A-358 - Efficacy, safety and willingness to be retreated with tirbanibulin 1% ointment in patients with actinic keratosis over a field treatment up to 100 cm² [Abstract]

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erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation and erosion/ulceration. Post-hoc analyses were performed by age group (≥80 years vs <80 years).

Results: Of 644 patients in the pooled safety population, 16.8% were ≥80 years (n=108), referred to as very elderly population. Mean baseline lesion count was similar across age groups (6.5 and 6.4, respectively). TF was predominantly the face (≥80 years: 71.3% face and 28.7% scalp; <80 years: 66.4% face and 33.6% scalp). At Day 57, very elderly patients achieved a mean 72.8% (95% CI: 66.4, 79.3) reduction in AK lesions (placebo: 26.9% [95% CI: 18.3, 35.5]), comparable to 77.5% (95% CI: 74.9, 80.0) for <80 years (placebo: 32.1% [95% CI: 28.3, 35.9]). TEAEs were also similar (38.9% and 36.4%, respectively). 6.5% of very elderly patients experienced severe TEAEs (vs 1.5% <80 years). LTS at Day 8 were consistent across groups, with mostly mild-to-moderate reactions; severe reactions were infrequent and similar: erythema (≥80 years: 9.3% vs <80 years: 7.4%), flaking/scaling (9.3% vs 7.2%), crusting (2.8% vs 1.7%), swelling (0.9% vs 0.4%), and vesiculation (0% vs 0.2%).

Conclusions: Tirbanibulin has shown efficacy and favorable safety/tolerability in very elderly patients. These outcomes support 5-day tirbanibulin treatment as a suitable field-directed therapy for AK in these high-risk patients.

References: [1] Szeimies RM, et al., (2024), Dermatol Ther (Heidelb), 1739–53, 14

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A-358

Efficacy, safety and willingness to be retreated with tirbanibulin 1% ointment in patients with actinic keratosis over a field treatment up to 100 cm²

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Background: Actinic keratosis (AK) is a pre-cancerous skin disease resulting from the atypical proliferation of keratinocytes that may progress to invasive squamous cell carcinoma (SCC). Tirbanibulin 1% ointment is approved for treating AK on the face or scalp in Europe over a field up to 25 cm2, and in the United States over a field up to 100 cm2.[1] This study aimed to evaluate tirbanibulin's efficacy and safety when applied to fields larger than 25 cm² and up to 100 cm², including up to two 5-day treatment courses, and to assess patients' and investigators' reported outcomes such as willingness to retreat with tirbanibulin.

Methods: This is a phase 3, multicenter, randomized, double-blind, vehicle-controlled study (NCT06135415). Patients with ≥4 to ≤12 AK lesions in a field of between 25 and 100 cm2 were randomized 2:1 to tirbanibulin or vehicle. All received a 5-day course; those not achieving complete clearance (CC) at Day (D) 57 received a second course. Primary endpoint was percent change from baseline in AK lesion count at D57. Key secondary endpoints were CC, defined as 100% clearance of AK lesions and partial clearance (PC), defined as ≥75% clearance of AK lesions, assessed at D57 and D113. Willingness to be retreated was evaluated at D113 by patient and investigator using a 5-point Likert scale (from very unlikely to very likely). For this subanalysis we merged "somewhat" and "very likely" categories.

Results: 187 patients were randomized to tirbanibulin and 93 to vehicle (mean age: 73.4 years; male: 83.9%). Tirbanibulin demonstrated a statistically significantly greater percent reduction in AK lesions from baseline to D57 versus vehicle (least-square mean: 64.2% vs 25.2%; p<0.001; median: 84.5% vs 20.0%; nominal p<0.001). At D57, a higher percentage of patients achieved CC and PC with tirbanibulin (41.2% and 58.8%, respectively) compared to vehicle (15.1% and 20.4%), and the improvement was further increased at D113 (CC and PC with tirbanibulin: 56.1% and 65.2% vs CC and PC with vehicle: 23.7% and 25.8%), the differences being statistically significant between groups both at D57 and D113 (p<0.001). Most treatment emergent adverse events (TEAEs) were mostly mild/moderate local skin reactions. Basal cell carcinoma occurred in 1.1% of both groups; and SCC occurred in 1.1% in the vehicle group. No SCC was reported in the tirbanibulin group. Willingness to be retreated (somewhat/very likely) was high in the tirbanibulin arm, both in patients (83.8%) and investigators (85.2%).

Conclusions: Tirbanibulin showed significantly greater efficacy and favorable safety/tolerability for AK treatment fields up to 100 cm² compared to vehicle, and was associated with high willingness to retreat, among both patients and investigators.

References: [1] Bhatia N, et al, (2024), JAAD Int, 6-14, 17

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A-355

Gene Signatures as Predictive Biomarkers for PD-1 Blockade in Cutaneous Squamous Cell Carcinoma

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Background: Anti-PD-1 therapy has substantially improved clinical outcomes in patients with advanced cutaneous squamous cell carcinoma (cSCC). However, approximately 50% of patients do not respond to PD-1 inhibition.

Methods: To explore the molecular mechanisms underlying treatment response and to find potential biomarkers, we performed whole-transcriptome profiling using the HTG EdgeSeq technology on 26 tumor samples of advanced cSCC who subsequently received anti-PD-1 therapy. Baseline clinical characteristics and treatment outcomes were collected, and differentially expressed genes (DEGs)