TIRBANIBULIN OINTMENT 1% FOR ACTINIC KERATOSIS (AK): POOLED DATA FROM TWO PHASE 3 STUDIES

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SYNOPSIS

- Tirbanibulin is a novel inhibitor of tubulin polymerization, also associated with disruption of Src kinase signaling, developed as a topical formulation for AK. We have previously shown that 5 days of tirbanibulin ointment is safe and superior to vehicle in AK clearance at 2 months post-treatment in two Phase 3 studies (FCD 2019).

OBJECTIVE

- Here we present pooled data analyses on efficacy, safety and 1-year follow-up.

METHODS

- Two identical Phase 3 randomized, double-blinded, vehicle-controlled studies evaluated efficacy and safety of tirbanibulin ointment 1% vs. vehicle in adults with AK on face/scalp.
- Eligible subjects with 4–8 clinically visible AK lesions in a 25 cm^2 area were randomized 1:1 to receive tirbanibulin or vehicle (5-day once-daily self-application).
- Primary and secondary endpoints were complete (100%) and partial (≥75%) clearance of AK lesions at Day (D) 57.
- Safety including adverse events (AEs) and local skin reactions (LSRs; Grade 0[none]-3[severe]) was assessed up to D57. Composite LSR scores represents the grades sum of all 6 LSR categories with a possible range from 0 to 18.
- Subjects with complete AK clearance at D57 were followed for 1-year to assess safety and clearance durability.

RESULTS

- Eligible subjects, predominantly Caucasian males with mean age of 70, skin type I-II and had median of 6 AK in the treatment area, were randomized to receive tirbanibulin (n=353) or vehicle ointment (n=349). Over 99% completed treatment. Baseline characteristics are shown in **Table 1**.

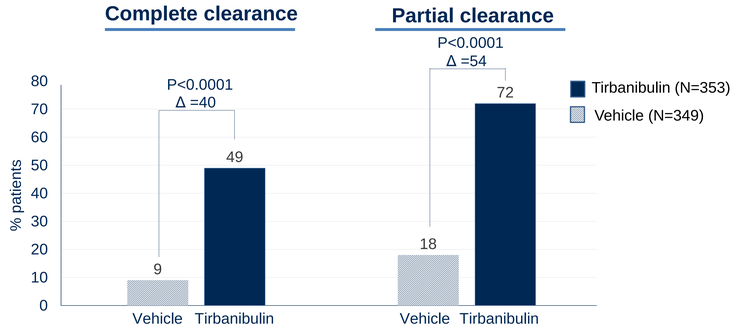
Table 1. Baseline characteristics

	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	15 (4)	7 (2)
Type V	0	1 (<1)
Type VI	1 (<1)	0
Median Baseline AK lesion count (min - max)	6.0 (4 - 8)	6.0 (4 - 8)

AK, actinic keratosis; SD, standard deviation

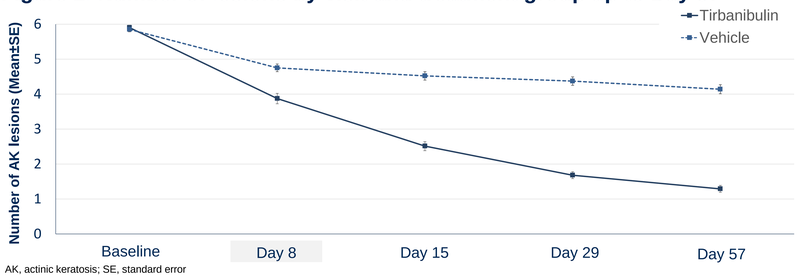
- At D57, complete clearance rates were significantly higher with tirbanibulin vs. vehicle, 49% vs. 9% (P<0.0001); partial clearance rates were 72% vs.18%, respectively (P<0.0001) (**Figure 1**). Median reduction in AK lesion count at D57 was greater with tirbanibulin vs. vehicle (87.5% vs. 20%).

Figure 1. Complete and partial clearance rates of AK lesions (ITT population)



- AK lesion count to Day 57 is shown in **Figure 2**. Reduction in AK lesion count to Day 57 was significantly greater than vehicle for all post-Baseline visits until Day 57 (**Table 2**).

Figure 2. Number of lesions by visit and treatment group up to Day 57



AK, actinic keratosis; SE, standard error

Table 2. Summary of AK Lesion Counts Up to Day 57

		Tirbanibulin (n=353)	Vehicle (n=349)
Baseline	Mean (±SE)	5.90 (0.07)	5.85 (0.07)
Day 8	Mean (±SE)	3.87 (0.15)	4.75 (0.11)
	Change from baseline, mean (%)	-2.05 (-35%)	-1.10 (-19%)
	p-value	<0.0001	
Day 15	Mean (±SE)	2.51 (0.13)	4.52 (0.12)
	Change from baseline	-3.38 (-58%)	-1.33 (-24%)
	p-value	<0.0001	
Day 29	Mean (±SE)	1.68 (0.10)	4.37 (0.12)
	Change from baseline	-4.23 (-72%)	-1.48 (-26%)
	p-value	<0.0001	
Day 57	Mean (±SE)	1.29 (0.10)	4.14 (0.13)
	Change from baseline	-4.61 (-79%)	-1.72 (-31%)
	p-value	<0.0001	

AK, actinic keratosis; SE, standard error

- At 1-year post-D57 follow-up, Kaplan-Meier estimate of proportion of tirbanibulin-treated patients (n=174) with at least one recurrent lesion present at baseline in the treated area recurring during follow-up was 47% and estimated rate of subjects with any AK lesion (recurred or new) was 73% (**Figure 3**). A total of 27% of patients had sustained AK clearance at 1-year.

Figure 3. Proportion of patients with any recurrence by number of lesions at baseline

- Treatment-related AEs were few and mostly mild transient application-site pruritus (tirbanibulin vs. vehicle: 9% vs 6%) and pain (tirbanibulin vs vehicle: 10% vs 3%) (**Table 3**).

Table 3. Treatment-Related Adverse Events Up to Day 57 (Safety Population)

	Safety population (n=702)	
n (%)	**Tirbanibulin (n=353)**	**Vehicle (n=349)**
Number of subjects with any treatment-related AEs	56 (16%)	35 (10%)
Application site pain	35 (10%)	11 (3%)
Application site pruritus	32 (9%)	21 (6%)

- LSR signs were present at baseline, increased after treatment, peaked on D8 with tirbanibulin, decreased significantly by D15, and mostly resolved by D29.
- Maximum mean±SD composite LSR scores were 4.1±2.32 and 1.0±1.14 for tirbanibulin and vehicle group, respectively.
- LSRs were mostly transient mild or moderate erythema and flaking/scaling. Severe LSRs were few. All LSRs resolved or returned to baseline and did not require intervention.
- No deaths, discontinuations, or serious AEs related to tirbanibulin occurred.
- No treatment-related AEs throughout 1-year follow-up were reported.

CONCLUSIONS

- Tirbanibulin ointment 1% applied for 5 days was well tolerated, safe and effective, potentially making it a valuable new addition to AK treatment.

ACKNOWLEDGEMENTS

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