COMPLETE CLEARANCE OF ACTINIC KERATOSIS WITH TIRBANIBULIN OINTMENT 1% IS NOT CORRELATED WITH THE SEVERITY OF LOCAL SKIN REACTIONS

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SYNOPSIS

- Tirbanibulin is a synthetic inhibitor of tubulin polymerization and Src kinase signaling. Tirbanibulin ointment 1% has been approved by the FDA (2020) for the treatment of actinic keratosis (AK) on the face or scalp.

OBJECTIVE

- The objective of this *post-hoc* pooled analysis of the two Phase 3 studies is to describe the tolerability profile of tirbanibulin ointment 1% in adults with AK on face or scalp who achieved complete (100%) clearance (CC) in the treatment area (two phase 3 randomized, double-blinded, vehicle-controlled studies: NCT03285477 - NCT03285490)

METHODS

- Patients with 4-8 clinically visible AK lesions in a 25 cm^2 area were randomized 1:1 to tirbanibulin ointment 1% or vehicle (5 consecutive day, once-daily self-application).
- For the current analysis, data of local skin reactions (LSR) up to Day (D) 57 (i.e.: erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration) in patients achieving CC (100%) with tirbanibulin were analyzed. LSRs were graded 0-3 (absent-severe).
- The distribution of highest LSR grades from baseline to D57 was described by LSR.
- An LSR composite score (sum of all 6 LSRs) was also calculated for each participant visit (range 0-18), and maximum composite scores were averaged for the study period.

RESULTS

- Of the 353 patients randomized to tirbanibulin (intention-to-treat, ITT) in the Phase 3 trials, 174 (49.3%) had CC in the treatment area. Baseline characteristics are shown in **Table 1**. There were no major differences between ITT and patients achieving CC, except for a lower percentage of males among the latter.

Table 1. Baseline characteristics

	With CC (N=174)	ITT (N=353)
Mean (SD) age, years	68.5 (8.7)	69.3 (8.6)
Male, n (%)	140 (80.5)	305 (86.4)
BMI (kg/m²), mean (SD)	29.0 (5.8)	28.8 (5.1)
Fitzpatrick skin type, n (%)		
Type I	25 (14.4)	49 (13.9)
Type II	98 (56.3)	200 (56.7)
Type III	43 (24.7)	88 (24.9)
Type IV-VI	8 (4.6)	16 (4.5)
AK lesion count, median (min-max)	5.0 (4-8)	6.0 (4-8)

AK, actinic keratosis; BMI, body mass index; CC, complete clearance; ITT, intention-to-treat; Max, maximum; Min, minimum; SD, standard deviation.

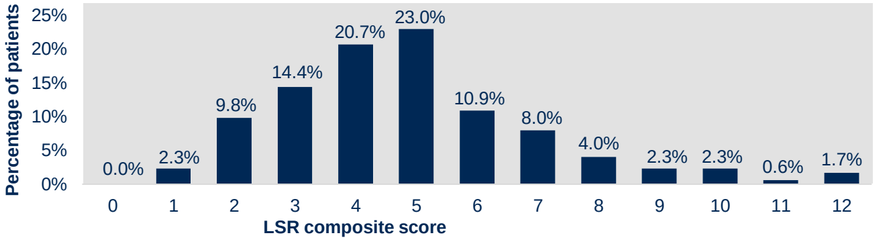
- The highest mean (SD) composite LSR score from baseline to D57 was 4.9 (2.2) for CC patients, on a scale from 0 to 18, with 70% of patients presenting LSRs score of 5 or less. Composite LSR score was ≤3 in 26.5% and ≤5 in 70.2% of CC patients (**Figure 2**). **Figure 3** illustrates the evolution of AK lesions in a patient with CC and a maximum LSR composite score of 4.
- In patients with CC, most LSRs were mild or moderate. Severe reactions were reported by 0.0%-10.9% in the overall CC population and in none of the patients with LSR≤3 (**Table 2**). No patients discontinued the study due to LSRs.

Table 2. Highest grade of LSRs from Baseline to D57 by severity among patients who achieved CC (Safety population)

	Patients with CC	
n (%)	**LSR ≤3 (N=46)**	**Overall (N=174)**
Erythema		
Mild	24 (52.2)	30 (17.2)
Moderate	22 (47.8)	128 (73.6)
Severe	0 (0.0)	16 (9.2)
Flaking/scaling		
Mild	31 (67.4)	47 (27.0)
Moderate	8 (17.4)	100 (57.5)
Severe	0 (0.0)	19 (10.9)
Crusting		
Mild	6 (13.0)	57 (32.8)
Moderate	0 (0.0)	32 (18.4)
Severe	0 (0.0)	6 (3.4)
Swelling		
Mild	4 (8.7)	51 (29.3)
Moderate	0 (0.0)	18 (10.3)
Severe	0 (0.0)	2 (1.1)
Vesicles/pustules		
Mild	0 (0.0)	11 (6.3)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.6)
Erosions/ulcers		
Mild	0 (0.0)	15 (8.6)
Moderate	0 (0.0)	4 (2.3)
Severe	0 (0.0)	0 (0.0)

CC, complete clearance; D, day; LSR, local skin reactions.

Figure 2. Distribution of LSR composite scores from Baseline to D57 among patients achieving CC



LSR composite scores range from 0 (no reaction) to 18 (maximum reaction). No patients presented a highest composite score in the more severe range of 13-18. CC, complete clearance; D, day; ITT, intention-to-treat; LSR, local skin reaction.

CONCLUSIONS

- This *post-hoc* analysis shows that CC of AK using tirbanibulin 1% ointment is associated with mild to moderate LSRs, with 70.2% of patients showing a composite LSR score ≤5. Moreover, tirbanibulin ointment 1% showed a good efficacy/tolerability profile for most patients, being a good alternative to current treatments.

REFERENCES

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

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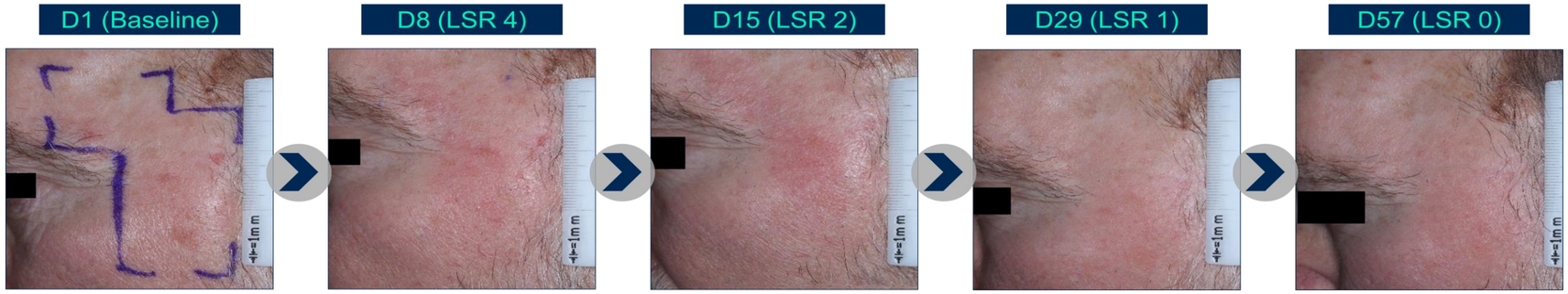
CONFLICTS OF INTEREST

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; **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; **AG**, **LP**, **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.

Figure 3. Evolution of facial AK lesions in a patient achieving CC with tirbanibulin at D29



The patient was a white (Fitzpatrick II), 67 year-old male. Previous dermatological conditions included facial reconstruction (1982), AK (September 2016). LSRs: D1 none; D8 flaking/scaling moderate, erythema moderate; D15 erythema moderate; D29 erythema mild; D57 none. AK, actinic keratosis; CC, complete clearance; D, day; LSR, local skin reaction.