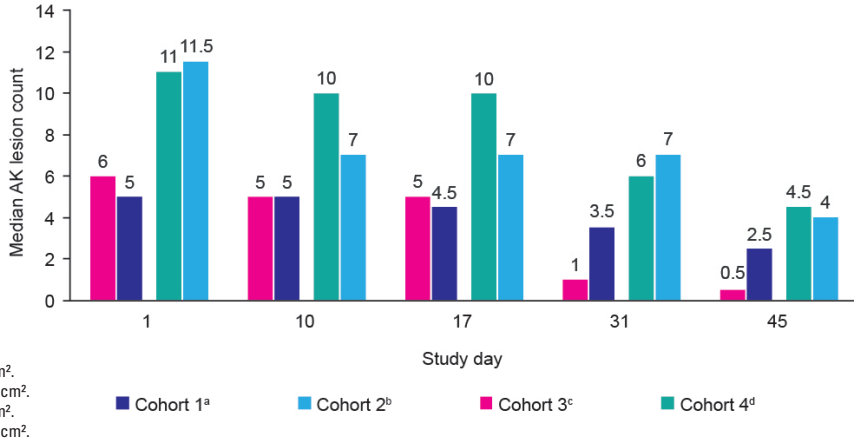
TABLE 1.

Demographic and Baseline Characteristics of Participants from the Phase 1 and Phase 2 Studies

	Phase 1 Study					Phase 2 Study		
	Cohort 1[b] (n = 4)	Cohort 2[c] (n = 10)	Cohort 3[d] (n = 8)	Cohort 4[e] (n = 8)	Overall (N= 30)	5-day cohort[d] (n = 84)	3-day cohort[b] (n = 84)	Overall (N = 168)
Age (years)								
Mean (SD)	63.0 (6.5)	61.8 (8.2)	63.0 (8.6)	64.9 (7.5)	63.1 (7.6)	69.0 (8.9)	67.7 (8.3)	68.3 (8.6)
Sex, n (%)								
Male	3 (75)	6 (60)	5 (63)	5 (63)	19 (63)	76 (90)	72 (86)	148 (88)
Female	1 (25)	4 (40)	3 (38)	3 (38)	11 (37)	8 (10)	12 (14)	20 (12)
Race, n (%)								
White	4 (100)	9 (9)	8 (100)	8 (100)	29 (97)	84 (100)	83 (99)	167 (99)
Other	0 (0)	1 (10)	0 (0)	0 (0)	1 (3)	0	1 (1)	1 (1)
Ethnicity, n (%)								
Hispanic or Latino	0	0	0	0	0	3 (4)	9 (11)	12 (7)
Not Hispanic or Latino	4 (100)	10 (100)	8 (100)	8 (100)	30 (100)	81 (96)	75 (89)	156 (93)
AK lesion count at baseline								
Mean (SD)	4.8 (0.5)	11.9 (2.6)	5.6 (0.5)	11.5 (2.1)	9.2 (3.7)	5.8 (1.4)	5.4 (1.2)	5.6 (1.3)
Median	5.0	11.5	6.0	11.0	10.0	6.0	5.0	5.0
Min, Max	4, 5	8, 16	5, 6	10, 16	4, 16	4, 8	4, 8	4, 8
Location of treatment area, n (%)								
Face						44 (52)	66 (79)	110 (65)
Scalp						40 (48)	18 (21)	58 (35)
Fitzpatrick skin type[a], n (%)								
Type I						11 (13)	13 (15)	24 (14)
Type II						39 (46)	39 (46)	78 (46)
Type III						26 (31)	29 (35)	55 (33)
Type IV						7 (8)	3 (4)	10 (6)
Type V						1 (1)	0	1 (1)
Type VI						0	0	0

AK, actinic keratosis; Max, maximum; Min, minimum; SD, standard deviation.
[a]The Fitzpatrick skin type classification system ranges from very fair (Type I) to very dark (Type VI). Data not collected for Phase 1 study.
[b]50 mg once-daily for 3 days over 25 cm^2.
[c]200 mg once-daily for 3 days over 100 cm^2.
[d]50 mg once-daily for 5 days over 25 cm^2.
[e]200 mg once-daily for 5 days over 100 cm^2.

FIGURE 1. Median AK lesion count by cohort and visit in participants treated with tirbanibulin ointment 1% in the Phase 1 study.



AK, actinic keratosis.
[a]50 mg once-daily for 3 days over 25 cm^2.
[b]200 mg once-daily for 3 days over 100 cm^2.
[c]50 mg once-daily for 5 days over 25 cm^2.
[d]200 mg once-daily for 5 days over 100 cm^2.

TABLE 2.

AK Clearance Rate at Day 45 in the Phase 1 Study and Day 57 in the Phase 2 Study in Participants Treated With Tirbanibulin Ointment 1%		
Phase 1 Study	**100% Clearance n (%)**	**≥75% Clearance n (%)**
Cohort 1: 50 mg once-daily for 3 days over 25 cm^2 (n = 4)	1 (25)	2 (50)
Cohort 2: 200 mg once-daily for 3 days over 100 cm^2 (n = 10)	0	3 (30)
Cohort 3: 50 mg once-daily for 5 days over 25 cm^2 (n = 8)	4 (50)	5 (63)
Cohort 4: 200 mg once-daily for 5 days over 100 cm^2 (n = 8)	1 (12.5)	4 (50)
Phase 2 Study	**100% Clearance Proportion of Participants (95% CI)**	**≥75% Clearance Proportion of Participants (95% CI)**
5-day cohort: 50 mg once-daily for 5 days over 25 cm^2 (n = 84)	0.43 (0.32, 0.54)	0.56 (0.45, 0.67)
3-day cohort: 50 mg once-daily for 3 days over 25 cm^2 (n = 84)	0.32 (0.22, 0.43)	0.52 (0.41, 0.63)

CI, confidence interval.

counts occurred by day 15 in the 5-day (-2.5 [2.48]) and 3-day cohorts (-2.5 [2.22]) that continued up to day 57 (-3.9 [2.00] and -3.4 [1.75], respectively) (Figure 2) . Even with small participant numbers, consistency in AK clearance among subgroups was noted.

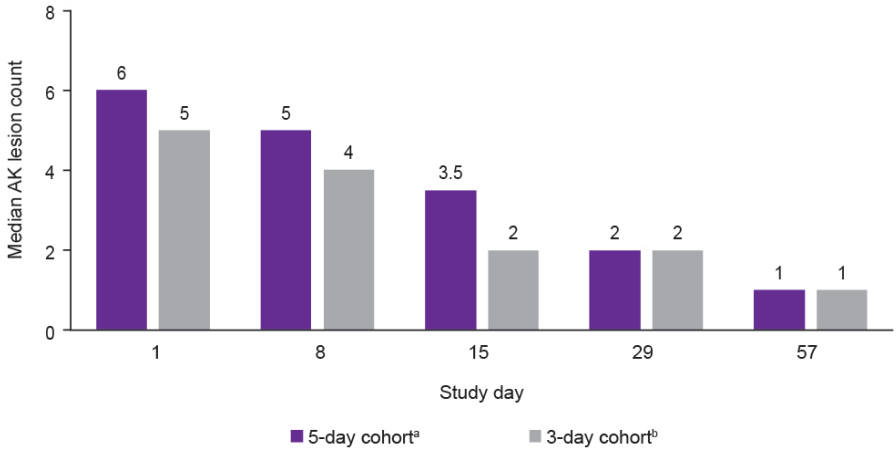
All 63 participants who had 100% clearance at day 57 in the Phase 2 study were included in the Recurrence Follow-up Set. Based on Kaplan-Meier analysis, at 12 months post-day 57, recurrence rates for the proportion of 5 day cohort participants were lower than the 3-day cohort (57% [95% CI, 41, 73] vs 70% [95% CI, 51, 87]). Most recurrence occurred within 6 months post-day 57.

Safety

In the Phase 1 study, no TEAEs were treatment-related, severe, or resulted in withdrawal from the study or treatment. There were no deaths or SAEs. No clinically significant changes in laboratory tests, vital signs, physical examinations, or electrocardiograms were reported. Application-site symptoms, collected separately from AEs, were mostly transient mild pruritus, and less frequently stinging/burning sensation. These were observed predominantly in Cohorts 3/4; all resolved without treatment.

In the Phase 2 study, all participants completed treatment and follow-up to day 57, and both regimens were well tolerated. There were no deaths, SAEs, or discontinuations due to treatment. Twelve of 168 participants (7%) had treatment-related AEs: 9 (11%) in the 5-day cohort and 3 (4%) in the 3-day cohort. Treatment-related AEs were mostly mild, transient application-site pruritus and application-site pain that resolved spontaneously. Three participants reported four treatment-related non-specific systemic AEs: transient mild-to-moderate dizziness and mild headache. One participant reported mild hair darkening near the treatment area, and another was

FIGURE 2. Median AK lesion count by cohort and visit in participants treated with tirbanibulin ointment 1% in the Phase 2 study.



AK, actinic keratosis.
[a]50 mg once-daily for 5 days over 25 cm^2.
[b]50 mg once-daily for 3 days over 25 cm^2.

TABLE 3.

Overview Of Adverse Events (AEs) and Treatment-Related AEs Prior to the Recurrence Follow-up Period in the Phase 2 Study

n (%)	5-day Cohort[c] (n = 84)	3-day Cohort[d] (n = 84)	Overall (N = 168)
AEs	35 (42)	21 (25)	56 (33)
TEAEs[a]	34 (40)	18 (21)	52 (31)
Treatment-related AEs[b]	9 (11)	3 (4)	12 (7)
SAEs	2 (2)	2 (2)	4 (2)
Severe AEs	1 (1)	2 (2)	3 (2)
AEs leading to treatment discontinuation	**0**	**0**	**0**
Deaths	**0**	**0**	**0**
Treatment-related AEs[b]			
Application site pruritus	5 (6)	1 (1)	6 (4)
Application site pain	3 (4)	2 (2)	5 (3)
Dizziness	2 (2)	0	2 (1)
Headache	1 (1)	1 (1)	2 (1)
Hair color changes	1 (1)	**0**	1 (1)
Overdose	1 (1)	**0**	1 (1)

AEs are coded with Medical Dictionary for Regulatory Activities. v18.1. SAEs, serious adverse events
[a]TEAEs are treatment-emergent adverse events that started on or after the first dose or that worsened after the first dose.
[b]Treatment-related AEs are those events considered definitely, probably, or possibly related to study treatment or of an unknown relationship to study treatment.
[c]50 mg once-daily tirbanibulin ointment 1% for 5 days over 25 cm^2.
[d]50 mg once-daily tirbanibulin ointment 1% for 3 days over 25 cm^2.

inadvertently given 10 times the assigned dose but did not report any other AEs or excessive LSRs (Table 3). Concurrent plasma concentrations were undetectable or <0.5 ng/mL. Results of laboratory evaluations, physical examinations, vital signs, and electrocardiograms were within expectations for an elderly population and were unrelated to treatment. From the Recurrence Follow-up Period, there were no treatment-related AEs or skin cancer in the treatment area.

Local Skin Reactions

LSR signs in the Phase 1 study were mostly mild-to-moderate erythema and flaking/scaling, generally appearing on day 4 and peaking ~days 5 or 8 (Cohorts 1/2) and ~days 8 or 10 (Cohorts 3/4), before spontaneously resolving/stabilizing within ~2 weeks. No participants experienced vesiculation/pustulation. No LSR required treatment.

In the Phase 2 study, even though LSRs were frequently observed with tirbanibulin ointment 1%, these were generally minimal/mild (Grade 1/2) erythema and flaking/scaling, were transient, and required no intervention. Less frequently reported were moderate (Grade 3) erythema and flaking/scaling, and minimal/mild (Grade 1/2) crusting. Only one participant (5-day cohort) had transient, severe erythema and flaking/scaling that

TABLE 4.

Maximal post-Baseline LSRs by Grade in Participants Treated With Tirbanibulin Ointment 1% in the Phase 2 Study (N = 84 per Cohort)

	Erythema		Flaking/scaling		Crusting		Swelling		Vesicula-tion/ pustulation		Erosion/ ulceration	
Cohort	5-day[a] n (%)	3-day[b] n (%)	5-day n (%)	3-day n (%)	5-day n (%)	3-day n (%)	5-day n (%)	3-day n (%)	5-day n (%)	3-day n (%)	5-day n (%)	3-day n (%)
LSR Grade												
0	9 (11)	15 (18)	23 (27)	20 (24)	49 (58)	53 (63)	66 (79)	76 (90)	80 (95)	83 (99)	71 (85)	78 (93)
1	22 (26)	34 (40)	20 (24)	33 (39)	27 (32)	20 (24)	16 (19)	8 (10)	4 (5)	**0**	12 (14)	6 (7)
2	35 (42)	29 (35)	24 (29)	23 (27)	8 (10)	10 (12)	1 (1)	**0**	**0**	1 (1)	1 (1)	**0**
3	17 (20)	6 (7)	16 (19)	8 (10)	**0**	1 (1)	1 (1)	**0**	**0**	**0**	**0**	**0**
4	1 (1)	**0**	1 (1)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

LSR, local skin reaction; n, number of participants with LSR; %, percentages are based on the number of participants dosed, 84 per cohort.
LSR rated for each category on a 5-point scale of 0 = none, 1 = minimal, 2 = mild, 3 = moderate or 4 = severe.
[a]50 mg once-daily for 5 days over 25 cm^2.
[b]50 mg once-daily for 3 days over 25 cm^2.

resolved. Few participants experienced erosions/ulcerations or vesiculation/pustulation and none were greater than mild (Grade 2) in severity. In both cohorts, LSRs began by day 2, peaked by the end of treatment, and returned to baseline or resolved by day 29. Slightly more participants in the 5-day cohort experienced LSRs compared with the 3-day cohort. Maximal post-baseline LSR grades are provided to show the highest LSR grade assessed by the investigators regardless of visit in Table 4. Representative photographs of typical and maximal LSRs for both studies are presented in Figure 3.

Pharmacokinetics

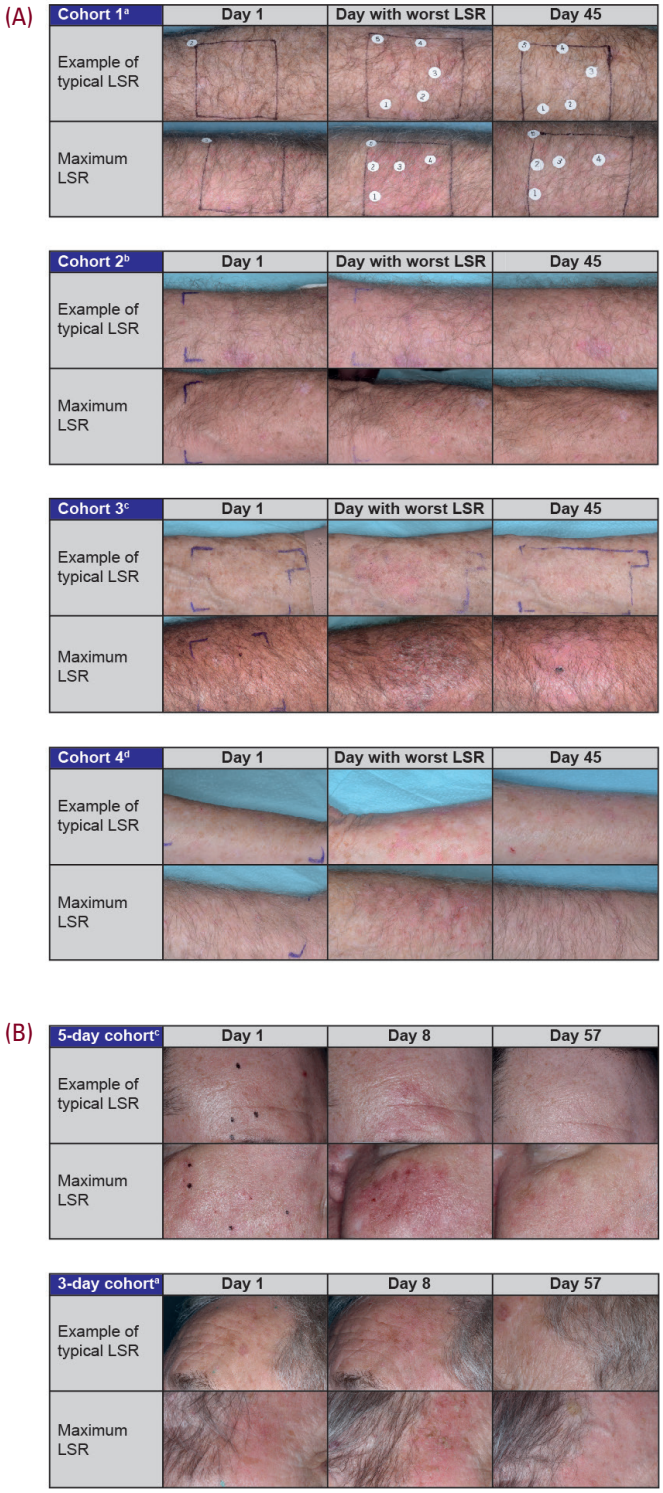
Phase 2 study results demonstrated that tirbanibulin was minimally absorbed following 3 or 5 consecutive days of treatment. For the majority of plasma samples collected, tirbanibulin was below the lower limit of quantification of 0.1 ng/mL. The maximum individual plasma concentration across both cohorts and all days of pharmacokinetics sampling did not surpass 2 ng/mL.

DISCUSSION

AK is very common and a major health concern due to its progression to non-melanoma skin cancers such as iSCC.[6,14,18] Treatment is generally encouraged as predicting which AK lesion will become cancerous is difficult.[6] Commonly used topical therapies include 5-fluorouracil, that is a cytotoxic agent, imiquimod, that acts by immunomodulation, and ingenol mebutate, that induces cell necrosis and inflammation.[8-10] These treatments often lead to moderate-to-severe application-site reactions or LSRs (itching, burning, erythema, flaking/crusting, edema, induration, excoriation, erosion, and ulceration),[8-10] and negatively impact treatment compliance and patients' quality of life.[5,19] Additionally, 5-fluorouracil (twice daily for 2–4 weeks) and imiquimod (twice weekly for ≤16 weeks) require long treatment durations,[8,9] which may prolong patient discomfort from local adverse reactions at both AK lesions and uninvolved areas. Thus, development of an effective and more tolerable topical AK treatment of short duration, having a new targeted mechanism of action, is needed to improve compliance that may lead to better treatment outcomes.

Tirbanibulin ointment 1% is a topical formulation of a novel synthetic molecule that has potent antiproliferative activity against keratinocyte growth in vitro based on inhibition of tubulin polymerization and Src kinase signalling. The reported studies were early-phase development of tirbanibulin ointment 1% in AK among participants with typical demographics and disease characteristics of the target population. Collectively, these studies showed that, firstly, short courses of tirbanibulin ointment 1% are active in reducing AK lesions in multiple locations. Secondly, the low incidence of severe local reactions may serve to differentiate tirbanibulin ointment from other topical treatments for AK. Lastly, these studies supported the

FIGURE 3. Representative photographs of typical and maximum LSRs in tirbanibulin treated participants in (A) Cohorts 1–4 from Phase 1 study and (B) 5-day and 3-day cohorts from Phase 2 study.



LSR, local skin reaction.
[a]50 mg once-daily for 3 days over 25 cm^2.
[b]200 mg once-daily for 3 days over 100 cm^2.
[c]50 mg once-daily for 5 days over 25 cm^2.
[d]200 mg once-daily for 5 days over 100 cm^2.

further development of the 5-day regimen of tirbanibulin ointment 1% in treating AK on the face or scalp in Phase 3 studies.

The Phase 1 study was a proof-of-concept study with a dose-escalating design in treatment area and treatment duration on the dorsal forearm. AK lesion count was consistently reduced in all cohorts, with the 5-day regimen over 25 cm^2 showing the highest complete clearance rate. This 5-day regimen was further evaluated on the face or scalp in the Phase 2 study. Results of the Phase 2 study showed that both 3-day and 5-day regimens had substantial activity against AK, with the 5-day regimen demonstrating numerically higher 100% clearance (43% vs 32%) and sustained response at 12 months post-day 57 (43% vs 30%) than the 3-day regimen. Although both studies were small and uncontrolled, complete AK clearance rates of tirbanibulin ointment 1% at day 57 for the 5-day regimen over 25 cm^2 on the face/scalp or dorsal forearm align well with topical treatment like ingenol mebutate (face/scalp, 42%; trunk/extremities, 32%) administered over 2-3 days.[20]

The favorable safety profile of tirbanibulin ointment was supported by the paucity of systemic, severe, or serious side effects and minimal systemic absorption. Although tirbanibulin ointment did cause some local irritation, it induced mostly mild and transient erythema, flaking/scaling, pruritus, and pain that resolved quickly and spontaneously. The low incidence of severe LSRs and LSRs of greater concern (vesiculation/pustulation and erosions/ulceration) that distinguishes tirbanibulin ointment 1% from other approved topical AK treatments warrant evaluation in future studies.

In summary, these Phase 1/2 studies supported our hypothesis that tirbanibulin ointment 1%, given as a short, once-daily treatment for AK lesions on the forearm, face, or scalp, could reduce lesions and is well tolerated with low-grade LSRs that quickly resolve without intervention. This allowed the 5-day treatment regimen of tirbanibulin ointment 1% to be selected for efficacy and safety evaluation in two double-blinded, placebo-controlled, randomized, parallel-group, multicenter, Phase 3 trials for AK on the face/scalp.

DISCLOSURES

Steven Kempers has no conflicts of interests to disclose.
Janet DuBois has received investigator fees for her institution from Aclaris Therapeutics, Inc., Allergan, Inc., BioPharmX, Botanix Pharmaceuticals, Brickell Biotech, Inc., Cara Therapeutics, Dermata Therapeutics, Dermavant Sciences, Dermira, Inc., Dr Reddy's Laboratories, Endo International plc., Escalier Biosciences, Foamix Pharmaceuticals Ltd., Galderma, GlaxoSmithKline, Glenmark Generics Inc., LEO Laboratories Ltd., Moberg Pharma North America LLC, MOE Medical Devices LLC, Novan, Inc., Perrigo Company plc, Pfizer Inc., Naked Biome Inc., Novartis Pharmaceuticals Corp., SeegPharm SA, Sienna Biopharmaceuticals, Inc., Sol-Gel Technologies Ltd., Taro Pharmaceutical Industries Ltd., Therapeutics Inc., and Valeant Pharmaceuticals North America LLC.
Seth Forman has received consultancy fees from AbbVie and Dermira, Inc., and principal investigator fees from Pfizer Inc. He has also received grants/research funding for his role as a principal investigator for AbbVie, AstraZeneca plc, Celgene Corporation, Cutanea Life Sciences, Eli Lilly Company, Incyte Corporation, Innovaderm Research Inc., Novartis, Promius Pharma, LLC., Regeneron Pharmaceuticals, Inc., and Valeant Pharmaceuticals North America LLC. Seth Forman has received honoraria from AbbVie (advisory board), Eli Lilly Company, and Novartis (speaker).
Amy Poon is a former employee of Athenex, Inc., and may own stock/stock options in Athenex, Inc.
Eva Cutler is an employee of Athenex, Inc.
Hui Wang is an employee of Athenex, Inc., and may own stock/stock options in Athenex, Inc.
David Cutler is an employee of Athenex, Inc., and may own stock/stock options in Athenex, Inc.
Jane Fang is a consultant of Athenex, Inc., and may own stock/stock options in Athenex, Inc.
Rudolf Kwan is an employee of Athenex, Inc., and may own stock/stock options in Athenex, Inc.

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