

Topical tirbanibulin resolves recalcitrant condyloma acuminata: Retrospective case series



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Condyloma acuminata (CA) are anogenital warts caused by human papillomavirus (HPV) infections. Currently, available treatments for CA include cryotherapy, imiquimod, sinecatechins, and podophyllotoxin. These topicals are limited by marked local skin reactions (LSRs), high recurrence rates, or limited accessibility. Clinical response of anogenital warts and HPV-16 (+) vulvar high-grade squamous intra-epithelial lesions with topical tirbanibulin has been published recently.^{1,2} Tirbanibulin 1% ointment is a synthetic antiproliferative agent approved by the Food and Drug Administration in 2020 for the treatment of actinic keratoses as a once-daily topical treatment for 5 days. Tirbanibulin exhibits a dual mechanism of action, inhibiting microtubule polymerization by binding tubulin and disrupting Src kinase signaling in actively dividing cells.³ Here, we report real-world experience with topical tirbanibulin on CA in 5 patients.

CASE SERIES

This a retrospective case series of 5 patients treated with off-label tirbanibulin 1% ointment for recalcitrant CA. The patient demographics, failed treatments, and results are shown in [Table I](#).

Case 1

A 26-year-old Fitzpatrick skin type V man with no notable medical history presented with recalcitrant CA on the distal shaft of the penis ([Fig 1, A](#)). The

Abbreviations used:

CA: condyloma acuminata
HPV: human papillomavirus
LSR: local skin reactions

patient had failed treatment for 10 months with nightly sinecatechins 5% ointment and cryotherapy every 2 to 3 weeks for 20 sessions over the 10 months. The patient then opted for off-label treatment with tirbanibulin 1% ointment. Treatment consisted of once-nightly application of half of a sachet for 5 consecutive nights followed by no application for 2 weeks with clinical follow-up at week 3. Since the lesion had markedly decreased, the patient opted for another round of application with the remaining 2.5 sachets in the box. The patient experienced mild erythema, scaling, crusting, and dryness starting on day 3 of the first application round that peaked between days 5 and 8 but resolved over the next 2 weeks. Clinical resolution was noted on day 5 of the second round with persistent clinical resolution 18 months later ([Fig 1, B](#)).

Case 2

A 72-year-old Fitzpatrick skin type V man presented with CA on the penis and scrotum that was recalcitrant to liquid nitrogen and sinecatechins 15% ointment for >2 years ([Fig 2, A](#)). The patient was treated with light cryotherapy followed by off-label

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Table I. Demographics and clinical data

Case no.	Age	Sex	Fitzpatrick skin type	Failed cryotherapy and sinecatechins	Failed other prior treatments	Concomitant cryotherapy	Resolved	No. of rounds	Adverse effects
1	26	M	V	Yes	None	No	Yes	2	Mild
2	72	M	V	Yes	None	Yes	Yes	1	Severe
3	61	M	II	Yes	None	Yes	Yes	1	Severe
4	44	F	IV	Yes	Imiquimod HPV vaccine	Yes	Yes	5	None
5	65	F	II	Yes	Imiquimod HPV vaccine	Yes	Yes	1	None

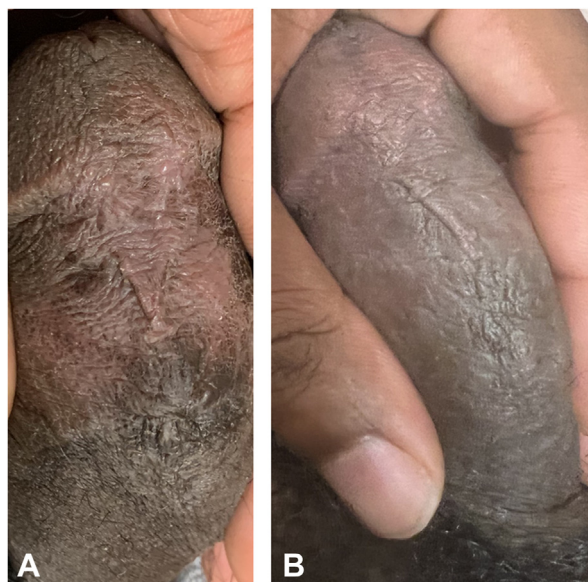


Fig 1. A, Persistent genital warts on the penile shaft in case 1 prior to topical tirbanibulin. **B,** Clinical resolution of genital warts on the penile shaft on day 28.

application of 1 full sachet of topical tirbanibulin that night and for the next 4 nights with resolution of the CA. Light cryotherapy is defined as a single freezing cycle with enough liquid nitrogen for a 1-mm freezing halo around each lesion, so the duration for each lesion varied depending on lesion thickness. Cryotherapy was used with the primary intent of facilitating deeper delivery of tirbanibulin. LSRs included erythema, scaling, crusting, dryness, and blistering starting on day 4 and peaking between days 5 and 8 (Fig 2, B), but resolved within 3 weeks. Postinflammatory hyperpigmentation and hypopigmentation also occurred but resolved over the next 4 weeks. No recurrence has been observed after 1 year.

Case 3

A 61-year-old Fitzpatrick skin type II man presented with CA recalcitrant to sinecatechins 15% ointment and cryotherapy. On day 1, the patient was

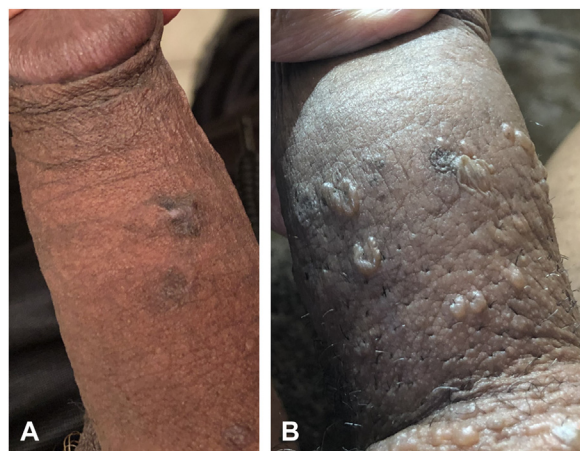


Fig 2. A, Persistent genital warts on the penile shaft in case 2 prior to topical tirbanibulin. **B,** Genital warts on the penile shaft on day 5 of treatment with severe local skin reactions that resolved over 2 weeks.

treated with light liquid nitrogen followed by application of 1 full sachet of tirbanibulin 1% ointment that night and for the next 4 nights. At clinical follow-up 1 month later the patient reported severe erythema, scaling, crusting, dryness, and blistering that resolved within 2 weeks. Physical examination revealed resolution. No recurrence has been observed for at least 1 year.

Case 4

A 44-year-old Fitzpatrick skin type IV woman presented with CA recalcitrant to sinecatechins 15% ointment, imiquimod 5% cream, and cryotherapy. Additionally, the patient received and completed the HPV 9-valent recombinant vaccine series. The patient was instructed to poke a hole in the sachet with a pin and express enough to apply a thin layer each night, with storage inside a sealed plastic bag until the next night. One sachet sufficed for the lesion over the 5 consecutive nights. The patient had clinical follow-up every 3 weeks, with improvement noted at each visit. After 5 rounds of application, the lesion resolved with no evidence of recurrence 18 months

later. Over the treatment course, the patient did not experience LSR or adverse effects.

Case 5

A 65-year-old Fitzpatrick skin type II woman presented with CA recalcitrant to sinecatechins 15% ointment, imiquimod 5% cream, cryotherapy, and the HPV 9-valent recombinant vaccine. Treatment consisted of light liquid nitrogen followed by once-nightly application of one-third to half of a sachet to the lesion for 5 consecutive nights. Clinical follow-up at week 3 revealed complete resolution. The patient reported no LSRs over the treatment course. The patient had no evidence of clinical recurrence at 1 year.

DISCUSSION

HPV is associated with a wide variety of clinical conditions, including warts and cancers of the cervix, vulva, vagina, penis, anus, and oropharynx. In fact, meta-analysis found that cutaneous squamous cell carcinomas were more likely to carry HPV than normal-appearing skin.⁴ Transmission primarily occurs through skin-to-skin contact. Over 180 subtypes of HPV have been identified. Anogenital warts have been historically associated with subtypes 6 and 11. A systematic review revealed that the prevalence of anogenital warts ranged from 0.13% to 0.56% based on a retrospective or prospective chart review, whereas it ranged from 0.2% to 5.1% based on genital examinations. Disparities in documentation likely exist because it is not required to report CA, unlike other sexually transmitted diseases.⁵

Studied extensively, HPV 16 up-regulates the Src family kinases (SFKs) Src and Yes by posttranscriptional mechanisms.⁶ SFKs are intracellular nonreceptor tyrosine kinases involved in various signaling pathways. It is currently understood that SFKs play an integral role in human epithelial cancers and have been shown to contribute to the proliferation of colon and breast cancers.⁷ HPV oncoproteins E6 and E7 inactivate p53 and Rb proteins, respectively, leading to uncontrolled proliferation. Szalmás et al⁶ demonstrated that HPV 16 E6 and E7 resulted in substantial increase in Src and Yes expression levels in human keratinocytes and enhanced the activating phosphorylation of all available SFKs. This intimates that inhibition of Src kinase signaling may be the mechanism of action in which tirbanibulin effectively treats CA.

Complete resolution of recalcitrant genital CA with topical tirbanibulin was observed in 5 patients requiring 1 to 5 rounds (Mean, 2; SD, 1.7) of application. The patients experienced LSRs ranging

from none to severe, with severe LSRs resolving within 21 days. Notably, LSR was not required for clinical resolution. Overall, patients were pleased with tirbanibulin treatment since all had previously failed treatment with sinecatechins 15% ointment. The patients experiencing severe LSRs applied a full sachet to the lesion each night. It is possible that the amount of ointment applied to the lesion correlated with the severity of LSR. Similarly, sinecatechins, imiquimod, and podophyllotoxin produce greater LSRs with thicker application.^{8,9} Based on the reported patients, one-third to half of a sachet per application may be better tolerated. Since 5 sachets are included in each box, 2 rounds are feasible with 1 prescription if the patient needs >1 round. Larger retrospective and prospective studies studying the efficacy and tolerability of tirbanibulin 1% ointment for the treatment of CA are warranted.

Conflicts of interest

Dr A.Y. Moore has received honoraria and/or research funds from Almirall, LLC. Authors Hurley, S. Moore, and L. Moore have no conflicts of interest to declare.

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