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Original Article

Patient- and Clinician-reported Outcomes, Safety and Efficacy Profile of Tirbanibulin 1% for Actinic Keratosis Under Conditions Close to Routine Clinical Practice in Spain and Italy (TIRBASKIN Study)

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ABSTRACT

Objective: To assess patient- and clinician-reported outcomes, efficacy, and safety of tirbanibulin 1% administered to patients with actinic keratoses (AKs) in Spain and Italy.

Methods: TIRBASKIN is a multicenter, single-cohort, phase IV, low-interventional clinical study conducted among adults with 4–8 AK lesions on the face or scalp in an area ≤25 cm^2. Patients applied tirbanibulin for 5 consecutive days. The primary endpoint was treatment satisfaction on day 57 (D57), assessed with the Treatment Satisfaction Questionnaire for Medication 9 (TSQM-9). Efficacy was assessed by the percentage of patients with complete clearance (CC) and partial clearance (PC) at D57. Tolerability was assessed by local tolerability signs (LTSs), also known as local skin reactions.

Results: A total of 328 patients (mean age, 74.8 years; male, 83.5%; Fitzpatrick skin type II, 53.7%; AKs on the scalp, 52.7%) completed study assessments at D57. Patients reported high levels of satisfaction with tirbanibulin as assessed by TSQM-9 (effectiveness mean score, 73.6; convenience mean score, 82.8; global satisfaction mean score, 76.9). Moreover, 87.7% of clinicians and 81.8% of patients reported overall satisfaction with tirbanibulin as much/somewhat better compared with previous topical treatment. In addition, 87.1% of clinicians and 86.3% of patients reported a likelihood of reconsidering tirbanibulin in the future, if needed. CC was achieved by 54.3% of patients and PC by 76.2%. At D8, the most frequent LTSs were erythema/redness (mild/moderate, 72.2%; severe, 2.2%) and flaking/scaling (mild/moderate, 34.6%; severe, 0.6%), which had mostly resolved by D57.

Conclusions: Patients' and clinicians' satisfaction was high, and both groups reported a high likelihood of using tirbanibulin again, if needed.

Introduction

Actinic keratoses (AKs) are common skin lesions caused primarily by prolonged exposure to ultraviolet light associated with chronic sun exposure.[1–3] If left untreated, these lesions may progress to squamous cell carcinoma (SCC).[1,2] It is estimated that nearly 60% of SCC develops from AKs.[4] In addition, AK prevalence is significantly higher in immunosuppressed patients.[3]

Currently, AK treatments include lesion-directed and field-directed therapies.[4] European guidelines[3] recommend that tirbanibulin 1% ointment be offered for the treatment of single or multiple AKs and field cancerization. Tirbanibulin is approved by health authorities worldwide for the topical treatment of nonhyperkeratotic, nonhypertrophic AKs

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Table 1
Baseline patient characteristics.

	Evaluable population (N = 328)
Age (years), mean (SD) [min; max]	74.8 (8.6) [42; 94]
Sex (male), n (%)	274 (83.5)
Fitzpatrick skin type, n (%)	
Type I	25 (7.6)
Type II	176 (53.7)
Type III	121 (36.9)
Type IV	5 (1.5)
Type V	1 (0.3)
Number of baseline AK lesions, mean (SD)	5.9 (1.4)
AK location, n (%)	
Face	155 (47.3)
Scalp	173 (52.7)
Patients naïve[a] to treatment, n (%)	
Yes	126 (38.4)
No	202 (61.6)
<END> [5pt] *Immunosuppressed patients, n (%)*	6 (1.8)
Age (years), mean (SD) [min; max]	71.5 (11.6) [57.0; 82.0]
Sex (male), n (%)	5 (83.3)
Fitzpatrick skin type, n (%)	
Type II	4 (66.7)
Type III	2 (33.3)
AK location, n (%)	
Face	1 (16.7)
Scalp	5 (83.3)
Renal transplant recipients	3 (50%)
Immunosuppression therapy, n (%)	
Apremilast	1 (0.3)
Azathioprine	1 (0.3)
Brodalumab	1 (0.3)
Mychophenolate mofetil	1 (0.3)
Mycophenolate sodium	2 (0.6)
Tacrolimus	1 (0.3)
Tacrolimus monohydrate	1 (0.3)

AK, actinic keratosis; SD, standard deviation.
[a] Naïve patients were patients never treated previously for AK lesions.

on the face or scalp[5] and has demonstrated efficacy and safety in prior phase II and III clinical trials (CTs),[6–8] including fields up to 100 cm^2.[9,10] Moreover, results from a phase IV study in the United States (US) demonstrated that tirbanibulin improved quality of life (QoL), as assessed by Skindex-16, as early as 8 weeks, and that both clinicians and patients reported high satisfaction with tirbanibulin.[11,12]

Although the presence of AK lesions in photoexposed areas constitutes one of the main reasons for dermatology consultation in Spain and Italy,[1] patient- and clinician-reported outcomes (PROs; ClinROs), such as well-being and treatment satisfaction, have been scarcely assessed in European patients treated with tirbanibulin.[13] Therefore, this study aimed to evaluate treatment satisfaction, PROs, and ClinROs and to assess efficacy and safety following treatment with tirbanibulin.

Patients and methods

Design

TIRBASKIN is an open-label, phase IV, multicenter, single-cohort, low-interventional CT (EudraCT No. 2022-001251-16) conducted in 30 centers in Spain and 7 in Italy from January 20, 2023, to January 19, 2024, in accordance with the Declaration of Helsinki, the International Council for Harmonisation Good Clinical Practice guidelines, and Spanish and Italian local laws. The study was reviewed by independent ethics committees in each country. All patients signed written informed consent, including consent for publication of photographs, before participating in the trial.

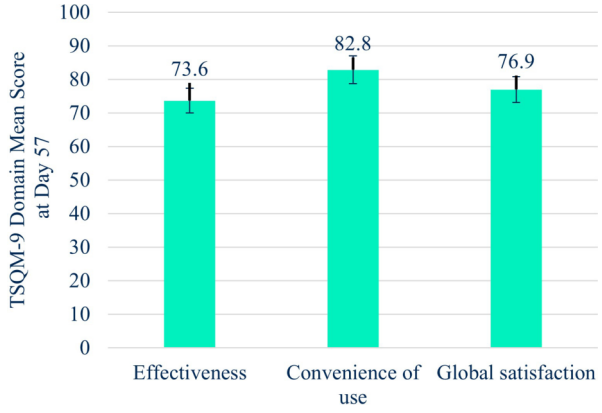

Fig. 1. Patients' reported satisfaction with tirbanibulin treatment (TSQM-9). TSQM, Treatment Satisfaction Questionnaire for Medication.

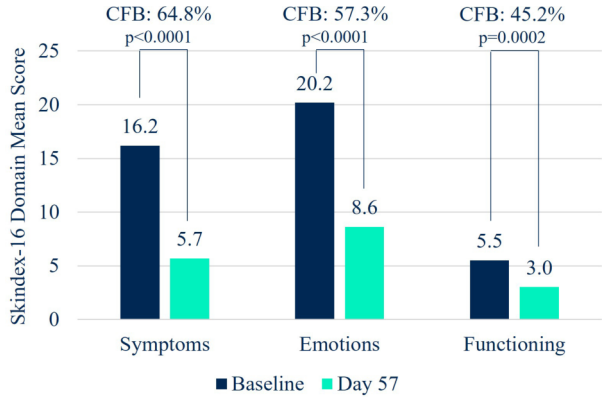

Fig. 2. Evaluation of PROs: AK symptoms and impact on emotions and functioning (Skindex-16). AK, actinic keratosis; CFB, change from baseline; PRO, patient-reported outcome.

Population

The study population consisted of adults with a clinically typical diagnosis of AK in 1 contiguous area of ≤25 cm^2 on the face or scalp containing 4–8 nonhyperkeratotic, nonhypertrophic AK lesions, who had not been previously treated in the same area during the previous 6 months. At least 30% of patients previously treated in other small areas (≤25 cm^2) within the previous >1 to <6 months were enrolled to avoid recall bias related to previous treatments. Patients with clinically atypical or rapidly changing AK lesions, incompletely healed wounds, or suspected basal cell carcinoma (BCC) or SCC were excluded. Moreover, patients receiving cosmetic procedures or treatments that could interfere with study results (ie, immunomodulators, cytotoxic drugs, interferons/interferon inducers, systemic retinoids, or systemic immunosuppressive agents [except for organ transplant recipients under stable immunosuppressive therapy for 6 months]) were also excluded.

Interventions

Tirbanibulin was applied according to the European Summary of Product Characteristics.[5] On day 1 (D1), treatment application was per-

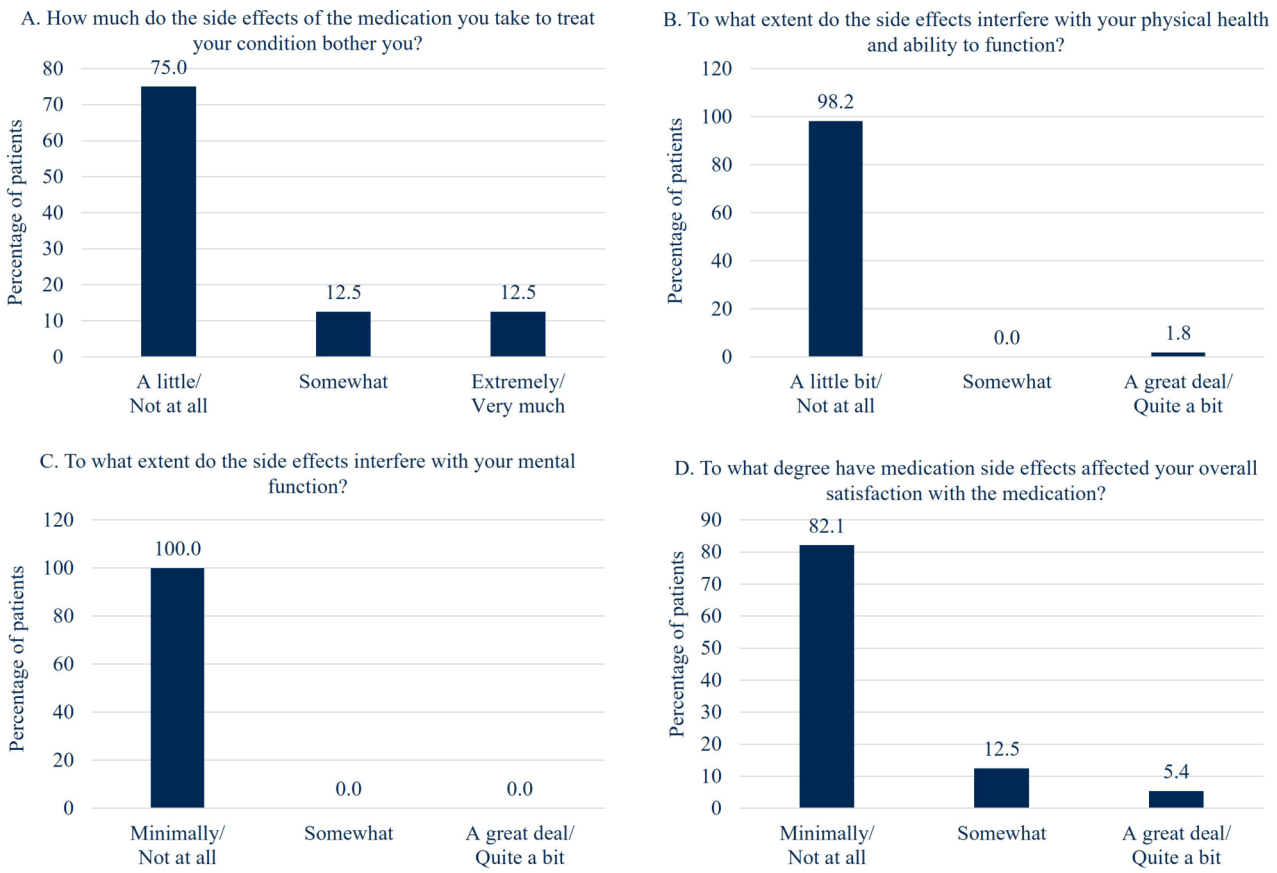

Fig. 3. Evaluation of PROs: tirbanibulin side effects (TSQM-1.4). PRO, patient-reported outcome; TSQM, Treatment Satisfaction Questionnaire for Medication.

formed at the investigational site. Between D2 and D5, treatment was self-administered once daily at home. Visits were conducted at screening and on D0 (baseline), D8, and D57 (end of study). Total study duration was 12 months, including recruitment, screening, treatment, and follow-up.

Endpoints

The primary endpoint was treatment satisfaction on D57, evaluated with the Treatment Satisfaction Questionnaire for Medication version 9 (TSQM-9).[14] TSQM-9 is a validated instrument comprising 3 domains: effectiveness (questions 1–3), convenience (questions 4–6), and global satisfaction (questions 7–9). Questions 1–6 and 9 are scored on a 7-point scale, whereas questions 7 and 8 are scored on a 5-point scale. Subscale scores are transformed to a 0–100 scale, with higher scores representing greater satisfaction.

Secondary endpoints were PROs and ClinROs, organoleptic properties of tirbanibulin, efficacy, safety, and adherence to treatment. PROs were assessed using Skindex-16, TSQM-1.4, and the Expert Panel Questionnaire (EPQ).

Skindex-16[15,16] was used to assess percent change from baseline (%CFB) to D57 in skin condition. Skindex-16 is a short, 16-item, patient-completed assessment with 3 domains: symptoms, emotional impact, and functioning. All items are scored on a 7-point numerical analog scale and transformed to a linear 0–100 scale. Higher scores indicate greater impairment.

TSQM-1.4[17] is an extended version of TSQM-9 focused on effectiveness, side effects, convenience, and global satisfaction domains. The global total score ranges from 0 to 100, with higher scores indicating greater satisfaction.

Regarding the EPQ[18] items were designed to be answered by both patients and clinicians, except for item 10, which was designed to be answered only by clinicians. Overall skin appearance was rated from 0 (much worse) to 4 (much improved), and satisfaction with "how skin looks" and "skin texture" was rated from 1 (extremely dissatisfied) to 7 (extremely satisfied). Duration and severity of local tolerability signs (LTSs), impact on daily activities, convenience, ease of use, and overall satisfaction compared with previous AK treatments were rated from 0 (much shorter/better) to 4 (much longer/worse). Likelihood of reconsidering treatment was rated from 0 (very unlikely) to 4 (very likely).

Organoleptic properties of tirbanibulin were assessed at D8 with a Likert-scale questionnaire composed of questions related to the product's characteristics. The Likert scale offered 7 possible responses, from "totally agree" to "totally disagree."

Efficacy profile was assessed by the percentage of patients with complete clearance (CC), defined as a 100% reduction in lesions within the application area, and the percentage of patients with partial clearance (PC), defined as a reduction of ≥75% of lesions, at D57. The percentage of patients with PC included patients with CC. Furthermore, the number of AK lesions at D57 and the percent reduction in AK lesion count were assessed. Efficacy was also assessed in patients defined as immunosuppressed and in subgroups according to lesion location (face vs scalp) and age (<65 vs ≥65 years).

Safety profile was assessed by the incidence and severity of adverse events (AEs) and LTSs (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, and erosions/ulcerations) on a grading scale ranging from 0 (absent) to 3 (severe). Application-site reactions such as itching, burning, stinging, tenderness, or pain were not classified as LTSs and were reported as AEs. LTSs were also evaluated in patients who achieved CC.

Treatment adherence was recorded using a self-administered patient diary (D0 to D4), including questions related to treatment dosage and frequency, AEs, and reasons for missed or delayed doses.

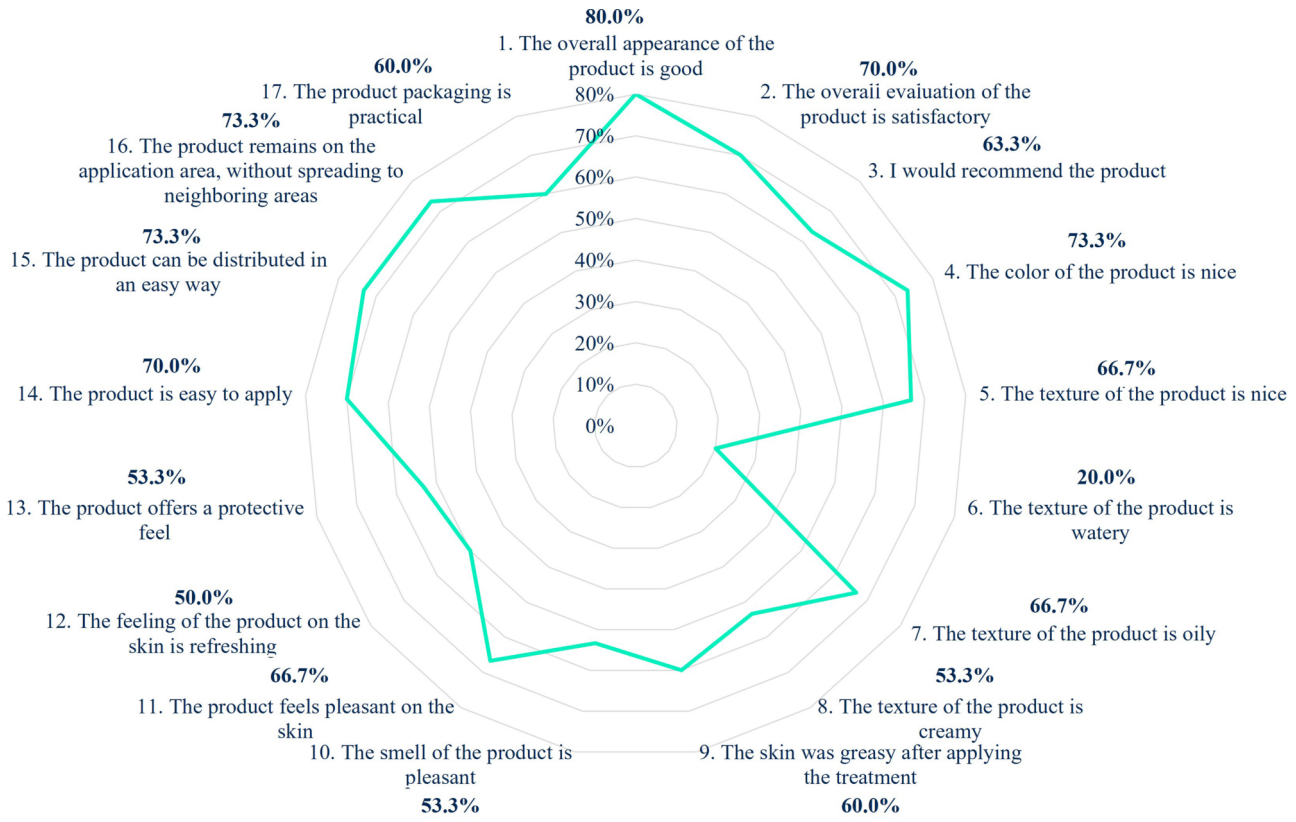

Fig. 4. Overall appreciation of organoleptic characteristics.

Statistical analysis

Variables were analyzed descriptively using appropriate statistical methods. Continuous data were summarized by mean, SD, 95%CI, median, first and third quartiles, minimum, and maximum. Categorical data were presented as absolute and relative frequencies (*n* and %). Bilateral 95% confidence limits are presented as appropriate. Patients were included in each analysis based on available data. No imputation was made for missing data. All analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC, USA).

Results

Baseline characteristics

A total of 334 patients (262 in Spain and 72 in Italy) applied at least 1 dose of tirbanibulin and were included in the full analysis set (FAS) and safety population. The evaluable population included 328 patients who completed the TSQM-9 assessment and the study at D57.

A total of 52.7% of patients were diagnosed with AK on the scalp, and the mean number of AK lesions at baseline was 5.9 (SD, 1.4). Mean age was 74.8 years (SD, 8.6), and most patients were male (83.5%). Moreover, 6 patients (1.8%) were immunosuppressed (Table 1).

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TSQM-9

Patients reported high satisfaction with tirbanibulin at D57 across TSQM-9 domains (Fig. 1). The highest satisfaction was reported for convenience of use (mean score, 82.8), followed by global satisfaction (mean score, 76.9) and effectiveness (mean score, 73.6); 95%CI are:

- Convenience of use: 82.8 (81.3; 84.3);
- Global satisfaction: 76.9 (74.9; 79.0);
- Effectiveness: 73.6 (71.3; 76.0).

Skindex-16

The %CFB in the symptoms, emotions, and functioning domains of Skindex-16 was 64.8%, $P < .0001$; 57.3%, $P < .0001$; and 45.2%, $P = .0002$, respectively (Fig. 2).

TSQM-1.4

Most patients (82.9%) did not experience any side effects, even slight ones, whereas 17.1% did. Side effects were reported as bothering patients a little or not at all (75.0% of patients), interfering a little or not at all with physical health and ability to function (98.2% of patients), interfering minimally or not at all with mental functioning (100% of patients), and affecting overall satisfaction minimally or not at all (82.1% of patients) (Fig. 3).

EPQ

Overall skin appearance in the treated AK area was considered much or somewhat improved from baseline to D57 by 96.3% of clinicians and 92.5% of patients. A total of 202 patients (61.6%) had received at least 1 prior AK therapy, the most common being cryotherapy (43.0% of pa-

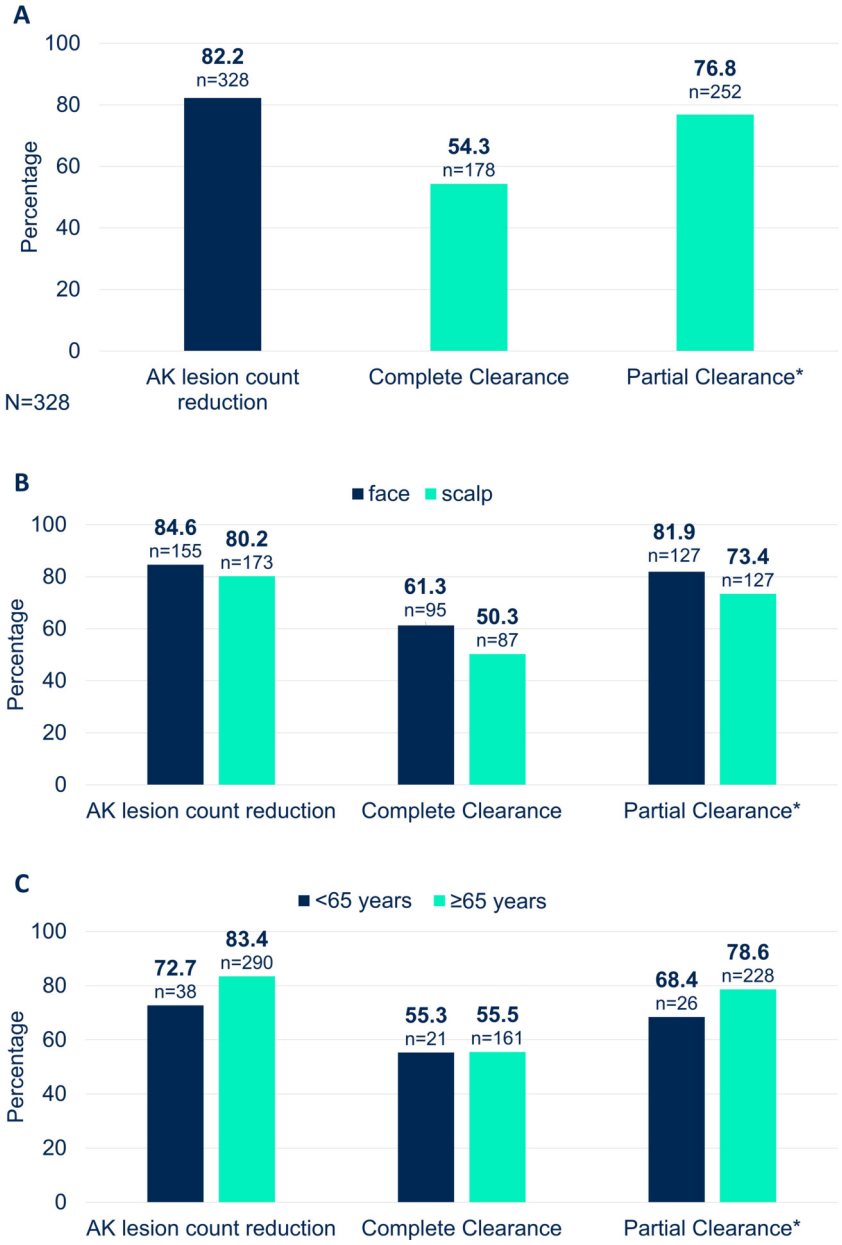

Fig. 5. Complete and partial clearance at day 57 for (A) the overall population; (B) patients with AK lesions on the face or scalp; and (C) patients aged <65 years or ≥65 years. AK, actinic keratosis. Partial clearance is defined as a reduction of ≥75% (includes patients with complete clearance).

tients), sensitizers used in photodynamic/radiation therapy (21.0% of patients), and diclofenac sodium (14.0%). Overall satisfaction with tirbanibulin compared with previous AK treatments was rated as much or somewhat better by 87.7% of clinicians and 81.8% of patients. Similarly, 87.1% of clinicians and 86.3% of patients reported that they would consider tirbanibulin again, if needed. More details are provided in Supplementary Fig. 1.

Organoleptic properties

Among the 328 evaluable patients, 327 (99.7%) completed the questionnaire at D8. Most patients found the general appearance (93.9% of patients) and texture (94.5% of patients) of the product agreeable. Patients also agreed that tirbanibulin was easy to apply (97.3% of patients) (Fig. 4).

Efficacy profile

At D57, the mean number of old and new AK lesions was 1.1 (SD, 1.6) and 0.1 (SD, 0.3), respectively. The percent reduction in AK lesion count was 83.0% when only old lesions were considered and 82.2% when both old and new lesions were considered (Fig. 5A). A total of 54.3% of patients achieved CC, and 76.8% achieved PC. Fig. 6 shows the evolution of AK lesions in 4 selected patients. Similar results were observed in subgroups according to location and age (Fig. 5B and C) and in immunosuppressed patients (percent reduction in lesion count, 83.3%; CC, 40.0%; PC, 100.0%). CC and PC according to baseline Olsen classification are presented in Supplementary Fig. 2.

Safety profile

A total of 153 patients (45.8%) reported at least 1 treatment-emergent AE (TEAE). In 38.6% of patients, TEAEs were considered

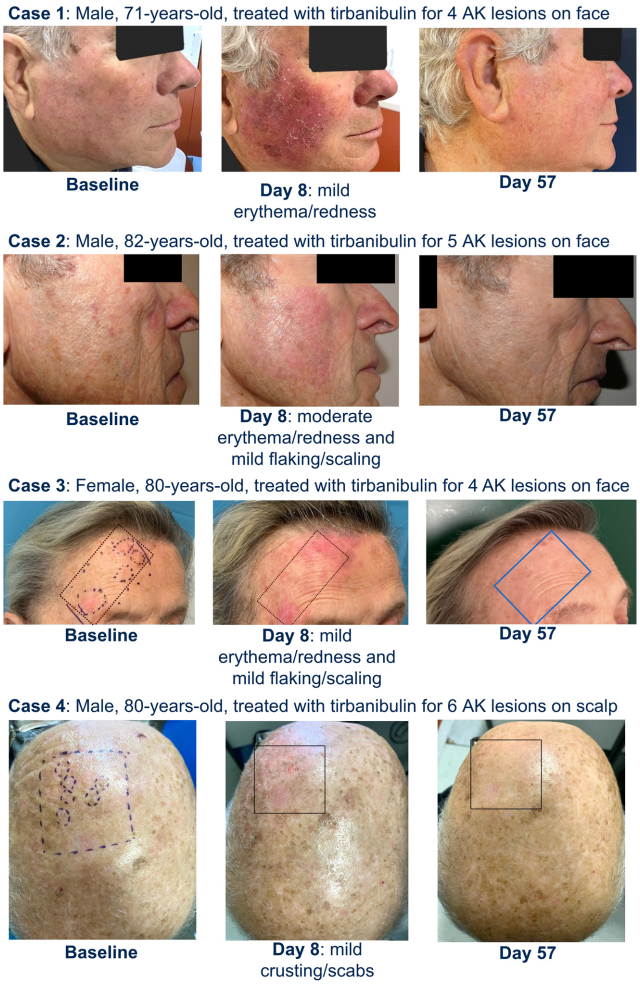

Fig. 6. Clinical clearance at day 8 and day 57 in four cases from the treated sample. AKs, actinic keratoses.

Table 2
Summary of TEAEs.

	Safety population (N = 334)
TEAEs, n (%)	153 (45.8)
Serious TEAEs, n (%)	0
TEAEs of special interest[a]*, n (%)*	3 (0.9)
TEAEs suspected related to treatment, n (%)	129 (38.6)
TEAEs leading to treatment discontinuation, n (%)	3 (0.9)
TEAEs by severity, n (%)	
Grade 1	131 (39.2)
Grade 2	17 (5.1)
Grade 3	3 (0.9)
Grade 4	1 (0.3)
TEAEs reported in >5%, n (%)	
Pruritus	92 (27.5)
Pain	31 (9.3)
Burning sensation	17 (5.1)

TEAE, treatment emergent adverse event.
[a] TEAEs of special interest were defined as skin cancers.

related to treatment (Table 2). Pruritus was the most frequent TEAE, occurring in 27.5% of patients. Regarding severity, grade 3 TEAEs were reported in 3 patients (0.9%) (hypersensitivity, 0.3%; BCC, 0.3%; and hypertension, 0.3%), and grade 4 TEAEs were reported in 1 patient (hypersensitivity, 0.3%). Regarding TEAEs of special interest, 3 patients (0.9%) experienced BCC; however, these BCCs were not located in the AK treatment area and were considered unrelated to treatment. Three patients (0.9%) discontinued treatment because of TEAEs.

At D8, most LTSs were mild or moderate (Table 3). Few patients experienced severe erythema/redness (2.2% of patients), flaking/scaling (0.6% of patients), or crusting/scabs (0.3% of patients). No severe cases of swelling, erosions/ulceration, or vesiculation/pustulation were reported. At D57, LTS assessment was comparable to baseline or better. The mean composite LTS score, calculated as the sum of the scores observed for each sign, was 1.8 (SD, 1.7) and 0.1 (SD, 0.3) out of 18 at D8 and D57, respectively. More than 75% of patients who achieved CC at D57 had an LTS composite score ≤2 at D8 (Supplementary Fig. 3). In the subgroup of patients who achieved CC, only 2.3% experienced severe erythema/redness. Immunosuppressed patients did not experience severe LTSs (Table 3).

Adherence

A total of 330 patients (98.8%) applied all tirbanibulin doses; 327 (97.9%) completed treatment, and 7 (2.1%) discontinued.

Discussion

Results of this study, conducted under conditions close to routine clinical practice in Spain and Italy, are comparable to those observed in phase III studies[8,10] and with existing topical treatments.[19]

As assessed by TSQM-9, at D57 patients reported high levels of global satisfaction (score = 76.9) and agreed on the convenience (score = 82.8) and effectiveness (score = 73.6) of tirbanibulin. These results were consistent with those reported in the PROAK study conducted in the US[11,12] and were higher than those reported in European studies evaluating other topical therapies for AK (imiquimod, diclofenac, and 5-fluorouracil [5-FU]).[20–22] In the RAPID-ACT study[23] conducted in Sweden and Denmark (N = 446), patients reported mean TSQM-9 scores for global satisfaction of 60.8 and 64.2, convenience scores of 79.3 and 78.4, and effectiveness scores of 52.9 and 60.8 with diclofenac and imiquimod, respectively.

The percentage of lesion reduction is proportionally related to the baseline lesion count, unlike CC rates, which are inversely associated with the number of lesions present at baseline.[24] In our study, the percent reduction in AK lesion count considering both old and new lesions was 82.2%, which is comparable to the reduction observed in phase III studies with 4% 5-FU (80.1%) and 5% 5-FU (79.0%).[25] Moreover, 54.3% of patients achieved CC, which is similar to the rate reported in an Italian retrospective study[26] of 250 patients treated with tirbanibulin (54.3%). Results obtained in the subgroups according to lesion location (face vs scalp) and age (<65 vs ≥65 years) further support the efficacy of tirbanibulin.

Tirbanibulin was also well tolerated and showed a favorable safety profile. Only 0.9% of patients discontinued treatment because of a TEAE. The most frequent TEAE was pruritus (27.5% of patients), which was higher than that reported in phase III studies.[8,10] As observed in previous studies,[8,10,12] most LTSs reported at D8 were mild or moderate erythema/redness and flaking/scaling. Furthermore, most patients who achieved CC experienced either no LTSs (24.1%) or mild/moderate LTSs (97.8%), indicating that treatment with tirbanibulin is not associated with bothersome local reactions. In contrast, commonly prescribed topical treatments for AK are associated with more severe LTSs.[27–29] Studies evaluating imiquimod 5% and 3.75% reported severe erythema/redness in 31% and 25% of patients, respectively, and severe scabbing/crusting in 24% and 13.7% of patients.[19] In an exploratory data analysis, CC and PC at week 8 in patients with AK treated with 5-FU 4% were significantly associated with the severity of LTSs, particularly severe erythema.[29]

Table 3
Summary of LTS on day 8.

	Safety population (N = 334)	Patients who achieved CC (N = 174)	Immunosuppressed patients (N = 6)
Erythema/redness, n (%)			
0 – Absent	83 (25.6)	47 (27.0)	1 (16.7)
1 – Mild	191 (59.0)	99 (56.9)	4 (66.7)
2 – Moderate	43 (13.3)	24 (13.8)	1 (16.7)
3 – Severe	7 (2.2)	4 (2.3)	0 (0.0)
Flaking/scaling, n (%)			
0 – Absent	210 (64.8)	107 (61.5)	4 (66.7)
1 – Mild	91 (28.1)	53 (30.5)	1 (16.7)
2 – Moderate	21 (6.5)	14 (8.1)	1 (16.7)
3 – Severe	2 (0.6)	0 (0.0)	0 (0.0)
Crusting/scabs, n (%)			
0 – Absent	262 (80.9)	139 (79.9)	3 (50.0)
1 – Mild	50 (15.4)	27 (15.5)	2 (33.3)
2 – Moderate	11 (3.4)	8 (4.6)	1 (16.7)
3 – Severe	1 (0.3)	0 (0.0)	0 (0.0)
Swelling, n (%)			
0 – Absent	277 (85.5)	155 (89.1)	6 (100)
1 – Mild	37 (11.4)	15 (8.6)	0 (0.0)
2 – Moderate	10 (3.1)	4 (2.3)	0 (0.0)
3 – Severe	0 (0.0)	0 (0.0)	0 (0.0)
Vesiculation/pustulation, n (%)			
0 – Absent	321 (99.1)	173 (99.4)	6 (100)
1 – Mild	2 (0.6)	1 (0.6)	0 (0.0)
2 – Moderate	1 (0.3)	0 (0.0)	0 (0.0)
3 – Severe	0 (0.0)	0 (0.0)	0 (0.0)
Erosions/ulcerations, n (%)			
0 – Absent	314 (96.9)	167 (96.0)	6 (100)
1 – Mild	6 (1.9)	5 (2.9)	0 (0.0)
2 – Moderate	4 (1.2)	2 (1.2)	0 (0.0)
3 – Severe	0 (0.0)	0 (0.0)	0 (0.0)

CC, complete clearance; LTS, local tolerability signs.

When considering side effects as assessed by TSQM-1.4, 17.1% of patients reported experiencing them (score = 97.5); however, these had minimal or no impact on physical health, mental functioning, or overall treatment satisfaction. Similarly, in an Italian observational study[30] involving 30 patients treated with tirbanibulin for AKs located on the face and scalp, the highest TSQM-1.4 scores at D57 were observed for convenience (score = 97) and side effects (score = 94), followed by global satisfaction (score = 83) and effectiveness (score = 80).

The impact of treatment on QoL was assessed using Skindex-16.[15,16] Tirbanibulin improved patients' QoL, as indicated by reductions in AK-related symptoms, emotional burden, and functional impact from baseline, consistent with findings from the PROAK study.[11,12] In contrast, studies evaluating health-related QoL using Skindex-17 reported only small improvements after other topical treatments for AK (imiquimod, diclofenac, and 5-FU).[20]

Results obtained from the EPQ survey help to better understand both the patient perspective and clinicians' daily experience. Both patients and clinicians reported similarly high levels of satisfaction with improvements in skin appearance and skin texture following treatment with tirbanibulin. In addition, both groups rated tirbanibulin more favorably than previous treatments in terms of LTS duration and severity, impact on daily activities, and convenience or ease of use, and both reported a willingness to consider tirbanibulin again if needed. These findings are similar to those reported in the PROAK study[11,12] and highlight the importance of short-duration, easy-to-use, effective treatments with favorable safety and tolerability profiles, such as tirbanibulin.

Potential limitations of this study include the absence of a control group, which prevents direct comparisons, and the study duration (12 months), which allows side effects evaluation and short-term but not long-term efficacy.

Conclusions

Our study supports previously published data[8,10,11] regarding the efficacy and safety of tirbanibulin 1% ointment for AKs on the face and scalp. Tirbanibulin improved QoL, and both clinicians and patients agreed on the convenience and effectiveness of this treatment, reporting high overall satisfaction. Although this comparison is indirect, tirbanibulin had a shorter treatment duration, was easier to use, and was associated with milder LTS severity compared with patients' previous treatments. Finally, despite the small number of immunosuppressed patients included (N = 6), this subgroup also benefited from tirbanibulin, showing efficacy and safety profiles comparable to those of immunocompetent patients. Under conditions close to routine clinical practice, these results support tirbanibulin as a valuable therapeutic option among the available treatments for AKs on the face and scalp.

Funding

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Conflicts of interest

YG has provided scientific advice, participated in medical meetings and sponsored training courses, and has served as principal investigator or collaborator in clinical research trials for AbbVie, Almirall, Leo Pharma, Cantabria Labs, Galderma, Isdin, Lilly, Pfizer, Rilastil, La Roche-Posay, and Sanofi.

OY has received consulting honoraria from Almirall, Leo Pharma, Isispharma, BMS, Bioderma-NAOS, and Novartis; and speakers' bureau/advisory board honoraria from Almirall, Leo Pharma, Isdin, Isispharma, BMS, MSD, and Kyowa Kirin.

JC has received research grants from Castle Biosciences and Regeneron; lecture honoraria from Sanofi, Almirall, AbbVie, Regeneron, and Sun Pharma; payments for expert testimony from Sanofi, Regeneron, and Almirall; support for attending meetings from Pfizer, Almirall, and Lilly; and advisory board honoraria from Almirall, Sanofi, Regeneron, Kyowa, Roche, and InflaRx.

CSG has participated as an investigator in clinical research trials for Galderma, Biofrontera, Leo Pharma, Almirall, Pierre Fabre, and Roche; and has provided advice and participated in scientific meetings and training courses for Galderma, Biofrontera, Leo Pharma, Almirall, Pierre Fabre, Roche, Cantabria Labs, and Sun Pharma.

AC has no conflicts of interest to declare.

FP, AL, VC, BK, and LP are employees of Almirall.

MR has received advisory board honoraria from AbbVie, Almirall, Lilly, Sanofi, Novartis, ConvaTec, and Urgo.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.ad.2026.104632.

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