doi:10.36849/JDD.19912

Tirbanibulin 1% Ointment: Clinical Trial and Real-World Evidence on Efficacy, Tolerability, Safety, and Patient-Reported Outcomes

Charlotte Jeong BS,[a] Leon Kircik MD,[b] Mark Lebwohl MD,[c] April W. Armstrong MD MPH[d]

[a]University of Arkansas for Medical Sciences College of Medicine, Little Rock, AR
[b]Icahn School of Medicine at Mount Sinai, New York, NY; Indiana University School of Medicine, Indianapolis, IN; Physicians Skin Care, PLLC, Louisville, KY; DermResearch, PLLC, Louisville, KY; Skin Sciences, PLLC, Louisville, KY
[c]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY
[d]Division of Dermatology, Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, CA

ABSTRACT

Actinic keratosis (AK) is a skin lesion that arises due to chronic sun exposure. Treatment of all AKs is recommended due to their risk of progressing to squamous cell carcinomas (SCCs). Many field-directed treatments for AKs involve burdensome treatment duration and frequency, compromising treatment compliance. Tirbanibulin 1% ointment is a first-in-class microtubule inhibitor that treats AKs by inhibiting Src kinase signaling and inducing pro-apoptotic effects. It is an approved treatment for field-directed therapy of AKs, administered once daily for 5 consecutive days. In addition to its convenience of use, tirbanibulin 1% ointment has demonstrated efficacy and safety in phases 1 to 3 clinical trials and favorable clinical outcomes in real-world clinical studies. This paper summarizes the comprehensive evidence from clinical trials and global clinical studies to guide clinical consideration of tirbanibulin 1% ointment in AK management.

J Drugs Dermatol. 2025;24:7(Suppl 1):s5-12.

INTRODUCTION

Actinic keratosis (AK) is a common skin lesion that develops due to long-term sun exposure. AKs are estimated to affect 14% of the global population.[1] Factors that increase the risk of developing AKs include male sex, older age, lighter skin color, red hair, and immunocompromise.[2] Clinically, AKs present as poorly demarcated, scaly areas with variable keratosis that may cause symptomatic or cosmetic discomfort.[3] However, the primary clinical significance of AKs is their potential for malignancy. AKs are characterized by atypia of keratinocytes,[3] and untreated lesions can progress to squamous cell carcinomas (SCCs) at a rate of 0.025% to 16% per year.[4] Therefore, treatment of all AKs is recommended.[2]

AK therapies can be categorized as lesion- or field-directed. Lesion-directed therapies target singular AK lesions for individuals with low disease burden and include cryotherapy and excisions.[3] In contrast, field-directed therapies target larger areas with multiple AKs and subclinical lesions for individuals with high disease burden. Field-directed therapies include photodynamic therapy and topical treatments such as imiquimod, 5-fluorouracil, and diclofenac sodium.[3] Although various field-directed therapies exist, they are often associated with prolonged treatment duration (ie, 12 or 16 weeks), frequent use (ie, twice daily), and prolonged inflammation.[2] These barriers limit patient adherence to many field-directed therapies.

Tirbanibulin 1% ointment is a field-directed therapy for AKs that gained initial approval from the United States Food and Drug Administration (FDA) in 2020.[5] Tirbanibulin inhibits microtubules and blocks Src kinase signaling, resulting in antiproliferative and proapoptotic effects.[6,7] Compared to other field-directed therapies, tirbanibulin is administered with lower frequency and treatment duration, with once-daily application for 5 consecutive days over a treatment area of up to 25 cm^2.[5] Additionally, tirbanibulin has been investigated and approved by the FDA in 2024 for larger treatment areas of up to 100 cm^2.[8] In this paper, we aim to review the efficacy, safety, tolerability, and clinical outcomes of tirbanibulin 1% ointment from clinical trials and real-world clinical studies.

Phase 1 and 2 Trials

A phase 1 trial assessed the safety and efficacy of tirbanibulin 1% ointment for AKs on the dorsal forearm across 4 different cohorts.[6] The cohorts varied in treatment dosage (50 vs 200 mg/day), treatment duration (3 vs 5 days), and surface area of application (25 vs 100 cm^2). Patients with 4 to 8 AK lesions received treatment over an area of 25 cm^2, whereas patients with 8 to 16 AK lesions received treatment over an area of 100

cm². On day 45, results showed the highest rate of complete clearance of AK lesions in patients using 50 mg/day for 5 days over a treatment area of 25 cm² (50%, N=4/8), followed by patients using 50 mg/day for 3 days over a treatment area of 25 cm² (25%, N=1/4).[6] Local skin reactions (LSR) included mild-to-moderate erythema and flaking/scaling that appeared on day 4, peaked between days 5 and 8, and spontaneously resolved within 2 weeks.[6] Adverse events (AEs) were limited to application site pruritus and pain.[6]

A phase 2 trial assessed the safety and efficacy of tirbanibulin 1% ointment for AKs on the face and scalp across 2 different cohorts.[6] Both cohorts used tirbanibulin 1% ointment 50 mg/day over an area of 25 cm², but the cohorts varied in treatment duration (3 vs 5 days). On day 57, patients in the 5-day cohort had a higher rate of complete clearance (43%, N=36/84) than the 3-day cohort (32%, N=27/84). LSRs primarily involved minimal/mild erythema and flaking/scaling, with few patients experiencing mild erosions/ulcerations or vesiculation/pustulation.[6] LSRs appeared on day 2, peaked at the end of treatment, and spontaneously resolved by day 29. AEs included application site pruritus and pain, transient dizziness, mild headache, and mild hair darkening near the treatment area.[6] Pharmacokinetics revealed minimal absorption of tirbanibulin after 3 or 5 days of treatment.[6]

In phase 1 and 2 trials, tirbanibulin 1% ointment led to clearance of AKs with self-resolving LSRs and minimal adverse effects. Based on these findings, the treatment regimen of tirbanibulin 1% ointment for 5 days was further evaluated in phase 3 trials.

Phase 3 Trials

Treatment Area of 25 cm²

Two identical phase 3 trials were conducted concurrently at 62 sites across the United States. Enrolled participants had 4 to 8 AKs on the face or scalp within a contiguous area of 25 cm².[7] They were randomized in a 1:1 manner to tirbanibulin 1% ointment or vehicle ointment (placebo). The primary outcome of these trials was to assess the efficacy of tirbanibulin 1% ointment once daily for 5 days over a treatment area of 25 cm², as measured by complete clearance of all AK lesions within the application area on day 57.[7]

Across the 2 trials, complete clearance was achieved in 49% (N=174/353) of participants on tirbanibulin and 9% (N=30/349) of participants on placebo (difference, 41%; 95% CI: 35 to 47).[7] Partial clearance was defined as a reduction of at least 75% in the number of AK lesions. Across the 2 trials, partial clearance was achieved in 72% (N=255/353) of participants on tirbanibulin and 18% (N=63/349) of participants on placebo (difference, 54%; 95% CI: 48 to 60).[7] Results for each phase 3 trial are shown in Figures 1 and 2. Additionally, participants with complete clearance on day 57 completed a 1-year follow-up, at which the development of new or recurrent AK lesions was assessed within the treatment area. At 1 year, 71% (N=124/174) of participants developed 1 or more AK lesions within the treatment area.[7] Of these participants, 58% (N=72/124) had recurrent lesions (reappearance of the same lesions from baseline), and 42% (N=52/124) had new lesions (different from those identified at baseline).[7]

FIGURE 1. Percentage of patients achieving complete clearance on tirbanibulin vs vehicle in each of the 2 phase 3 clinical trials.

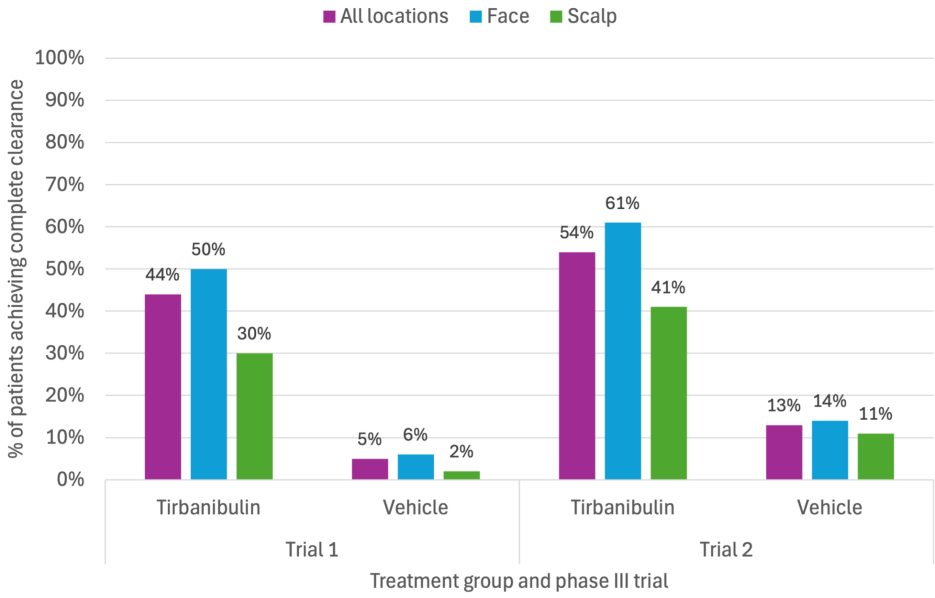
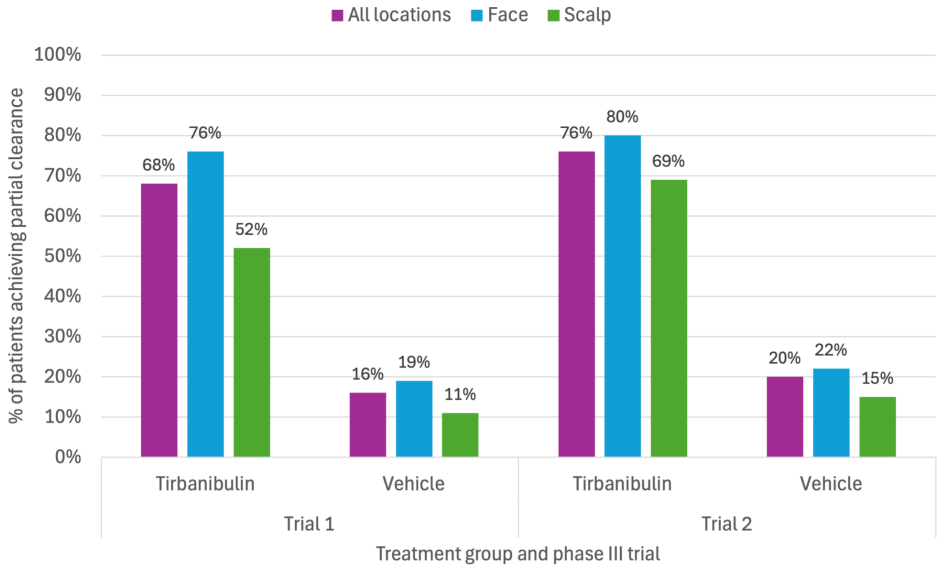


FIGURE 2. Percentage of patients achieving partial clearance on tirbanibulin vs vehicle in each of the 2 phase 3 clinical trials.



Consistent with that of the phase 1 and 2 trials, LSRs most commonly included moderate erythema (63%, N=223/353) and moderate flaking/scaling (47%, N=166/353), and less commonly included crusting, swelling, vesiculation/pustulation, and erosion/ulceration (Figure 3).[7] These local reactions peaked by day 8 and spontaneously resolved by day 29. Moreover, AEs included application site pain (10%, N=35/353) and pruritus (9%, N=32/353). Detailed results from each phase 3 trial are shown in Table 1.

Treatment Area of 100 cm²

Currently, there are limited treatment options for AK field-directed therapies that cover a treatment area greater than 25 cm². Thus, following FDA approval of tirbanibulin for 25 cm², a phase 3 trial using a larger treatment area was initiated.[8] Enrolled participants had 4 to 12 AKs on the face or balding scalp within a contiguous area of 100 cm². All enrolled participants received treatment with tirbanibulin 1% ointment once daily for 5 days over a treatment area of 100 cm².[8]

FIGURE 3. Maximal local skin reactions at the application site in the two phase 3 clinical trials (pooled data).

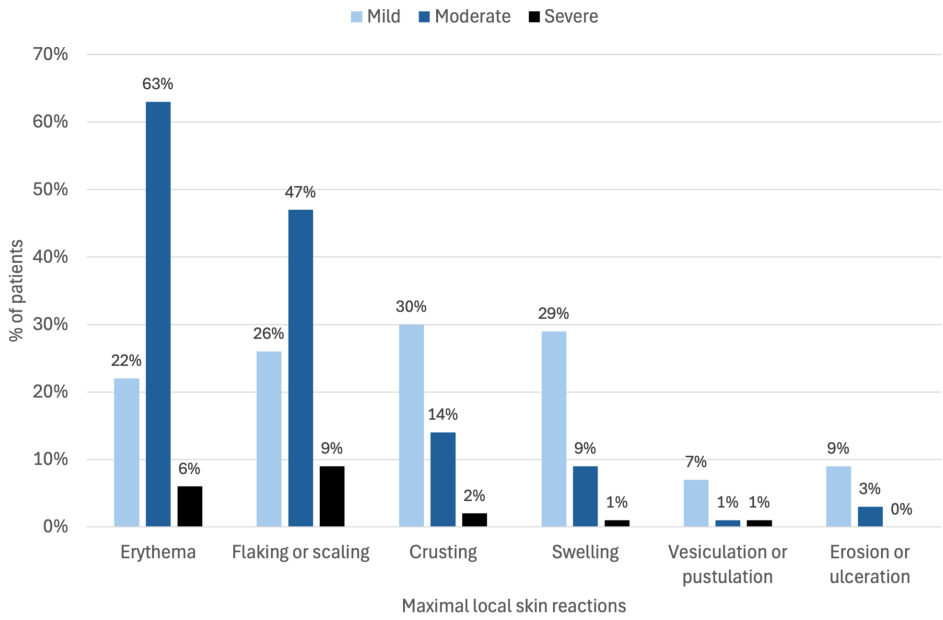


TABLE 1.

Summary of Clinical Trials Evaluating Tirbanibulin 1% Ointment

Clinical Trial Phase and Intervention	Efficacy	Tolerability and Safety
Phase 1[6] Cohort 1: 50 mg/day for 3 days over 25 cm^2 Cohort 2: 200 mg/day for 3 days over 100 cm^2 Cohort 3: 50mg/day for 5 days over 25 cm^2 Cohort 4: 200 mg/day for 5 days over 100 cm^2	**Complete clearance (on Day 57)** Cohort 1: 25% (N=1/4) Cohort 2: 0% (N=0/10) Cohort 3: 50% (N=4/8) Cohort 4: 12.5% (N=1/8)	**LSRs** Mild to moderate erythema Mild-to-moderate flaking/scaling Timeline: Appeared day 4, peaked days 5-8, resolved in 2 weeks **Treatment-related AEs*** Application site pruritus and pain
Phase 2[6] 3-day cohort: 50 mg/day for 3 days over 25 cm^2 5-day cohort: 50 mg/day for 5 days over 25 cm^2	**Complete clearance (on Day 57)** 3-day cohort: 32% (N=27/84) 5-day cohort: 43% (N=36/84)	**LSRs** Minimal/mild erythema (71%, N=120/168) Minimal/mild flaking/scaling (60%, N=100/168) Timeline: Appeared day 2, peaked day 5, resolved day 29 **Treatment-related AEs*** Application site pruritus and pain
Phase 3 (Trial 1)[11] Tirbanibulin 1% ointment once daily for 5 days over 25 cm^2	**Complete clearance (on Day 57)** Tirbanibulin: 44% (N=77/175) Placebo: 5% (N=8/176) **Partial clearance (on Day 57)** Tirbanibulin: 68% (N=119/175) Placebo: 16% (N=29/176) **Follow-up at 1 year** 71% (N=124/174) with new or recurrent lesions in the treatment area -New: 42% (N=52/124) -Recurrent: 58% (N=72/124)	**LSRs** Moderate erythema (63%, N=223/353) Moderate flaking/scaling (47%, N=166/353) Timeline: Peaked day 15, resolved day 29 **Treatment-related AEs*** Application site pruritus (9%, N=32/353) Application site pain (10%, N=35/353)
Phase 3 (Trial 2)[7] Tirbanibulin 1% ointment once daily for 5 days over 25 cm^2	**Complete clearance (on Day 57)** Tirbanibulin: 54% (N=97/178) Placebo: 13% (N=22/173) **Partial clearance (on day 57)** Tirbanibulin: 76% (N=136/178) Placebo: 20% (N=34/173)	
Phase 3[8] Tirbanibulin 1% ointment once daily for 5 days over 100 cm^2	**Mean % change (SD) in AK lesion count from baseline** Day 5: 22.3% (36.4) Day 8: 28.1% (47.3) Day 15: 50.5% (45.2) Day 29: 69.6% (35.0) Day 57: 77.8% (26.8)	**LSRs** Erythema (96.1%, N=99) Flaking/scaling (84.4%, N=87) Timeline: Peaked day 5-8, resolved day 29 **Treatment-related AEs*** Application site pruritus (N=11, 10.5%) Application site pain (N=9, 8.6%)

*No treatment-related changes in labs, vital signs, physical examination, or EKGs
LSR = local skin reaction; AE = adverse events; EKG = electrocardiogram; W = week; SD = standard deviation; AKASI = Actinic Keratosis Area and Severity Index; N/A = none applicable

Efficacy outcomes were measured by the mean percentage of change in AK lesion count from baseline. The mean (SD) percentage change from baseline was 22.3% (36.4) on day 5, 28.1% (47.3) on day 8, 50.5% (45.2) on day 15, 69.6% (35.0) on day 29, and 77.8% (26.8) on day 57.[8] There were no significant differences in mean percentage change in lesion count between different number of baseline lesions (≤ 8 AKs vs > 8 AKs), Fitzpatrick skin types (I/II vs III/IV), age (< 65 years vs ≥ 65 years), and sex (male vs female).[8] There was a small difference in mean percentage change in lesion count between treatment locations on the face (84.5% change on day 57) vs the scalp (63.7% change on day 57).[8]

The local tolerability signs (LTS) score consisted of a graded evaluation (0=absent, 1=mild, 2=moderate, and 3=severe) for erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, and erosion/ulceration. The maximum LTS score was defined as the highest severity reported for each category throughout the post-baseline visits. Similarly to earlier trials, the most common LTS observed were erythema (N=99, 96.1%) and flaking/scaling (N=87, 84.4%).[8] Photographs of local tolerability signs are shown in Figure 4. The majority of patients had a maximum LTS score of "moderate" for erythema (N=66, 64.1%), "moderate" for flaking/scaling (N=44, 42.7%), and "absent" for all other LTS. LTS peaked between days 5 and 8 and spontaneously resolved by day 29.[8] The most commonly reported treatment-emergent adverse events (TEAEs) were pruritus (N=11, 10.5%) and pain (N=9, 8.6%) at the application site.

In brief, tirbanibulin 1% ointment demonstrated efficacy in both treatment areas of 25 cm^2 and 100 cm^2, and patients commonly experienced local reactions of erythema and flaking/scaling. New or recurrent AK lesions occurred in patients who had achieved complete clearance of AKs 1 year prior; 58% had re-current lesions (reappearance during

FIGURE 4. Local tolerability signs at baseline (pre-treatment) and days 5, 8, 15, 29, and 57 (post-treatment) in 2 patients using tirbanibulin on a treatment area of 100 cm^2.

follow-up) and 42% had new lesions only (distinct from baseline).[11] A summary of clinical trial results is outlined in Table 1.

Real-World Clinical Studies

Patient-Reported Outcomes in Actinic Keratosis (PROAK) Study

Given the efficacy and safety demonstrated in clinical trials, tirbanibulin 1% ointment was investigated in a real-world clinical study called Patient-Reported Outcomes in Actinic Keratosis (PROAK) to evaluate patient-reported outcomes (PRO) and clinician-reported outcomes (ClinRO).[9] The PROAK study included patients from 32 real-world community practices in the United States diagnosed with AKs on the face or scalp and treated with tirbanibulin.[9]

ClinRO included assessments on treatment effectiveness measured by Investigator's Global Assessment (IGA). IGA success was defined as an IGA score of 0 to 1, equivalent to ≥ 75% clearance of AK lesions.[9] Clinicians reported IGA success in 73.8% of patients at week 8 and 71.9% of patients at week 24. There was a statistically significant difference in IGA success between males (70.4%) vs females (81.3%, P=0.0488), patients with AKs on the face (81.5%) vs scalp (64.1%) vs both (48.7%, P<0.0001), and patients with absent/mild skin photodamage (83.1%) vs severe/moderate skin photodamage (70.9%, P=0.0491).[9] Additionally, there was a statistically significant reduction in skin photodamage severity at week 24 compared to baseline (P<0.0001).[9] PRO included assessments on quality of life (QoL) measured by Skindex-16.[9] There was a statistically significant decrease in scores in all Skindex-16 domains (ie, symptoms, emotions, and functioning) at week 8 compared to baseline in the overall cohort (P<0.0001).[9]

Both clinicians and patients reported treatment satisfaction with the Treatment Satisfaction Questionnaire for Medication (TSQM-9) and Expert Panel Questionnaire (EPQ). On the TSQM-9, both clinicians and patients reported high satisfaction scores with tirbanibulin at week 8 and week 24 in effectiveness, convenience of use, and global satisfaction.[9] On the EPQ, the majority of patients and clinicians reported the highest satisfaction ratings at week 24 in all domains. Detailed results from the TSQM-9 and EPQ are summarized in Table 2.

TABLE 2.

Summary of Real-World Clinical Studies Evaluating Tirbanibulin 1% Ointment

Clinical Study *Study site*	Efficacy, Tolerability, and Safety	Patient- and Clinician-Reported Outcomes
PROAK study[9] *United States*	**≥ 75% clearance** *IGA success* W8: 73.8% W24: 71.9% **LSRs** Mild/moderate erythema (47.6%) Severe erythema (4.9%) Mild/moderate flaking/scaling (49.6%) Severe (3.3%) **AEs** 5% (N=15) had ≥ 1 AE	**Quality of life** *Skindex-16* Week 8: Statistically significant decrease in scores in all Skindex-16 domains (symptoms, emotions, and functioning) **Treatment satisfaction** *TSQM-9* Patients, mean (SD) score out of 100 at W24 Effectiveness: 73.3 (21.3) Convenience of use: 85.0 (14.6) Global satisfaction: 72.0 (24.6) Clinicians, mean (SD) score out of 100 at W24 Effectiveness: 74.3 (21.2) Convenience of use: 84.5 (15.6) Global satisfaction: 74.9 (23.9) *EPQ* % of patient response Much/somewhat improved overall appearance of skin: 78.5% Extremely/very satisfied/satisfied with improvement in "how skin looks": 73.3% Extremely/very satisfied/satisfied with improvement in "skin texture": 71.8% Somewhat/very likely to consider tirbanibulin to treat AK lesions in the future: 78.4% % of clinician response Much/somewhat improved overall appearance of skin: 83.6% Extremely/very satisfied/satisfied with improvement in "how skin looks": 68.5% Extremely/very satisfied/satisfied with improvement in "skin texture": 68.9% Somewhat/very likely to consider tirbanibulin to treat AK lesions in the future: 77.3%
Campione et al[10] *Italy*	**Complete clearance (on Day 57)** 70% (N=21) **Partial clearance (on Day 57)** 30% (N=9) **LSRs** Mild erythema (30%, N=9) Moderate erythema (53.3%, N=16) Mild scaling (26.6%, N=8) Moderate scaling (3.33%, N=1) Timeline: Appeared day 2-15, peaked day 8, resolved day 15-29	**Treatment satisfaction** *TSQM 1.4* Patients, mean (SD) score out of 100 on day 57 Effectiveness: 80 Convenience of use: 97 Global satisfaction: 83 Side effects: 94
Kirschberger et al[11] *Germany*	**Complete clearance** *AKASI score < 1* W4: 47% (N=14) 1-6 months: 57% (N=13) **LSRs** Erythema (80%, N=26) Flaking/scaling (43%, N=13) Timeline: Appeared day 2-10, resolved in 5 days	N/A
Li Pomi et al[12] *Italy*	**Complete clearance (at W8)** 51% of all lesions Olsen grade 1: 60% (N=51/85) Olsen grade 2: 49% (N=57/116) Olsen grade 3: 29% (N=8/27) **Partial clearance (at W8)** 73% of all lesions Olsen grade 1: 78% (N=67/85) Olsen grade 2: 72% (N=84/116) Olsen grade 3: 55% (N=15/27) **LSRs** Moderate erythema (60%, N=23/38) Moderate scaling (44%, N=17/38) Timeline: Appeared Day 7-9, peaked Day 10-12, resolved in 2-4 weeks	**Treatment compliance** *Patient-reported* Excellent: 71% (N=28) Good: 18% (N=7) Moderate: 8% (N=3) Poor: 3% (N=1)

PROAK = Patient-Reported Outcomes in Actinic Keratosis; LSR = local skin reaction; AE = adverse events; W = week; SD = standard deviation; IGA = investigator's Global Assessment; AKASI = Actinic Keratosis Area and Severity Index; TSQM = Treatment Satisfaction Questionnaire for Medication; EPQ = Expert Panel Questionnaire; N/A = none applicable

Fifteen patients (15%) reported at least one AE, and most of them were mild (4%).[9] Few patients developed SCC (2.3%) and basal cell carcinoma (1.3%), but only one patient developed skin cancer within the treatment site.[9] None of the cases were considered related to treatment. Severe AEs reported were not related to treatment, and there were no serious adverse drug reactions. Consistent with clinical trial results, the most commonly reported LSRs were erythema (47.6% mild/moderate and 4.9% severe) and flaking/scaling (49.6% mild/moderate and 3.3% severe).[9]

Single-Center Clinical Studies

Single-center studies have been conducted globally in real-world clinical settings. Campione et al, Kirschberger et al, and Li Pomi et al reported efficacy and safety results from cohorts in Italy and Germany consistent with those of the PROAK study.[10-12] All 3 studies used dermoscopic evidence in combination with clinical findings to demonstrate clearance of AK lesions. Detailed findings are reported in Table 2.

In addition to efficacy and safety data, Campione et al reported treatment satisfaction on day 57 using the TSQM, with mean satisfaction scores (on a scale of 0-100) of 97 in convenience of use, 94 in side effects, 83 in global satisfaction, and 80 in effectiveness.[10] Moreover, Li Pomi et al measured AK clearance at week 8, stratified by Olsen grading of AK lesions.[12] Olsen grade 1 lesions demonstrated the highest rate of complete clearance (60%, N=51/85), followed by Olsen grade 2 lesions (49%, N=57/116), then Olsen grade 3 lesions (29%, N=8/27). Similarly, Olsen grade 1 lesions demonstrated the highest rate of partial clearance (78%, N=67/85), followed by Olsen grade 2 lesions (72%, N=84/116), then Olsen grade 3 lesions (55%, N=15/27).[12] There was a statistically significant difference in the rate of complete clearance between Olsen grade 1 vs grade 3 lesions (60% vs 29%, *P*=0.01), as well as the rate of partial clearance between Olsen grade 1 vs grade 3 lesions (78% vs 55%, *P*=0.02).[12] Li Pomi et al also measured self-reported patient compliance to tirbanibulin treatment, which showed 71% (N=28) of patients reporting their compliance as "excellent", 18% (N=7) as "good", 8% (N=3) as "moderate", and 3% (N=1) as "poor".[12]

In summary, real-world clinical studies using tirbanibulin 1% ointment demonstrated high treatment satisfaction, improved quality of life, and robust treatment compliance. The highest efficacy was achieved by AK lesions in females, on the face, with absent/mild skin photodamage, and with milder Olsen grade.

DISCUSSION

Tirbanibulin 1% ointment has demonstrated strong clinical trial and real-world evidence for safe and effective treatment of AKs. While other field-directed therapies can be limited by poor treatment compliance due to prolonged treatment duration, tirbanibulin 1% ointment is administered with a lower frequency and duration of use. Phase 3 and real-world clinical studies demonstrated complete clearance of AKs by day 57 in most patients. Given efficacy data on different types of AK lesions and patient characteristics, tirbanibulin may be particularly effective for mild AKs on the face without significant hyperkeratosis, female patients, and individuals with limited skin photodamage. However, despite significant improvement in AK lesions, patients may experience recurrence of AKs in the treatment area after complete clearance.

Moreover, patients commonly experienced LSRs such as erythema and flaking/scaling that self-resolved in 2 to 4 weeks. Application site pruritus and pain were the most common AEs experienced by patients. Of note, tirbanibulin used in larger treatment areas of 100 cm^2 revealed promising efficacy and safety in a phase 3 clinical trial, which led to the FDA approval for field treatment up to 100 cm^2. Lastly, real-world clinical studies have contributed valuable patient and clinician perspectives on tirbanibulin use. Overall, both patients and clinicians reported high treatment satisfaction, with the highest scores reported in convenience of use. Patients also demonstrated strong treatment compliance, and quality of life improved in all domains of symptoms, emotions, and functioning.

This article summarizes the clinical evidence on tirbanibulin 1% ointment use from several studies. This comprehensive review of tirbanibulin 1% ointment can guide treatment considerations for the treatment of AKs for both clinicians and patients.

DISCLOSURES

Charlotte Jeong BS has no conflicts of interest to disclose. Leon Kircik MD has served on as an investigator, consultant, speaker, and/or advisory board member for Abbott Laboratories, AbbVie, Ablynx, Aclaris, Acambis, Allergan, Inc., Almirall, Amgen, Inc., Anacor Pharmaceuticals, AnaptysBio, Arcutis, Arena, Assos Pharmaceuticals, Astellas Pharma US, Inc., Asubio Pharma Co., Bausch Health, Berlex Laboratories,

Biogen-Idec, BioLife, BioMimetix, Biopelle, BMS, Boehringer-Ingleheim, Breckinridge Pharma, Cassiopea, Centocor, Inc., Cellceutix, Cipher, Coherus BioSciences, Colbar, Combinatrix, Connectics Corporation, Coria, Dermavant, Dermira, Dermik Laboratories, Dow Pharmaceutical Sciences, Inc., Dr. Reddy's Lab, Dusa, Embil Pharmaceuticals, Eli Lilly, EOS, Exeltis, Ferndale Laboratories, Inc., Foamix, Ferrer, Galderma, Genentech, Inc., GlaxoSmithKline, PLC, Glenmark, Health Point, LTD, Idera, Incyte, Intendis, Innocutis, Innovail, Isdin, Johnson & Johnson, Kyowa Kirin, Laboratory Skin Care Inc., Leo, L'Oreal, 3M, Maruho, Medical International Technologies, Merck, Medicis Pharmaceutical Corp., Merz, Nano Bio, Nektar, Nimbus, Novartis AG, Noven Pharmaceuticals, Nucryst Pharmaceuticals Corp, Obagi, Onset, OrthoNeutrogena, Pediapharma, Pfizer, Promius, PuraCap, PharmaDerm, QLT, Inc, Quinnova Pharmaceuticals, Quatrix, Rapt Therapeutics, Regeneron, Sanofi, Serono, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, TolerRx, Triax, UCB, Valeant Pharmaceuticals Intl., Ventyx Biosciences, Warner Chilcott, XenoPort, and ZAGE. Mark Lebwohl MD has served as a consultant for Aditum Bio, Almirall, AltruBio, AnaptysBio, Apogee Therapeutics, Arcutis, Arena Pharmaceuticals, Aristea Therapeutics, Arrive Technologies, AstraZeneca, Atomwise, Avotres Therapeutics, BiomX, Boehringer Ingelheim, Brickell Biotech, Bristol-Myers-Squibb, Cara Therapeutics, Castle Biosciences, CorEvitas, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, EPI, Evelo Biosciences, Evommune Inc., Facilitation of International Dermatology Education, Forte Biosciences, Foundation For Research and Education in Dermatology, Galderma Laboratories, L.P., Galderma Laboratories, L.P., Helsinn Therapeutics, Hexima Ltd, LEO Pharma AS, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, STRATA Skin Sciences, Inc, Sun Pharmaceutical Industries Inc, Takeda Pharmaceutical Company, Trevi, Verrica Pharmaceuticals, and Vial. April W. Armstrong MD MPH has served as a research investigator, scientific advisor, and/or speaker to AbbVie, Amgen, Almirall, Arcutis, ASLAN, Beiersdorf, BI, BMS, EPI, Incyte, Leo, UCB, Janssen, Lilly, Novartis, Ortho, Sun, Dermavant, Dermira, Sanofi, Takeda, Regeneron, and Pfizer.

REFERENCES

1. George CD, Lee T, Hollestein LM, et al. Global epidemiology of actinic keratosis in the general population: a systematic review and meta-analysis. *Br J Dermatol.* 2024;190(4):465-476.
2. Del Rosso JQ, Kircik L, Goldenberg G, et al. Comprehensive management of actinic keratoses. *J Clin Aesthet Dermatol.* 2014;7(9 Suppl S2-S12):S2-S12.
3. Arcuri D, Ramchatesingh B, Lagacé F, et al. Pharmacological agents used in the prevention and treatment of actinic keratosis: a review. *Int J Mol Sci.* 2023 Mar 5;24(5):4989.
4. Glogau RG. The risk of progression to invasive disease. *J Am Acad Dermatol.* 2000;42(1, Part 2):S23-S24.
5. Klisyri [package insert]. Malvern, PA: Almirall, LLC; 2024.
6. Kempers S, DuBois J, Forman S, et al. Tirbanibulin ointment 1% as a novel treatment for actinic keratosis: phase 1 and 2 results. *J Drugs Dermatol.* 2020;19(11):1093-1100.
7. Blauvelt A, Kempers S, Lain E, et al. Phase 3 trials of tirbanibulin ointment for actinic keratosis. *N Engl J Med.* 2021;384(6):512-520.
8. Bhatia N, Lain E, Jarell A, et al. Safety and tolerability of tirbanibulin ointment 1% treatment on 100 cm2 of the face or scalp in patients with actinic keratosis: a phase 3 study. *JAAD Int.* 2024;17:6-14.
9. Schlesinger T, Kircik L, Lebwohl M, et al. Patient- and clinician-reported outcomes for tirbanibulin in actinic keratosis in Clinical Practice Across the United States (PROAK). *J Drugs Dermatol.* 2024;23(5):338-346.
10. Campione E, Rivieccio A, Gaeta Shumak R, et al. Preliminary evidence of efficacy, safety, and treatment satisfaction with tirbanibulin 1% ointment: a clinical perspective on actinic keratoses. *Pharmaceuticals (Basel).* 2023;16(12):1686.
11. Kirchberger MC, Gfesser M, Erdmann M, et al. Tirbanibulin 1% ointment significantly reduces the actinic keratosis area and severity index in patients with actinic keratosis: results from a real-world study. *J Clin Med.* 2023;12(14):4837.
12. Li Pomi F, Vaccaro M, Pallio G, et al. Tirbanibulin 1% ointment for actinic keratosis: results from a real-life study. *Medicina (Kaunas).* 2024;60(2):225.

AUTHOR CORRESPONDENCE

April W. Armstrong MD MPH
E-mail:..... armstrongpublication@gmail.com