Safety, Tolerability and Efficacy of Tirbanibulin Ointment 1% Treatment on 100 cm² of the Face and Scalp in Patients with Actinic Keratosis: A Phase 3 Study

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Synopsis

- Actinic keratosis (AK) is a pre-cancerous skin disease resulting from the atypical proliferation of keratinocytes that may progress to squamous cell carcinoma.[1]
- Tirbanibulin ointment 1% has demonstrated safety, tolerability, and efficacy for AK and is approved in the US and Europe for treating AK on the face or scalp over an area up to 25 cm².[2]

Objective

- The objective of this study was to evaluate the safety and tolerability of tirbanibulin ointment 1% applied to a larger area, a field of 100 cm², on the face or balding scalp in adult patients with AK.

Methods

- A phase 3, multicenter, open-label, single-arm study (NCT05279131) was conducted among adult patients having a treatment field on the face (excluding lips, eyelids, inside nostrils, and ears) or balding scalp that measured approximately 100 cm² and contained 4 to 12 clinically typical, visible, and discrete, non-hypertrophic, non-hyperkeratotic AK lesions.
- Enrolled patients received tirbanibulin once daily to the treatment area for 5 consecutive days and a follow-up period up to Day 57.
- All patients were evaluated for safety, tolerability, and the presence of AKs until Day 57.
- Safety was assessed by evaluating treatment emergent adverse events (TEAEs).
- Tolerability endpoints included scores of 6 local tolerability signs (LTS: erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosion/ulceration) scored at each timepoint from 0 (absent) to 3 (severe) and summed to a composite score (0-18).
- Exploratory efficacy was measured as percentage change from baseline (CFB) in AK lesion count.

Results

- A total of 105 patients (20 sites in US) were included in the safety analysis set (males: 69%; ≥65 years: 65%; Fitzpatrick skin type II: 63%; AK on the face: 68%; mean number of AKs: 7.7).
- The most common LTS after tirbanibulin administration were erythema (96% of patients) and flaking/scaling (85% of patients), mainly were mild-to-moderate in severity, peaked at Day 8, and resolved or returned to baseline by Day 29. Severe erythema was only reported in 6% of patients and severe flaking/scaling in 9% of patients. No severe cases were reported for the rest of LTS (**Figure 1**). Overall, the tolerability profile of treating a 100 cm² area was consistent with that seen when treating an area of 25 cm².[2]
- The most frequent TEAEs were application site pruritus (11% of patients) and application site pain (9%), consistent with previous Phase 3 study results (25 cm² treatment area).[2] No serious TEAEs related to the drug were reported (**Table 1**).
- The maximum local tolerability composite score was 4 out of 18, consistent with prior pivotal trials.

Figure 1. Local tolerability signs after tirbanibulin administration (local tolerability severity scale: 0=Absent, 1=Mild, 2=Moderate, 3=Severe)

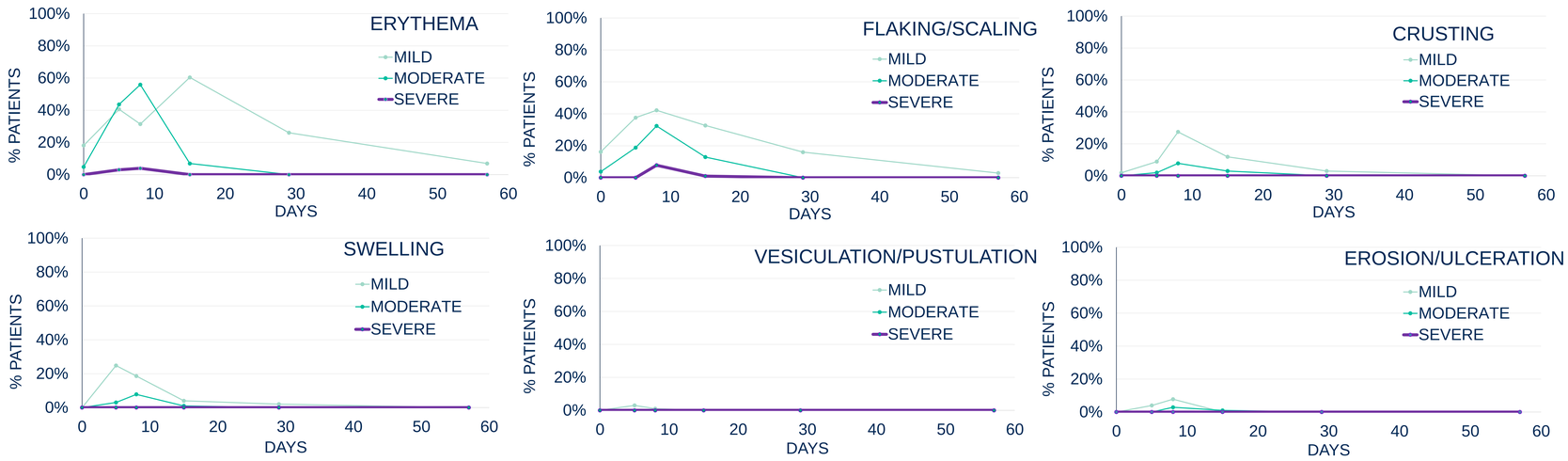

Table 1. Most frequent TEAEs in 100 cm² treatment area vs 25 cm² treatment area

Preferred Term	Tirbanibulin 100cm² (N=105)	Tirbanibulin arm Pooled Phase 3, 25cm² (N=353)
Patients with at least one TEAE, n (%)	**29 (27.6%)**	**124 (35.1%)**
Most frequent events (≥ 2%)		
Application site pruritus, n (%)	11 (10.5%)	32 (9.1%)
Application site pain, n (%)	9 (8.6%)	35 (9.9%)
Dizziness, n (%)	2 (1.9%)	1 (0.3%)
Paraesthesia, n (%)	2 (1.9%)	--
SCC, n (%)	2* (1.9%)	6 (1.7%)

Patient 75 y.o., SCC outside the treatment field, **4 days after treatment start, moderate, non-serious, considered non-related to the treatment. Patient 81 y.o., in situ SCC inside the treatment field, **59** days after treatment start, mild, non-serious, considered non-related to the treatment*
y.o., years old; SCC, squamous cell carcinoma; TEAE, treatment-emergent adverse event.

- Patients initiated the study with a mean of 7.7 AKs and completed the study with a mean of 1.8 AKs, indicating good efficacy.
- Mean percentage CFB in lesion count at Day 57 was 78%, consistent with the Phase 3 study with a 25 cm² treatment area.[2]

Conclusion

Good safety, local tolerability, and efficacy in patients with AK treated with tirbanibulin over a 100 cm² area were consistent with those previously reported in patients with AK treated in pivotal trials with tirbanibulin over a smaller area.

References

[1]Siegel JA *et al*. *Br J Dermatol*. 2017;177(2):350-358. [2]Blauvelt A *et al*. *N Engl J Med*. 2021;384(6):512–20.

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Conflicts of interest

NB: consulting honoraria from and investigator for Almirall, Biofrontera, Leo, Ortho, and Sun Pharma. **AB**: speaker (received honoraria) for AbbVie, Bristol-Myers Squibb, Eli Lilly and Company, Regeneron, and UCB, scientific adviser (received honoraria) for AbbVie, Abcentra, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Dermavant, EcoR1, Eli Lilly and Company, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, Janssen, Landos, Leo, Merck, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TrialSpark, UCB Pharma, Vibliome, and Xencor, and clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Concert, Dermavant, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB Pharma. **EL**: clinical investigator, consultant, advisor, and/or paid speaker for Almirall, Athenex, Gage Pharmaceuticals, UCB, Abbvie, Sanofi, Regeneron, Vyne Pharmaceuticals, Pfizer, Amgen, Novartis, Eli Lilly, Kadmon, Chemocentryx, Bausch Health, Galderma, Dermavant, Arcutis, Bristol Myers Squibb, Kiniksa, Mindera, Sebacia, Pulse BioSciences, Leo Pharmaceuticals, Aclaris, Biorasi, Brickell, Cassiopea, Dr Reddy, Endo Pharmaceuticals, and G&E Herbal Biotechnology. **AJ**: investigator of or received grants/research funding from AbbVie, Almirall, Arcutis Biotherapeutics, Arcutis, Inc., Asana Biosciences, LLC, BMS, Castle Biosciences, Concert Pharmaceuticals, Dermira, Foamix Pharmaceuticals Ltd, Incyte Corporation, Leo Pharma Inc., Lilly ICOS LLC, Novartis, Sanofi/Regeneron, UCB, Vivex Biomedical, Inc.; JD: investigator of or received grants/research funding from AbbVie, AiViva BioPharma, Allergan, Inc, Almirall, AnaptysBio, Arcutis Biotherapeutics, Bausch Health; Biofrontera; Bristol-Myers Squibb; Caliway Biopharmaceuticals Co., Ltd; Cara Therapeutics; Croma-Pharma GmbH Austria; Dermata Therapeutics; DermBiont; Dr. Reddy; Endo Pharmaceuticals; Evommune, Inc.; Galderma USA; Incyte Corporation; LEO Laboratories Ltd (LEO Pharma); Merck; Palvella Therapeutics; RAPT Therapeutics; Therapeutics Inc; Vial Health Technologies; **MLT**, **MF**, **VK**, **LP, RO**: Almirall Spain employee.