# EFFICACY OF TIRBANIBULIN OINTMENT 1% ACROSS DIFFERENT PATIENT POPULATIONS: POOLED RESULTS FROM TWO PHASE 3 STUDIES

**Brian Berman[1], Adrià Gual[2], Ayman Grada[3], Emilio Fumero[4], Laura Padullés[5], Francisco Hernández[4]**

[1] Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Florida, USA; [2] Hospital Quiron Salud, Barcelona, Spain; [3] Almirall, Malvern, PA, USA; [4] Almirall, Sant Feliu de Llobregat, Spain; [5] Almirall, Barcelona, Spain

## SYNOPSIS

- Tirbanibulin 1% ointment is indicated for the topical treatment of actinic keratosis (AK) of face or scalp based on the results of two Phase 3 studies[1].

## OBJECTIVE

- This *post-hoc* analysis aimed at assessing the efficacy of tirbanibulin in different patient subgroups by body mass index (BMI), Fitzpatrick skin type and previous AK treatment.

## METHODS

- Post-hoc pooled analysis from two identical Phase III, randomized, double-blinded, vehicle-controlled studies in adults with AK on the face or scalp. Eligible subjects 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 self-application for 5 consecutive days).
- The primary efficacy and key secondary endpoints were complete clearance (CC, 100% reduction from baseline) and partial clearance (PC, ≥75%) rates of AK lesions at Day 57. Logistic regression models to find independent predictors of CC and PC of AK lesions among tirbanibulin-treated patients were built.
- Safety was also assessed, including adverse events (AEs) and local skin reactions (LSRs: erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration; 4-point grading scale: 0 [absent] to 3 [severe]).

## RESULTS

- Eligible subjects were randomized to tirbanibulin (n=353) or vehicle (n=349). Over 99% of subjects completed treatment. Baseline characteristics are shown in **Table 1**.

### Table 1. Baseline characteristics

| | Tirbanibulin (n=353) | Vehicle (n=349) |
|---|---|---|
| **Age (years), mean (SD)** | 69.3 (8.6) | 70.2 (9.1) |
| **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) |
| **AK lesion count, median (min - max)** | 6.0 (4 - 8) | 6.0 (4 - 8) |

AK, actinic keratosis; SD, standard deviation.

- At Day 57, CC rates were significantly higher with tirbanibulin vs. vehicle (49.3% vs. 8.6%, p<0.0001), as were PC rates (72.2% vs. 18.1%, p<0.0001). Median percent reduction in AK lesion count at Day 57 was greater with tirbanibulin vs. vehicle (87.5% vs. 20.0%).
- At Day 57, CC/PC/median percent reduction were significantly higher for tirbanibulin vs. vehicle in the face (55.9% vs. 9.6% / 77.7% vs. 20.5% / 100% vs. 25.0%, p<0.0001 for all) and the scalp (35.7% vs. 6.4% / 60.9% vs. 12.7% / 83.3% vs. 18.3%, p<0.0001 for all).
- Logistic regression showed 2.1-fold greater odds of either CC or PC at Day 57 for face location vs. scalp. Odds of CC at Day 57 was 28% lower for every 1-lesion increase in number of baseline lesions (**Table 2**). **Figure 1** illustrates the evolution of Olsen 1-2 facial AK lesions in two patients who achieved CC with tirbanibulin**.**
- There was no significant relationship between baseline variables such as previous AK treatment (**Table 3**), as well as Fitzpatrick skin type (**Table 4**) or BMI ($kg/m^2$) (**Table 5**) and clearance rates at Day 57.

### Table 2. Logistic regression model at Day 57 (ITT population)

| Clearance | Factors | p-value | OR Estimate (95%CI) |
|---|---|---|---|
| **Complete** | Number of Baseline AK Lesions | 0.0003 | 0.723 (0.608 – 0.861) |
| | Treatment Area Location: Face | 0.0020 | 2.093 (1.310 – 3.347) |
| **Partial** | Age | 0.0232 | 0.968 (0.940– 0.996) |
| | Treatment Area Location: Face | 0.0030 | 2.099 (1.287– 3.422) |

CI, confidence interval; OR, odds ratio; ITT, intention to treat.

### Table 3. Clearance rates at Day 57 by previous AK treatment (ITT population)

| Previous AK treatment | Complete clearance | | Partial clearance | |
|---|---|---|---|---|
| | Yes (n=174) | No (n=179) | Yes (n=255) | No (n=98) |
| **No, n (%)** | 116 (52.02%) | 107 (47.98%) | 169 (75.78%) | 54 (24.22%) |
| **Yes, n (%)** | 58 (44.62%) | 72 (55.38%) | 86 (66.15%) | 44 (33.85%) |
| **p-value Chi-square** | 0.1797 | | 0.0513 | |

AK, actinic keratosis; ITT, intention to treat.

### Table 4. Clearance rates at Day 57 by Fitzpatrick skin type (ITT population)

| Fitzpatrick Skin Type | Complete clearance | | Partial clearance | |
|---|---|---|---|---|
| | Yes (n=174) | No (n=179) | Yes (n=255) | No (n=98) |
| **Type I, n (%)** | 25 (51.02%) | 24 (48.98%) | 35 (71.43%) | 14 (28.57%) |
| **Type II, n (%)** | 98 (49.00%) | 102 (51.00%) | 141 (70.50%) | 59 (29.50%) |
| **Type III, n (%)** | 43 (48.86%) | 45 (51.14%) | 65 (73.86%) | 23 (26.14%) |
| **Type IV, n (%)** | 7 (46.67%) | 8 (53.33%) | 13 (86.67%) | 2 (13.33%) |
| **Type V, n (%)** | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |
| **Type VI, n (%)** | 1 (100.00%) | 0 (0.00%) | 1 (100.00%) | 0 (0.00%) |
| **p-value Fisher** | 0.9900 | | 0.7209 | |

ITT, intention to treat.

### Table 5. BMI by clearance rates at Day 57 (ITT population)

| BMI | Complete clearance | | Partial clearance | |
|---|---|---|---|---|
| | Yes (n=174) | No (n=179) | Yes (n=255) | No (n=98) |
| **Mean, SD (%)** | 29.02 (5.81) | 28.62 (4.27) | 28.96 (5.44) | 28.44 (4.02) |
| **p-value t-test** | 0.4579 | | 0.3312 | |

BMI, body mass index; ITT, intention to treat; SD, standard deviation.

- 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%). No deaths, discontinuations, or serious AEs related to tirbanibulin occurred.
- LSR signs were present at baseline, increased after treatment, peaked on Day 8 with tirbanibulin, decreased significantly by Day 15, and mostly resolved by Day 29. Maximum mean ± standard deviation (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 observed in less than 10% in each group. All LSRs resolved or returned to baseline and did not require intervention.

## CONCLUSIONS

- Tirbanibulin ointment 1% applied once-daily for 5 days was generally well tolerated and effective. Previous AK treatment, Fitzpatrick skin type or BMI were not predictive for the clinical response. In contrast, AK location on the face and fewer number of lesions at baseline were predictors of treatment success after 2 months.

## REFERENCES

1) Blauvelt A et al. New Engl J Med 2021;384:512-20.
2) Olsen EA et al. J Am Acad Dermatol 1991;24:738-43.

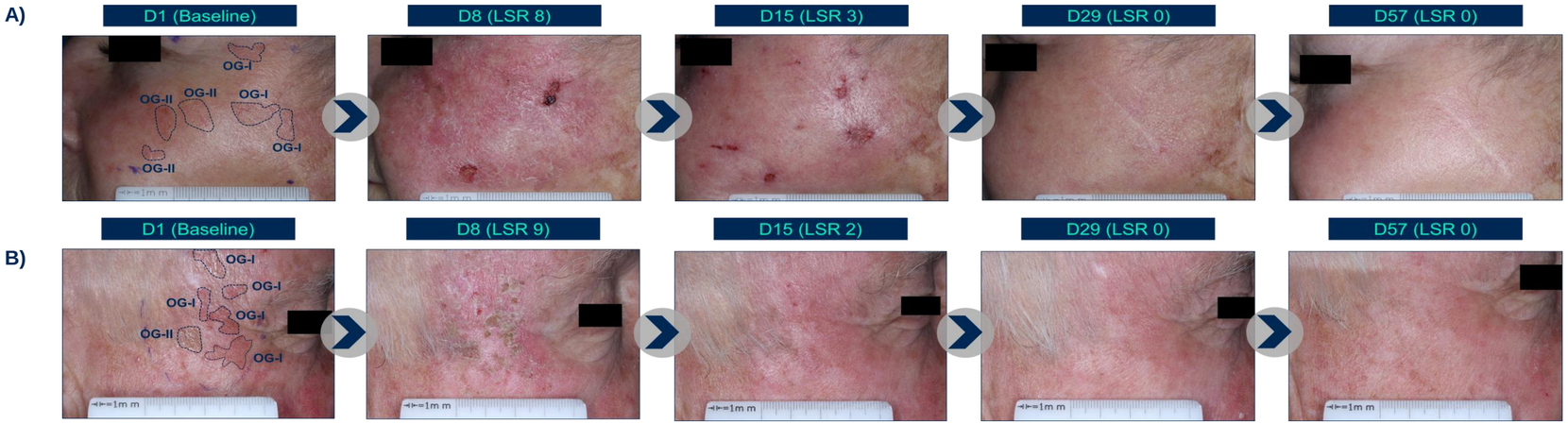
## ACKNOWLEDGEMENTS

- Phase III studies were funded by Athenex. *Post-hoc* analysis/medical writing was funded by Almirall.
- Writing support was provided by TFS HealthScience.

## 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; **AGu** has served as a consultant for Almirall; **AGr**, **EF**, **LP** and **FH** are employees of Almirall.

### Figure 1. Evolution of facial AK lesions in patients who showed complete clearance with tirbanibulin at Day 29 (A) and Day 15 (B)




Grading of lesions according to the Olsen classification[2] was performed *post-hoc*, and therefore was based on visual inspection only. AK, actinic keratosis; D, day; LSR, local skin reaction; OG, Olsen Grade. **A)** The patient was a white (Fitzpatrick III), 71 year-old female. Previous dermatological conditions included rosacea (1985), AK (2002), photoaging on face (2017), and seborrheic keratoses on bilateral upper and lower extremities. LSRs: D1 none; D8 flaking/scaling moderate, erythema moderate, crusting moderate, erosion/ulceration mild, swelling mild; D15 flaking/scaling mild, erythema mild, crusting mild; D29 and D57 none. **B)** The patient was a white (Fitzpatrick II), 69 year-old male. Previous dermatological conditions included basal cell carcinoma back (2009), AK (2009), AK (2017), and basal cell carcinoma on the left cheek (2017). LSRs: D1 none; D8 flaking/scaling severe, erythema moderate, crusting moderate, swelling mild, erosion/ulceration mild; D15 flaking/scaling mild, erythema mild; D29 and D57 none.