Safety and tolerability of tirbanibulin 1% treatment of Actinic Keratosis on face and scalp in routine clinical practice across the U.S. (PROAK study)

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Synopsis

- Actinic Keratosis (AK) has been shown to negatively affect emotional and social functioning and skin-related quality of life of patients.[1]

Objective

- The objective of this analysis was to evaluate safety and tolerability of tirbanibulin in AK treatment, among patients administered tirbanibulin in routine clinical practice across the U.S.

Methods

- A single-arm, multicenter, prospective cohort study (PROAK: NCT05260073) was conducted in adult patients with AKs on 25 cm^2 on the face or scalp who were newly initiated with once-daily tirbanibulin 1% ointment treatment (5 consecutive days course) as part of usual care.
- Safety and tolerability endpoints were assessed at week 8 and week 24 and included adverse events (AEs), serious AEs (SAE), adverse drug reactions (ADRs), serious ADRs, local skin reactions (LSR), skin scarring and hypo/hyperpigmentation.
- Number of patients discontinuing treatment because of AEs, ADRs and for any other reasons were also reported.
- LSR (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, and erosion/ulceration) were scored from 0 (absent) to 3 (severe) and summed to a composite score (0-18).

Results

- A total of 300 patients were included in the safety analysis population (**Table 1**).
- A total of 98% of patients completed the 5-day treatment course. No patients discontinued the study due to AEs or ADRs.
- During the study, 5% of patients reported at least one AE, 4% of patients at least 1 SAE, and no patients reported serious ADR (**Table 2**).
- Basal Cell Carcinoma was reported in 1% (n=4) of patients and Squamous Cell Carcinoma in 2% (n=7) of patients; all cases were considered not related to treatment and only one patient had a confirmed location as the same as the treatment.
- At week 8, scarring, hypopigmentation, and hyperpigmentation were observed in 1%, 5% and 3% of patients, respectively.
- At week 8, the most reported LSR were erythema and flaking/scaling, mostly mild to moderate with few severe cases (5% and 3%, respectively). No severe cases were reported for the rest of LSR (**Figure 1**).
- At week 8, mean (min-max) LSR composite score was 0.94 (0-11) which was lower than the composite score registered in Phase 3 trials (4.0 [0-11] in trial NCT03285477 and 4.3 [0-12] in trial NCT03285490).[2]

Table 1. Baseline characteristics

Character	Safety Population (N=300)
Age (years), mean (SD)	66.5 (11.5)
Sex (male), n (%)	205 (68.3)
Caucasian, n (%)	295 (98.3)
Fitzpatrick Skin Type, n (%)	
Type I	25 (8.3)
Type II	268 (89.3)
Type III	0 (0)
Type IV	4 (1.3)
Type V	3 (1.0)
Treatment Area, n (%)*	
Face	235 (78.3)
Scalp	102 (34.0)

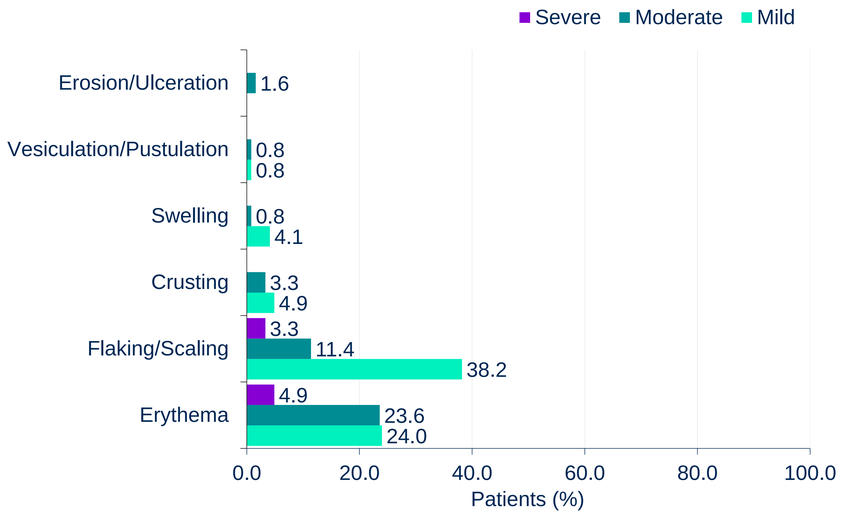
**Some patients had both locations. SD, standard deviation*

Table 2. Summary of safety events

Safety Event	Safety Population (N=300)
Patients with at least one AE, n (%)	**15 (5.0)**
Mild	12 (4.0)
Moderate	2 (0.7)
Severe	1 (0.3)
Patients with at least one SAE*, n (%)	**6 (4.0)**
Patients with at least one ADR, n (%)	**1 (0.3)**
Mild	1 (0.3)
Patients with at least one Serious ADR, n (%)	**0 (0)**
Patients with at least one not-related AE, n (%)	**14 (4.7)**

ADR, adverse drug reaction; AE, adverse event; SAE, serious adverse event.
**SAEs were one hospitalization due to a Pneumothorax, one slip and fall accident, one Bowen's Disease, three Squamous Cell Carcinoma, and two Basal Cell Carcinoma (note that one patient reported 3 different SAEs).*

Figure 1. Local skin reactions at week 8 after tirbanibulin administration



Conclusion

- **In real world, once-daily tirbanibulin 1% ointment for 5 consecutive days showed a good safety and tolerability profile in the treatment of AK on the face or scalp, in line with results obtained in Phase 3 trials[2] even with a lower mean LSR composite score in PROAK study (0.9 vs 4.0 and 4.3).**
- **This good safety/tolerability suggests a more favorable profile compared to other AK topical treatments currently available in the market.**

References

[1]Schlesinger T et al. Skin. 2023;7(3):771-787. [2]Blauvelt A *et al*. *N Engl J Med*. 2021;384(6):512–20.

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Conflicts of interest

TS: consulting honoraria from Abbvie, Allergan, Almirall, Arcutis, Biofrontera, BMS, Castle Bioscience, CMS Aesthetics DCME, EPI Health, Foundation for Research and Education in Dermatology, Galderma, Genentech, Kintor, Lilly, Merz, Nextphase, Novartis, Ortho Dermatologics, Pharmatecture, Pierre Fabre, Plasmed, Prolacta Bioscience, Pulse Biosciences, Regeneron, Skinceuticals/L'Oreal, RBC Consultants, Sun Pharma, UCB, and Verrica. Grant/Research funding from Abbvie, Aclaris, Allergan, Amgen, Anterios, AO Biome, Arcutis Premier Research, ASLAN, Astellas Pharma US, Athenex, Biofrontera, Biorasi, Boehringer Ingelheim, Brickell Biotech, BMS, Cara Therapeutics, Castle Bioscience, Celgene, Chemocentryx, Coherus Bioscience, Concert Pharmaceutical, Corrona, Cutanea Life Sciences, Dermavant, Dermira, DT Pharmacy & DT Collagen, EPI Health, Galderma, Janssen, Kiniksa, Leo, Lilly, Merz, Nestle, Nimbus, Novartis, Pfizer, Processa, Pulse Biosciences, Regeneron, Sanofi Genzyme, Sisaf, Trevi, and Verrica. Speakers' Bureau/Advisory Board honoraria from Abbvie, Almirall, Amgen, Arcutis, Bioderma, BMS Biofrontera, Celgene, DUSA/Sun Pharma, EPI Health, Leo, Lilly, Regeneron, Remedly, Sanofi Genzyme, and Sun Pharma. Owns stock from Amgen, BMS, Lilly, and Remedly. **JDR**: researcher, consultant, and speaker for Almirall. **VAP**: speakers bureau for Regeneron, advisory board/consultant for Regeneron, Almirall, PhD Biosciences, Castle Biosciences, and shareholder for Science 37, Avestra. **LK**: has served as an investigator, speaker, advisory board member, or consultant for Abbott Laboratories, Aclaris, Inc, Allergan, Inc, Almirall, Anacor Pharmaceuticals, Inc, Assos Pharma, Astellas Pharma US, Inc, Asubio Pharma Co, Ltd, Berlex Laboratories (Bayer Healthcare Pharmaceuticals), Biogen-Idec, Inc, Biolife, Biopelle, Boehringer Ingelheim, Breckinridge Pharma, Celgene Corporation, Centocor, Inc, Colbar, CollaGenex, Combinatrix, Connetics Corporation, Coria, Dermik Laboratories, Dermira, Inc, Dow Pharmaceutical Sciences, Inc, Dusa Pharmaceuticals, Inc, Eli Lilly & Co, Embil Pharmaceutical Co, Ltd, EOS, Ferndale Laboratories, Inc, Galderma Laboratories, LP, Genentech, Inc, GlaxoSmithKline, PLC, Health Point Ltd, Idera, Inc, Innocutis Medical, LLC, Innovail, Intendis, Inc, Johnson & Johnson, Laboratory Skin Care, Inc, Leo Pharmaceuticals, Inc, L'Oreal SA, 3M, Maruho Co, Ltd, Medical International Technologies, Medicis Pharmaceutical Corp, Merck & Co, Inc, Merz, Nano Bio Corporation, Novartis Pharmaceutical Corporation, Noven Pharmaceuticals, Inc, Nucryst Pharmaceuticals Corporation, Obagi Medical Products, Inc, Onset, Ortho Dermatologics, OrthoNeutrogena, PediaPharma, Inc, Promius Pharma, LLC, PharmaDerm, Pfizer, Inc, PuraCap, QLT, Inc, Quatrix, Quinnova, Serono (Merck-Serono International SA), SkinMedica, Inc, Stiefel Laboratories, Inc, Sun Pharmaceutical Industries, Ltd, Taro, TolerRx, Inc, Triax, UCB, Inc, Valeant Pharmaceuticals North America LLC, Warner-Chilcott, XenoPort, Inc, and ZAGE. **AA**: served as a research investigator and/or scientific adviser to AbbVie, BI, BMS, EPI, Incyte, LEO, UCB, Janssen, Lilly, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron, and Pfizer. **BB**: consulting honoraria from Almirall, Biofrontera, BMS, Pfizer, Evommune, Aiviva, Sirnaomics, Pulse, Mediwound, BPGBio, Lemonex and Minolabs. **NB**: consulting honoraria from and investigator for Almirall, Biofrontera, Leo, Ortho, and Sun Pharma. **ML**: research funds from: Abbvie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, Dermavant Sciences, Eli Lilly, Incyte, Janssen Research & Development, LLC, Ortho Dermatologics, Regeneron, and UCB, Inc.Consultant for Aditum Bio, Almirall, AltruBio Inc., AnaptysBio, Arcutis, Inc., Aristea Therapeutics, Avotres Therapeutics, Brickell Biotech, Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Celltrion, Corevitas, Dermavant Sciences, Dr. Reddy, EPI, Evommune, Inc., Facilitatation of International Dermatology Education, Forte Biosciences, Foundation for Research and Education in Dermatology, Galderma, Helsinn, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Seanergy, Strata, Trevi, and Verrica. **DR**: has served as a consultant for Almirall, Castle BioSciences, DermTech, and SciBase. **SN**: consulting honararia or research funding from Almirall, Biogen, Johnson and Johnson, Sarepta Therapeutics, SeaGen, and Takeda. **VK** and **IK**: Almirall employees.