TIRBANIBULIN OINTMENT 1%, A NOVEL INHIBITOR OF TUBULIN POLYMERIZATION AND SRC KINASE SIGNALING, FOR THE TREATMENT OF ACTINIC KERATOSIS (AK): RESULTS FROM TWO PIVOTAL PHASE III STUDIES

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SYNOPSIS

- Actinic keratosis (AK) are precancerous lesions that if left untreated may lead to invasive squamous cell carcinoma[1]
- Tirbanibulin (KX2-391, KX01) is a synthetic, highly selective, novel inhibitor of tubulin polymerization and Src kinase signaling developed as a first-in-class topical formulation for the treatment for AK[2]
- Previous Phase I and II studies demonstrated that tirbanibulin ointment 1% was active against AK lesions on the forearm and face or scalp, respectively. Local skin reactions (LSRs) were mostly transient and mild-to-moderate in severity, and tirbanibulin was well tolerated[3,4]
- This poster presents results from two Phase III, double-blinded, vehicle-controlled, randomized, parallel-group, multicenter studies (KX01-AK-003 [NCT03285477]; KX01-AK-004 [NCT03285490]) that evaluated the efficacy and safety of tirbanibulin versus vehicle in adults with AK lesions on the face or scalp

OBJECTIVE

- To assess the efficacy and safety of tirbanibulin compared with vehicle in participants with AK lesions on the face or scalp

METHODS

- Adult participants with 4–8 typical, visible AK lesions in a 25 cm^2 treatment area on the face or scalp were enrolled (2:1) in the study
- Participants were randomized to receive either tirbanibulin ointment 1% or vehicle (1:1); treatment was self-applied once-daily for 5 consecutive days and left in place for ~12 hours
- The primary efficacy endpoint was complete (100%) clearance of AK lesions at Day 57
- Partial (≥75% reduction of AK lesions) clearance was a secondary efficacy endpoint
- Safety assessments included adverse events (AEs) and monitoring of LSRs including erythema, flaking/scaling, crusting, swelling, vesicles/pustules, and erosions/ulcers as graded on a 4-point scale (0 [absent] to 3 [severe]); composite LSR score was the sum of all six LSR grades (possible range: 0–18)

RESULTS

Study participants

- Overall 702 participants were enrolled from 62 study sites in the US (n=351 from 31 sites per study where each site participated in only one study); over 99% of participants were treatment compliant
- Demographics and baseline characteristics were similar between treatment groups; most participants were White males (mean age, 70 years) and had a Fitzpatrick Skin Type of I–II (**Table 1**)
- The Intent-to-Treat and Safety Population were the same for both studies and included all randomized participants who were dosed. Participants who discontinued early were considered non-responders

Table 1. Demographics and baseline characteristics (ITT population)

	KX01-AK-003 (n=351)		KX01-AK-004 (n=351)	
	Tirbanibulin (n=175)	Vehicle (n=176)	Tirbanibulin (n=178)	Vehicle (n=173)
Mean age, years	69.5	70.2	69.1	70.2
Male, n (%)	147 (84)	154 (88)	158 (89)	150 (87)
White, n (%)	175 (100)	175 (99)	177 (99)	173 (100)
Fitzpatrick Skin Type I-II, n (%)	123 (70)	142 (81)	126 (71)	120 (69)
Median baseline AK lesion count	6	6	6	6
Treatment area face:scalp ratio	119:56	121:55	119:59	118:55

AK actinic keratosis; ITT, intent-to-treat

Efficacy

- Complete (100%) and partial (≥75%) clearance rates were significantly higher in participants administered tirbanibulin compared with vehicle in both studies (p<0.0001) (**Table 2**)
  - KX01-AK-003: 44% vs 5% (complete clearance); 68% vs 16% (partial clearance), respectively
  - KX01-AK-004: 54% vs 13% (complete clearance); 76% vs 20% (partial clearance), respectively
- Significantly higher complete and partial clearance rates for tirbanibulin compared with vehicle were also demonstrated in subgroup analyses for age, baseline AK lesion count, gender, skin type, and treatment location (face or scalp) in both studies (p<0.001)

Table 2. Complete (100%) and partial (≥75%) clearance rates of AK lesions (ITT population)

	KX01-AK-003 (n=351)			KX01-AK-004 (n=351)		
	Tirbanibulin (n=175)	Vehicle (n=176)	p-value	Tirbanibulin (n=178)	Vehicle (n=173)	p-value
100% clearance, n (%)	77 (44%)	8 (5%)	<0.0001	97 (54%)	22 (13%)	<0.0001
Face	50%	6%	<0.0001	61%	14%	<0.0001
Scalp	30%	2%	<0.0001	41%	11%	0.0003
≥75% clearance, n (%)	119 (68%)	29 (16%)	<0.0001	136 (76%)	34 (20%)	<0.0001
Subgroup analysis						
Age						
<65 years old	45%	2%	<0.0001	63%	10%	<0.0001
≥65 years old	44%	5%	<0.0001	51%	13%	<0.0001
Gender						
Female	61%	14%	0.0007	85%	13%	<0.0001
Male	41%	3%	<0.0001	51%	13%	<0.0001
Baseline AK lesion count						
4–6 AK lesions	49%	6%	<0.0001	61%	13%	<0.0001
7–8 AK lesions	31%	2%	<0.0001	42%	11%	0.0002
Fitzpatrick Skin Type						
I or II	45%	5%	<0.0001	54%	13%	<0.0001
III, IV, V, or VI	42%	3%	<0.0001	56%	13%	<0.0001

AK actinic keratosis; ITT, intent-to-treat

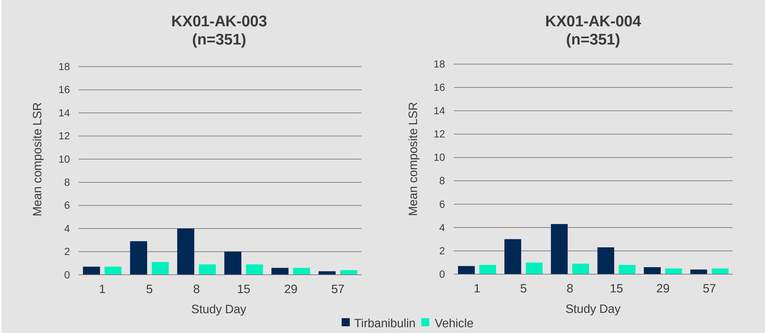
Safety

- Treatment-related treatment-emergent AEs (TEAEs) were reported in 56 participants receiving tirbanibulin (KX01-AK-003, n=20 [11%]; KX02-AK-004, n=36 [20%]) and 35 participants treated with vehicle (KX01-AK-003, n=16 [9%]; KX02-AK-004, n=19 [11%])
  - Most treatment-related TEAEs were mild-to-moderate, transient application site pruritus or pain that did not require treatment
- Two tirbanibulin-treated participants did not complete treatment for reasons unrelated to study drug but remained in the study
- In the vehicle-treated group, two participants discontinued early from the study for reasons unrelated to treatment
- No discontinuations or serious AEs related to tirbanibulin were reported
- No ocular exposure led to ocular AEs, and there were no clinically significant abnormal electrocardiograms, laboratory findings, physical examinations, or vital signs

Local skin reaction assessments

- LSRs were mostly mild-to-moderate erythema and flaking/scaling
- Mean composite LSR scores were low for tirbanibulin, peaked on Day 8 and were resolved by Day 29 (**Figure 1**)
- The most common maximal post-baseline severe (Grade 3) LSRs were erythema and flaking/scaling (**Table 3**)

Figure 1. Mean composite LSR scores (Safety Population)



LSRs were graded on a 4-point scale (0=absent; 1=mild [slightly or barely perceptible]; 2=moderate [distinct presence]; 3=severe [marked/intense]). Composite LSR score is the sum of all six LSR (erythema, flaking/scaling, crusting, swelling, vesicles/pustules, erosions/ulcers) grades with a possible range of 0–18
LSR, local skin reaction

Table 3. Maximal post-baseline severe (Grade 3) LSRs (Safety Population)

	KX01-AK-003 (n=351)		KX01-AK-004 (n=351)	
n (%)	Tirbanibulin (n=175)	Vehicle (n=176)	Tirbanibulin (n=178)	Vehicle (n=173)
Erythema	5 (3)	0	17 (10)	0
Flaking/scaling	11 (6)	0	20 (11)	1 (<1)
Crusting	2 (1)	0	5 (3)	0
Swelling	1 (<1)	0	1 (<1)	0
Vesicles/pustules	1 (<1)	0	1 (<1)	0
Erosions/ulcers	0	0	0	0

LSRs, local skin reactions

CONCLUSIONS

- Tirbanibulin ointment 1% once-daily for 5 days resulted in higher overall complete AK clearance rates at Day 57 than vehicle in two Phase III studies (KX01-AK-003: 44% vs 5%; KX01-AK-04: 54% vs 13%, respectively; p<0.0001)
- Statistically significant differences were demonstrated in all subgroups analyzed for the face and scalp
- Most treatment-related TEAEs were mild-to-moderate, transient application site pruritus, or pain that did not require treatment
- Mean composite LSR scores were low and peaked at Day 8 before resolving by Day 29
- Over 99% of participants completed the full 5-day self-application of tirbanibulin

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DISCLOSURES

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