IMPACT OF PRIOR TREATMENT IN THE EFFICACY AND TOLERABILITY OF TIRBANIBULIN OINTMENT 1% FOR ACTINIC KERATOSIS: POOLED RESULTS FROM TWO PHASE 3 STUDIES

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SYNOPSIS

- Tirbanibulin was evaluated as a field treatment for actinic keratosis (AK) of face or scalp in two Phase 3, randomized, double-blind, vehicle-controlled studies (NCT03285477, NCT03285490)[1].
- Pooled data showed complete (100%) clearance (CC) and partial (≥75%) clearance (PC) rates of 49% and 72% for tirbanibulin-treated versus 9% and 18% for vehicle-treated participants, respectively
- Local skin reactions (LSR) were mostly mild-to-moderate, the mean±standard deviation (SD) maximum LSR severity composite score being 4.4±2.2 for tirbanibulin-treated and 1.6±1.4 for vehicle-treated participants.

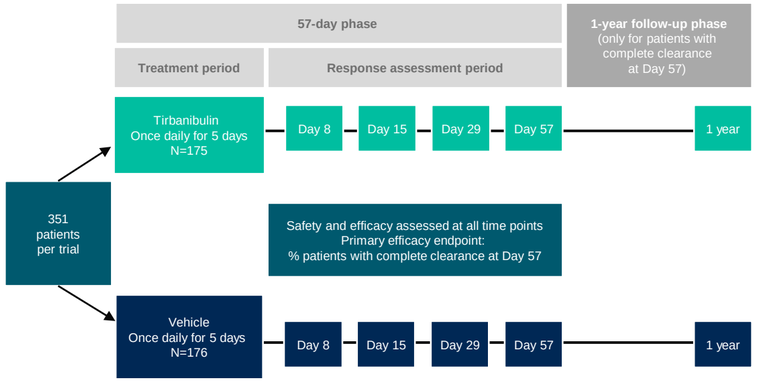
OBJECTIVE

- This *post-hoc* analysis of the pooled Phase 3 data assessed efficacy and tolerability according to prior AK treatment in the treatment area.

METHODS

- In the Phase 3 trials, patients with 4-8 clinically visible AK lesions in a 25 cm^2 area were randomized 1:1 to tirbanibulin ointment 1% or vehicle (once-daily, 5 consecutive days, self-application). The study design is shown in **Figure 1**.

Figure 1. Design of Phase 3 studies



- Count of clinically visible AK lesions (lesion count) was performed for all patients at different time points.
- In each of the safety evaluations performed from baseline to D57, LSR (i.e., erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosions/ulceration) were graded 0-3 (absent-severe). An LSR composite score (sum of scores) was calculated for each participant visit (range 0-18), and maximum composite scores were averaged for the study period.
- For the current analysis, participants were considered pretreated if receiving prior treatment in the same area as tirbanibulin/vehicle.

RESULTS

- Pretreated participants were 130/353 (37%) of those randomized to tirbanibulin and 141/349 (40%) of those randomized to vehicle.
- Of tirbanibulin-pretreated participants, 91/130 (70%) had received cryosurgery and 45/130 (35%) topicals in the same treatment area (22 in each group had received both).
- There were no major differences in the baseline characteristics between pretreated and non-pretreated participants. Baseline characteristics are shown in **Table 1**.

Table 1. Baseline characteristics

	Tirbaninulin (N=353)		Vehicle (N=349)	
	Pretreated (N=130)	Non-pretreated (N=223)	Pretreated (N=141)	Non-pretreated (N=208)
Age (years), mean (SD)	69.8 (9.1)	69.1 (8.3)	70.7 (9.1)	69.9 (9.1)
Male, n (%)	112 (86.2)	193 (86.5)	124 (87.9)	180 (86.5)
BMI (kg/m^2), mean (SD)	28.4 (4.9)	29.1 (5.2)	28.7 (4.9)	28.1 (4.6)
Fitzpatrick skin type, n (%)				
Type I	10 (7.7)	39 (17.5)	13 (9.2)	25 (12.0)
Type II	80 (61.5)	120 (53.8)	94 (66.7)	130 (62.5)
Type III	35 (26.9)	53 (23.8)	31 (22.0)	48 (23.1)
Type IV-VI	5 (3.8)	11 (4.9)	3 (2.1)	5 (2.4)
AK lesion count, median (min-max)	6.0 (4.0-8.0)	6.0 (4.0-8.0)	6.0 (4.0-8.0)	6.0 (4.0, 8.0)

AK, actinic keratosis; BMI, body mass index; max; maximum; min, minimum; SD, standard deviation.

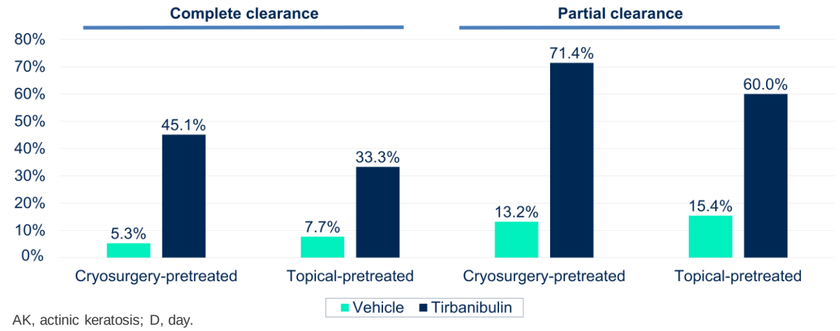
- Median (minimum-maximum) time since previous treatment was available in a subset of patients, being 23.7 (1.0-157.8) and 22.7 (0.2-157.8) months in cryosurgery-pretreated and topical-pretreated participants receiving tirbanibulin, respectively (**Table 2**).
- Tirbanibulin treatment resulted in CC in 45.1% of cryosurgery-pretreated and in 33.3% of topical-pretreated participants (**Figure 2**).
- Moreover, PC was achieved by 71.4% of cryosurgery-pretreated and by 60.0% of topical-pretreated participants receiving tirbanibulin (**Figure 2**).
- Maximum mean LSR composite scores were similar between pretreated and non-pretreated participants in both tirbanibulin and vehicle groups; and between cryosurgery- and topical-pretreated participants in the tirbanibulin and vehicle groups (**Table 3**).

Table 2. Time (months) since previous treatment

		No complete clearance	Complete clearance	Overall
Cryosurgery-pretreated	**n**	26	23	49
	Mean (SD)	31.4 (32.6)	24.2 (21.7)	28.0 (28.0)
	Median (min-max)	26.7 (1.9-157.8)	20.7 (1.0-65.5)	23.7 (1.0-157.8)
Topical-pretreated	**n**	12	7	19
	Mean (SD)	33.0 (41.4)	14.0 (12.7)	26.0 (34.5)
	Median (min-max)	25.0 (2.3-157.8)	14.6 (0.2-35.2)	22.7 (0.2-157.8)

Time since previous treatment was only available in a subset of patients. Max, maximum; min, minimum; SD, standard deviation.

Figure 2. Complete and partial clearance rates of AK lesions at D57



AK, actinic keratosis; D, day.

Table 3. Highest mean LSR composite score from Baseline to D57

Population	Tirbanibulin	Vehicle
Overall pretreated (t=130/v=141)	4.1 ± 2.0	1.7 ± 1.5
Cryosurgery-pretreated (t=91/v=114)	4.1 ± 1.9	1.8 ± 1.5
Topical-pretreated (t=45/v=39)	3.9 ± 1.8	1.8 ± 1.9
Non-pretreated (t=223/v=208)	4.6 ± 2.3	1.5 ± 1.4

Mean ± standard deviation. Twenty-two patients had prior treatment with cryosurgery and topicals. These are included in both cryosurgery- and topical-pretreated categories. D, day; LSR, local skin reactions; t, tirbanibulin; v, vehicle.

CONCLUSIONS

- Compared to pooled Phase 3 trials, in this *post-hoc* analysis the efficacy of tirbanibulin in pretreated areas was similar, and there were no differences in tolerability in terms of LSR.
- Although sample sizes were limited and statistical significance was not tested, results show that tirbanibulin has a favorable safety/efficacy profile to be used either as first-line or after other treatments, and warrant further research on the most suitable treatment sequence in individuals with AK.

REFERENCES

1) Blauvelt A et al. New Engl J Med 2021;384:512-20.

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CONFLICTS OF INTEREST

TS has served as a consultant/speaker with honorarium, advisor and/or investigator for Almirall, Biofrontera, Galderma, Leo, Ortho and Sun Pharmaceuticals; **NB** has served as a consultant with honorarium and investigator for Almirall, Biofrontera, Leo, Ortho, and SunPharma; **BB** has served as a consultant, speaker, and/or investigator for Almirall, Biofrontera, LEO and Pierre-Fabre, and also participated in the US Biofrontera PDT Advisory Council; **AG**, **LP** and **FH** are employees of Almirall; **DC** is an employee of Athenex; **ML** is an employee of Mount Sinai and receives research funds from: Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant Sciences, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc., and is a consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis, Inc., Aristea Therapeutics, Arrive Technologies, Avotres Therapeutics, BiomX, Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Dr. Reddy's Laboratories, Evelo Biosciences, Evommune, Inc., Facilitatation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Helsinn Therapeutics, Hexima Ltd., LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, and Verrica.