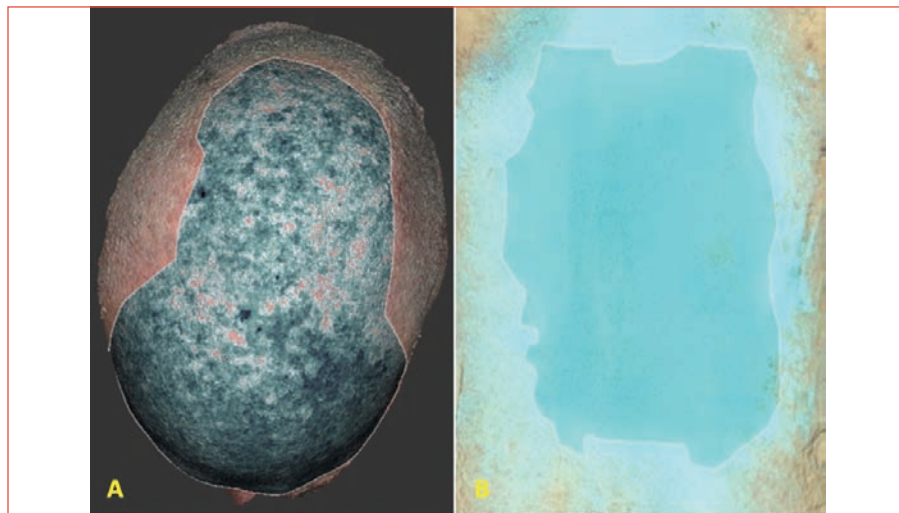


## THE AREA CAPABLE OF BEING COVERED BY THE APPLICATION OF 250MG OF TIRBANIBULIN OINTMENT

Dear Editor:

The United States (US) Food and Drug Administration (FDA) recently approved the field treatment for actinic keratoses (AK) on the face and scalp with topical tirbanibulin ointment 1%. Tirbanibulin inhibits tubulin polymerization and alters Src kinase signaling, resulting in antiproliferative and pro-apoptotic effects. FDA approval was based on the application of the contents of one packet of 2.5mg tirbanibulin in 250 mg ointment to a 25cm<sup>2</sup> contiguous area of skin on the face and scalp, once daily for five consecutive days. However, clinically relevant field treatment of actinic keratoses most often requires application to an area greater than 25 cm<sup>2</sup>. Although the area able to be covered by 250mg of imiquimod 5% cream has been studied<sup>1</sup>, to our knowledge, there are no published data regarding the surface area of skin able to be covered by a single packet of 2.5mg tirbanibulin in 250mg ointment (TRB).

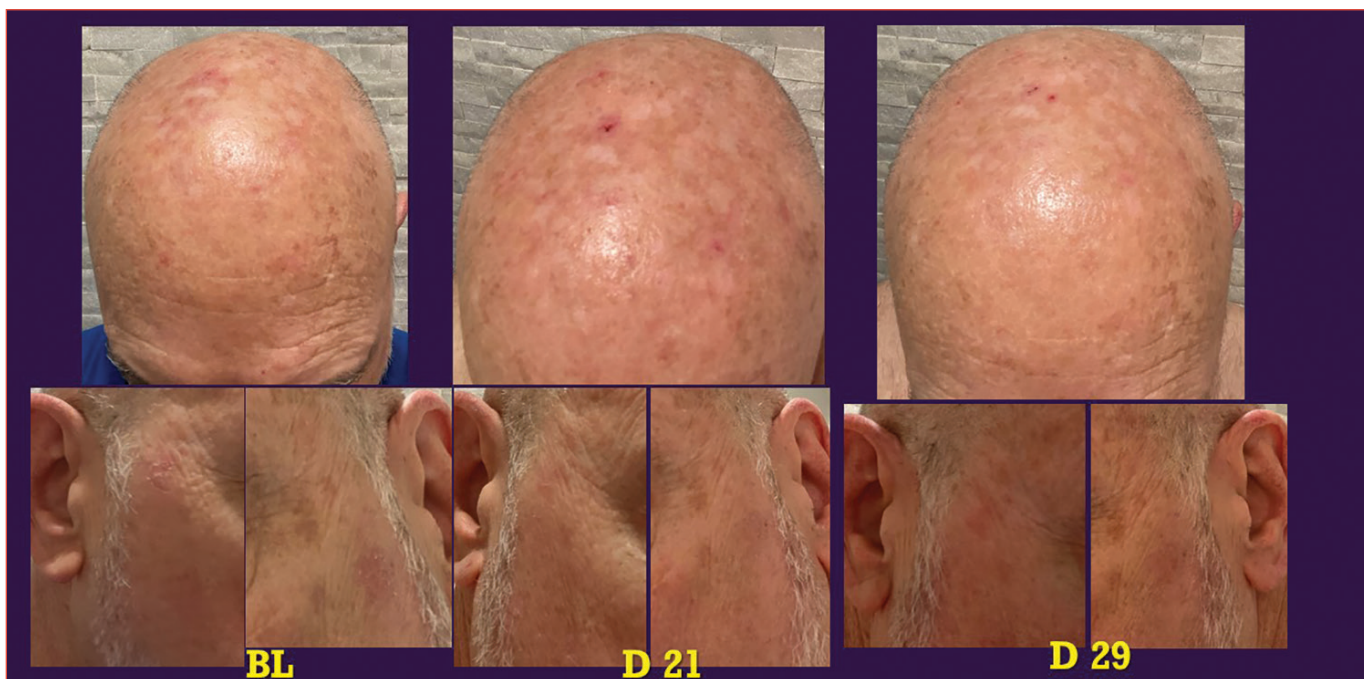


**FIGURE 1.** A) 3D visualization of scalp and forehead to which of one 250-mg packet of tirbanibulin ointment 1% (TRB) was applied; B) 3D visualization of midback application of one 250-mg packet of TRB following fluorescent powder dusting

**Case report.** The contents of one TRB was evenly applied to the balding scalp and forehead to the hairline of a 72-year-old male patient with multiple actinic keratoses. In addition, two targeted facial AKs were treated with a thin layer of the remaining residual ointment from the sachet. This was repeated daily for five 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). Using the Trace™ software, three separate measurements of area of application were calculated to be 317.82 cm<sup>2</sup> (Standard Deviation=2.06).

The area of application of the contents of



**FIGURE 2.** Mild local skin reactions peaked at Day 8 after initiation of the five consecutive day application of 250mg tirbanibulin ointment 1% and resolved by Day 29.

one 250-mg packet of TRB applied to the hair-bearing area of the midback was visualized by dusting the midback with a green, fluorescent powder (Art 'N Glow, Plano, Texas) which selectively adhered to the applied ointment (Figure 1). Using the 3D high resolution imaging technique, the area of the fluorescent powder adhering to the evenly applied ointment was calculated to be 210.27cm<sup>2</sup> (SD=2.10).

### CONCLUSION

A single TRB was sufficient to be applied to the patient's balding scalp and forehead up to the hairline and down to the top of the eyebrows. In addition, two targeted AKs on the left and right lateral canthal areas were treated with a thin layer of the final remaining ointment from the packet. As expected, local skin reactions (LSRs) peaked at Day 8 in the treatment areas and resolved by Day 39 (Figure 2), similar to the findings in the Phase

III trials.<sup>2</sup> Presence of LSRs, and clearance of the two target AK lesions last to be treated at each of the five applications suggest that the layer of ointment applied was sufficient to be effective. The calculated 317.82cm<sup>2</sup> area of application in the patient was over 12 times the 25-cm<sup>2</sup> area treated in the Phase III trials. These results suggest that the contents of a single packet of 250mg tirbanibulin 1% ointment can be applied therapeutically to areas larger than 25cm<sup>2</sup>, allowing for successful treatment of whole cosmetic units within pharmacy dispensing limitation to one packet/day for the five-day treatment.

With regard,

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