FAVORABLE SAFETY PROFILE OF TIRBANIBULIN OINTMENT 1% FOR ACTINIC KERATOSIS: POOLED RESULTS FROM TWO PHASE III STUDIES

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SYNOPSIS

- Tirbanibulin is a first-in-class, novel inhibitor of tubulin polymerization and associated with disruption of Src kinase signaling for actinic keratosis (AK).
- No cases of contact sensitization or phototoxicity were observed in two phase I studies (KX01-AK-006/KX01-AK-008).

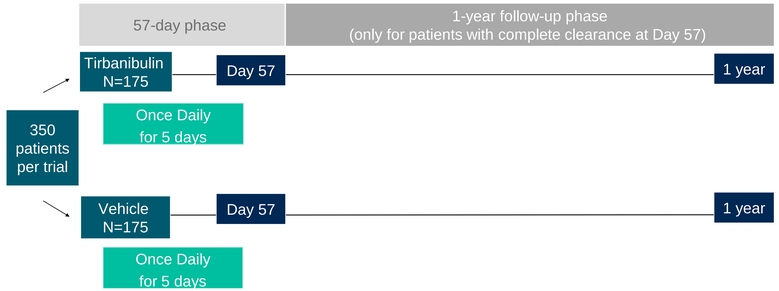
OBJECTIVE

- The objective was to report pooled safety data in adults with AK on the face/scalp from two pivotal phase III randomized, double-blinded, vehicle-controlled, parallel-group studies (KX01-AK-003/KX01-AK-004).

METHODS

- Eligible adult patients with 4-8 clinically visible AK lesions in a 25 cm^2 area were randomized 1:1 to receive tirbanibulin ointment 1% or vehicle (5-day once-daily self-application). The study design is shown in **Figure 1**.
- ITT Population: included all randomized patients. Safety Population included all subjects who received at least one dose of tirbanibulin ointment 1%

Figure 1. Design of both studies



- Safety assessments included local skin reactions (LSRs: erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration; scale of 0-3 [absent-severe]) and adverse events (AEs) up to Day (D) 57.
- Incidence of maximal post-baseline LSR grades greater than baseline was described by treatment and LSR sign. Pooled LSR composite scores (the sum of all 6 LSRs) by visit and treatment were analyzed.

RESULTS

- 702 subjects were included in the pooled safety population (tirbanibulin n=353; vehicle n=349). Treatment compliance was >99%. Demographics were similar between treatment groups; most were Caucasian males, Fitzpatrick skin type II and median of 6 baseline AK lesions. Baseline characteristics are shown in **Table 1**.

Table 1. Baseline characteristics

	Tirbanibulin (N=353)	Vehicle (N=349)
Mean Age (SD), years	69.3 (8.61)	70.2 (9.13)
Gender: Male, n (%)	305 (86)	304 (87)
Race: White, n (%)	352 (>99)	348 (>99)
Fitzpatrick Skin Type, n (%)		
Type I	49 (14)	38 (11)
Type II	200 (57)	224 (64)
Type III	88 (25)	79 (23)
Type IV-VI	16 (5)	8 (2)
Median Baseline AK lesion count (min - max)	6.0 (4 - 8)	6.0 (4 - 8)

AK, actinic keratosis; SD, standard deviation

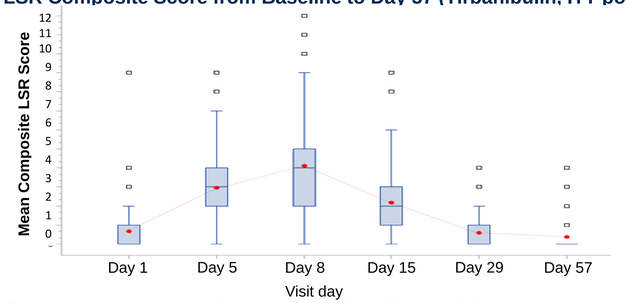
- Treatment-related AEs were few: 16% of tirbanibulin-treated patients and 10% of vehicle-treated patients had ≥1 treatment-related AE (mostly transient mild-to-moderate application-site pain and pruritus that did not require treatment). No deaths, discontinuations, or serious AEs related to tirbanibulin occurred.
- Incidence and severity of LSRs greater than baseline were higher with tirbanibulin vs. vehicle (**Table 2**):
  - For tirbanibulin, the most commonly occurring LSRs were mild to moderate erythema (22% and 63%) and flaking/scaling (26% and 47%), followed by mild crusting (30%) and mild swelling (29%).

Table 2. Maximal post-baseline LSRs by severity (Safety Population)

	Safety population (n=702)	
n (%)	**Tirbanibulin (n=353)**	**Vehicle (n=349)**
Erythema		
Mild	76 (22)	98 (28)
Moderate	223 (63)	20 (6)
Severe	22 (6)	0
Flaking/scaling		
Mild	92 (26)	86 (25)
Moderate	166 (47)	33 (9)
Severe	31 (9)	1 (<1)
Crusting		
Mild	107 (30)	31 (9)
Moderate	50 (14)	8 (2)
Severe	7 (2)	0
Swelling		
Mild	102 (29)	15 (4)
Moderate	32 (9)	1 (<1)
Severe	2 (<1)	0
Vesicles/pustules		
Mild	25 (7)	3 (<1)
Moderate	2 (<1)	0
Severe	2 (<1)	0
Erosions/ulcers		
Mild	32 (9)	10 (3)
Moderate	9 (3)	0
Severe	0	0

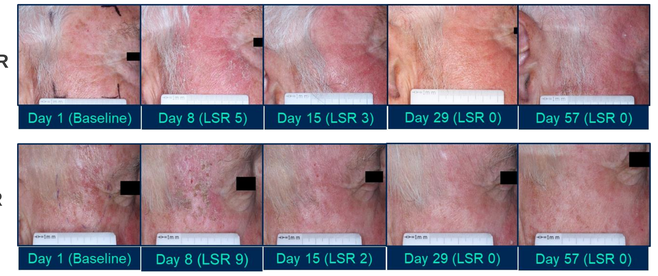
- Regarding composite LSR scores, LSR peaked on D8 with tirbanibulin with a maximum mean composite LSR score of 4.1, decreased significantly by D15, and resolved by D29-D57. By D29 and D57, mean composite LSR scores were similar between tirbanibulin (0.6 and 0.4, respectively) and vehicle groups (0.6 and 0.5) (**Figure 2 and Figure 3**).
- No significant difference was observed in mean composite LSR score in patients less and above 65 year old (maximum mean LSR: 4)

Figure 2. LSR Composite Score from Baseline to Day 57 (Tirbanibulin, ITT population)



The length of the box represents the interquartile range (the distance between the 25th and 75th percentiles). The symbol in the box interior represents the group mean. The horizontal line in the box interior represents the group median.

Figure 3. Evolution of moderate and severe LSR from baseline to Day 57



- There were no differences in treatment-related AEs according to age, gender, and baseline AK lesions. Overall incidence of treatment-related AEs was slightly higher for face (17% and 11%) than scalp subjects (13% and 7%) in the tirbanibulin and vehicle groups, respectively (**Table 3**).

Table 3. Treatment-Related Adverse Events Up to Day 57 of Incidence ≥2% by Treatment Location Subgroups (face/scalp)

	Safety population (n=702)			
n (%)	**Tirbanibulin (n=353)**		**Vehicle (n=349)**	
	Face	**Scalp**	**Face**	**Scalp**
Number of subjects with any treatment-related AEs	41 (17)	15 (13)	27 (11)	8 (7)
Application site pain	26 (11)	9 (8)	9 (4)	2 (2)
Application site pruritus	23 (10)	9 (8)	18 (8)	3 (3)

CONCLUSIONS

- Pooled data from phase III studies showed a favorable safety and tolerability profile of tirbanibulin ointment 1% once daily for 5 consecutive days in the treatment of AK on the face or scalp.

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