

## BRIEF ARTICLE

**Bullous Eruption After Off-Label Use of Topical Tirbanibulin on The Chest**

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**ABSTRACT**

Tirbanibulin 1% ointment (Klisyri), an FDA-approved topical treatment for actinic keratosis, is advertised to serve as a first-in-class topical with high efficacy and low adverse effects compared to other field therapies. We report a case of severe bullous eruption associated with application of tirbanibulin in an adult female. Though application of tirbanibulin did resolve the actinic keratoses on the patient's chest, the severe local skin reaction precludes future use of tirbanibulin in her case.

**INTRODUCTION**

Actinic keratoses are premalignant skin growths, may progress to squamous cell carcinoma, and most commonly affect the sun-exposed regions of the body like the face, scalp, extensor forearms, and dorsal hands.<sup>1</sup> Current topical field-directed medications include 5-fluorouracil, imiquimod, and diclofenac sodium<sup>1</sup>, with clearance rates around 75%<sup>2</sup>, 85%<sup>3</sup>, and 58%<sup>3</sup> respectively.

Tirbanibulin is a fairly new topical treatment for actinic keratosis approved by the FDA in December 2020. Advertised as a first-in-class topical with high efficacy and fewer adverse effects compared to alternative field therapies, its proposed molecular target is by indirect inhibition of Src.<sup>4</sup> This decreases microtubule polymerization and Src kinase signaling, effectively downregulating the growth of human keratinocytes and inducing apoptosis.<sup>5,6</sup> Recommended usage of

tirbanibulin is once daily application to the face or scalp, to an area up to 25 cm<sup>2</sup>, for five consecutive days.<sup>7</sup> Excipients in the commercially available formulation of tirbanibulin 1% ointment include propylene glycol and glycerol monostearate 40-55.<sup>8</sup>

**CASE REPORT**

A 56-year-old Caucasian female with a history of actinic keratoses and cutaneous squamous cell carcinoma presented for re-evaluation of scattered actinic keratoses on the upper chest status post application of tirbanibulin 1% ointment once daily for 5 days. With prior actinic keratoses treated with cryotherapy, tirbanibulin was the first field-directed topical agent used by the patient. The patient reported the appearance of small vesicles on day 3 of application which worsened by day 5. She noted pruritus and denied pain. She reported meticulous sun avoidance during the treatment duration. The patient denies a history of allergic contact

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dermatitis, rash secondary to any topical medicaments, history of lupus erythematosus, porphyria, or polymorphous light eruption.

Examination revealed a well-demarcated erythematous plaque studded with tense vesicles and bullae of her upper chest (**Figure 1**).



**Figure 1.** Erythema and brisk vesiculation on the upper chest following tirbanibulin application.

Management included drainage of larger bullae with sterile needle and application of triamcinolone 0.1% cream twice daily for 2 weeks.

The patient reported resolution of symptoms and bullae by 2 weeks. At her follow-up visit 2 months later, there was mild post-inflammatory erythema without scarring. No actinic keratoses were noted in the treatment field at that time.

## DISCUSSION

In the Phase 1 study of tirbanibulin ointment with 30 participants, no participants experienced any vesiculation or pustulation post application to their forearm.<sup>9</sup> In the Phase 2 study with 168 participants applying tirbanibulin to their face and scalp, 5 patients

experienced minimal or mild vesiculation and pustulation, as rated by investigators; no moderate or severe vesicular reactions were noted.<sup>9</sup> In the Phase 3 study with 702 participants, 353 patients received tirbanibulin and 349 received a placebo, 10% experienced application-site pain.<sup>5</sup> Interestingly, only 1% (2/353) of patients experienced severe vesiculation or pustulation while erythema (91%) and flaking or scaling (82%) were common side-effects.<sup>5</sup>

In trial 1 and 2 of Phase 3, there was a pooled complete clearance rate of actinic keratoses among 49% of participants compared to a 9% clearance rate in the placebo group at day 57.<sup>5</sup> In trial 1 and 2 of Phase 3, there was a pooled partial clearance rate among 72% of participants compared to 18% in the placebo group at day 57.<sup>5</sup>

Though the clearance rate with tirbanibulin is not as high as other field-directed topicals<sup>7</sup>, this patient did experience complete clearance of her actinic keratoses. However, she fell in the minority of patients (<1%) who experience severe adverse skin reactions. The reason for this is unclear. One hypothesis to explore is whether the skin of the chest metabolizes the medicine differently than the face or scalp. Other explanations for her intense vesiculation include an idiosyncratic sensitivity to tirbanibulin's pharmacologic effect or a brisk allergic contact dermatitis to one of the ointment's excipients.

## CONCLUSION

Though tirbanibulin ointment is generally associated with mild adverse reactions<sup>8</sup> and increased user compliance due to its short duration of application, clearance rates may be lower than other topical field-directed therapies for actinic keratoses.<sup>7</sup> Despite the

low percentage (<1%)<sup>7</sup> of patients who experience severe bullous reactions, patients who are using tirbanibulin ointment in off-label locations or in areas greater than 25 cm<sup>2</sup> should be counseled to report atypical side effects to their healthcare provider.

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