

Determination of the Area of Skin Capable of Being Covered by the Application of 250 mg of Tirbanibulin Ointment, 1%

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Background

- A newly FDA-approved treatment for actinic keratoses (AK) on the face and scalp is topical tirbanibulin ointment, whose mechanism of action, inhibition of tubulin polymerization and alteration of Src kinase signaling, results in antiproliferative and pro-apoptotic effects.
- FDA approval was based on Phase III studies of the safety and effectiveness of the application of the contents of 1 packet of 2.5mg tirbanibulin in 250 mg ointment to an AK affected 25cm² area of skin on the face and scalp, OD x 5 days
- Clinically relevant field treatment of actinic keratoses most often requires application to an area greater than 25 cm².

Objective

To determine the surface area of skin that's able to be covered by a single packet of 2.5mg tirbanibulin in 250 mg ointment

Methods

Part 1: Clinical subject

The contents of one packet of tirbanibulin ointment, 1% was evenly spread across the balding scalp and forehead to the hairline of a 72 year old male with multiple actinic keratoses (Figure 1A). In addition, 2 targeted facial AKs were treated with a thin layer of the remaining residual ointment from the sachet. This was repeated daily for 5 consecutive days. A 3D image of the subject's scalp and forehead was created using a 3D high-resolution imaging technique (Cherry Imaging, Ltd, Yokneam, Israel). 3 separate measurements of area of application was calculated using the Trace™ software (Figure 1B).

Part 2: Visualization of applied ointment

The contents of one packet of tirbanibulin ointment, 1% was emptied onto the hair-bearing area of the midback of a 29 year old male. The boundaries of the area of application were visualized by dusting the midback with a green fluorescent powder (Art 'N Glow, Plano, TX) which selectively adhered to the applied ointment (Figure 2). 3 measurements of the area of the fluorescent powder adhering to the applied ointment were taken on a 3D image of the subject's back.

Baseline & Post-Treatment with Tirbanibulin Ointment, 1% OD x 5 Days

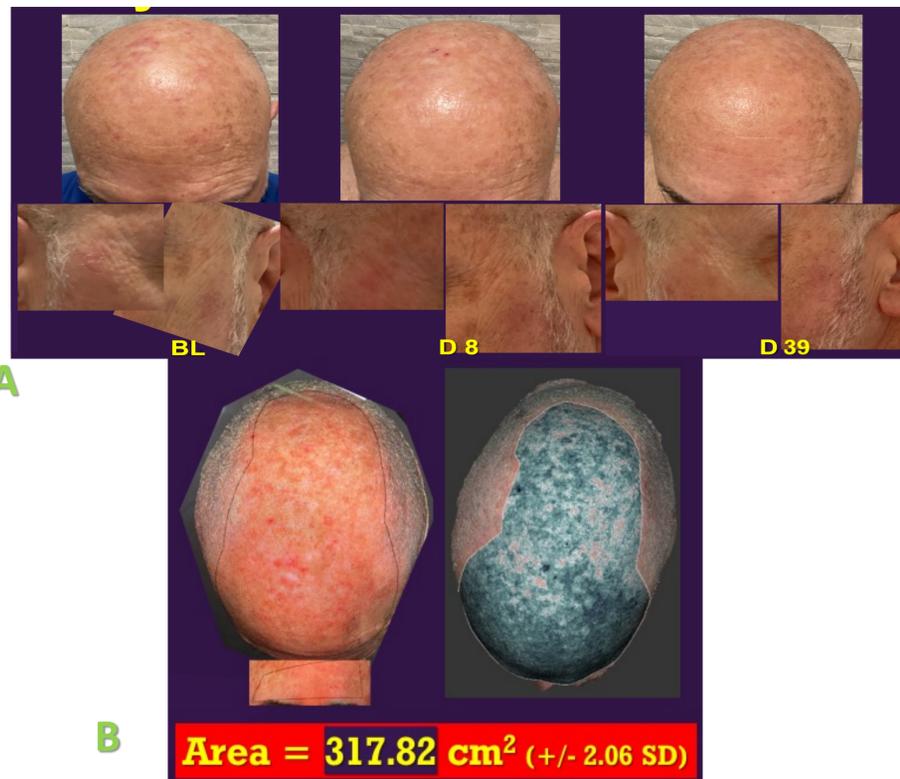


Figure 1: A. The contents of one 250 mg packet of 1% tirbanibulin ointment was applied at baseline (BL) once daily for 5 consecutive days. B. Digitalized 3D images for calculation of application area. Figure 1: B. 3D measurement of the area of application

Results

Area of scalp and forehead application was **317.82 cm²** (SD 2.06) [Figure 1B].

Area of midback application was **210.27 cm²** (SD 2.10) [Figure 2].

Mild Local Skin Reactions (LSRs) peaked at Day 8 and resolved by Day 39 (Figure 1), which corresponds to the results in the published phase III trials.¹ Both facial target AK lesions cleared by Day 39.

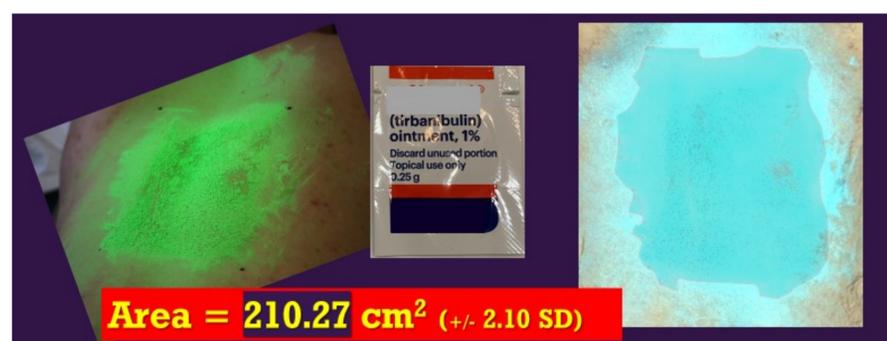


Figure 2: Midback application of a packet of TRB visualized with fluorescent powder dusting and 3D imaging to calculate area of application.

Discussion

A single 250 mg packet of TRB was sufficient to be applied to the patient's entire balding scalp and forehead up to the hairline and down to the top of the eyebrows. In addition, 2 targeted AKs on the left and right lateral canthal areas were treated with a thin layer of the final remaining ointment from the sachet. As expected, LSRs peaked at Day 8 in the treatment areas. Presence of LSRs, and clearance of 2 AK lesions last to be treated at each of the 5 applications, as well as the complete clearance of both AK lesions suggest that the thin layer of ointment applied was sufficient to be effective. The calculated 317.82 cm² area of application in the patient was over 12 times the 25 cm² area treated in the phase 3 trials. Fluorescent visualization detected the even quality of application to 210.27 cm² of hair-bearing, non-actinically damaged skin.

Conclusion

These results suggest that the contents of a single packet of 2.5mg tirbanibulin in 250 mg ointment can be applied therapeutically to clinically relevant areas larger than 25 cm², allowing for treatment of whole cosmetic units over 5 days despite pharmacy dispensing limitations of a total of 5 packets for a once-daily, 5-day treatment regimen.

References

1. Blauvelt A, Kempers S, Lain E, et al. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis. *N Engl J Med.* 2021;384(6):512-520.
2. Berman B, Ricotti CA Jr, Cazzaniga A, Davis SC. Determination of the area of skin capable of being covered by the application of 250 mg of 5% imiquimod cream. *Dermatol Surg.* 2004;30(5):784-786.