

1% Tirbanibulin Ointment for Actinic Keratoses on Upper Extremities: A Retrospective Case Review Study

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The anatomical distribution of actinic keratoses (AKs) is the result of chronic and prolonged sun exposure, with more than 80% of cases located in the head, neck and upper extremities (1). However, since most drug studies have been performed on the face and scalp, data on treatment of AK in other frequently affected areas, such as the upper extremities, may be under-represented (2). 1% Tirbanibulin ointment has been developed as a first-in-class anti-proliferative and pro-apoptotic agent for the treatment of AKs and has been approved by the European Medicines Agency and the U.S. Food and Drug Administration for usage on face and scalp area (3). Its mechanism of action promotes the eradication of lesions through the inhibition of tubulin polymerization and Src signalling, among others (4). The aim of the current study is to examine the efficacy and safety of 1% tirbanibulin ointment for treating AKs in the upper extremities under daily practice conditions.

MATERIALS AND METHODS

This retrospective case review study was conducted between March and June 2023 at a single centre in Madrid, Spain. Subjects aged 18 years or above with clinically typical non-hyperkeratotic AK lesions (grade I–II according to Olsen's classification) on their upper extremities were included. Patients were excluded if they were pregnant, had a known history of sensitivity to tirbanibulin or vehicle components, or had received another therapy within the study area during the previous 3 months. In all cases, dosage

followed indications from the summary of product characteristics (once daily, 5 consecutive days, covering up to a 25 cm² area). A clinical assessment of target lesions was performed at screening and at 60 days after treatment. The primary outcome was a complete clearance rate, defined as the proportion of subjects with no AKs in the treatment area. Secondary assessments included percentage change of the number of lesions from baseline, partial clearance rate (defined as 75% reduction or more in baseline AK count), adverse events and treatment adherence. χ^2 test was used to analyse the association between the AK grade and complete clearance rate. *p*-values <0.05 were considered statistically significant for this analysis.

Local skin reactions, such as erythema, scaling, swelling, crusting, vesiculation and erosions, were classified according to a 4-point scale of severity (none, mild, moderate, severe) 5–7 days after ending the treatment. Adherence was considered correct if 1% tirbanibulin ointment was applied daily for 5 consecutive days. Demographic data, skin phototype, personal history of skin cancer, and previous treatments for AKs were also collected.

RESULTS

This study reviewed the data on 17 patients with AK, for 22 treatment cycles (14% located on the arms, 41% on the forearms, and the remainder 45% on the dorsum of the hands). The majority of patients included were female (59%) and assigned to skin type II (59%) according to Fitzpatrick. Most of the patients (68%) reported a previous history of skin cancer, with all arising in a different location of the study area and had been diagnosed more than 1 year previously (7 patients with basal cell carcinoma (BCC), 5 with squamous cell carcinoma (SCC), 1 with melanoma and 1 with BCC and SCC). All patients had undergone previous treatments in the same location, most commonly cryotherapy. No recurrent lesions were included. The main demographic characteristics of patients are shown in **Table I**.

Complete clearance occurred in 45% (10 of the 22 patients) of subjects on day 60. The mean percentage change from baseline in the number of AK lesions in the selected treatment area was -86.2 ± 14.5 and partial clearance ($\geq 75\%$) was observed in 18 of the 22 patients (82%) (**Table II**). No difference was found in the efficacy of tirbanibulin in terms of location or AK severity ($p > 0.05$). Regarding treatment adherence, all study participants completed the therapy with 1% tirbanibulin ointment according to the data sheet. Local skin reactions were recorded in 8 patients (36%), while most of these reactions were categorized as mild (7 of the 8, 88%). All

Table I. Patients' demographic data at baseline

Variable	
Age, years, mean \pm SD	73.9 \pm 10.5
Sex, <i>n</i> (%)	
Male	7 (41)
Female	10 (59)
Phototype, <i>n</i> (%)	
I	4 (24)
II	10 (59)
III	3 (17)
Personal history of skin cancer, <i>n</i> (%)	
Basal cell carcinoma	8 (47)
Squamous cell carcinoma	6 (35)
Melanoma	1 (6)
Previous treatments for the same location, <i>n</i> (%)	
Cryotherapy	12 (70)
Diclofenac	3 (18)
Imiquimod	4 (24)
Ingenol mebutate	2 (12)
Photodynamic therapy	6 (35)
5-fluorouracil/10% salicylic acid	4 (24)

SD: standard deviation.

Table II. Data for tirbanibulin 1% ointment for all treatment cycles (n = 22)

Variable	
Location, n(%)	
Dorsal hands	10 (45)
Forearms	9 (41)
Arms	3 (14)
Grade of AKs, n(%)	
I	13 (59)
II	9 (41)
Lesions per area, N; mean ± SD	3.86 ± 1.35
Complete clearance rate, n(%)	10 (45)
Change of the number of lesions from baseline, %, mean ± SD	-86.2 ± 14.5
Partial clearance rate (≥ 75%), n(%)	18 (82)
Adverse events, n(%)	
None	14 (64)
Mild	7 (32)
Moderate	1 (4)
Severe	0 (0)
Treatment adherence, n(%)	
Partial	0 (0)
Complete	22 (100)

SD: standard deviation.

events consisted primarily of erosions, irritation, and pain and were already healed or regressive at the time of the report (median duration: 4 days).

DISCUSSION

AKs generally arise on sun-exposed skin regions and therefore tend to be located on the face, scalp, and extremities (1). Although 1% tirbanibulin ointment has demonstrated a high efficacy in pivotal studies for AKs on the face or scalp, fewer data are available on AK treatment in non-facial areas (4). The phase I study was a proof-of-concept study with a dose-escalating design in which tirbanibulin was efficacious at reducing all AK lesions regardless of dosing on the dorsal forearm (4, 5). The current study extends these results by demonstrating a higher efficacy with confirmed good safety and adherence to treatment when applied on the upper extremities under daily practice conditions. It is important to note that there was approximately a 45% complete clearance of grade I and II AKs in these locations. Moreover, comparable levels were observed for mean percentage change in the AK lesion count $-86.2 \pm 14\%$, as well as partial clearance at day 60 (82%), which are at least in the range of other therapies licensed for AKs (1, 6–12). Efficacy achieved may be considered even higher, especially if we take into account the reduced number of sessions (5 applications) in conjunction with the increased resistance of AKs in this treatment area. Unlike other available therapies, 1% tirbanibulin ointment eliminates both clinically visible and subclinical lesions with no substantial tissue necrosis and/or inflammation, which usually translates into good tolerability and treatment adherence (13). In the current study, the safety profile of AK treatment of the upper extremities with tirbanibulin was better than that which has already been reported for treatment of the approved indication areas of the face and

scalp (4). This can be explained by the fact that skin on the upper extremities has a robust barrier function and a consequent lower tendency to local skin reactions (9). Moreover, patients showed a high degree of treatment adherence (100%), which is unsurprising due to its simple dosing regimen that facilitates patient completion (5, 13).

This study has some limitations. It was developed in a single institution, with a relatively small sample size and retrospectively collected data. Moreover, self-reported information about compliance or adverse events may constitute a potential recall bias.

The results suggest that 1% tirbanibulin ointment is an effective and tolerable option for treating mild to moderate AKs of the upper extremities under daily practice conditions. Further studies are needed in order to optimize the suitable therapeutic strategies for this group of usually difficult-to-treat AKs.

The authors have no conflicts of interest to declare.

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