



REVIEW

New Developing Treatments for Molluscum Contagiosum

Francesco Lacarrubba · Giuseppe Micali · Andrea Calogero Trecarichi ·
Enrica Quattrocchi · Giuseppe Monfrecola · Anna Elisa Verzi

Received: August 1, 2022 / Accepted: September 27, 2022 / Published online: October 14, 2022
© The Author(s) 2022

ABSTRACT

A large variety of treatments for molluscum contagiosum (MC) are available, but none are Food and Drug Administration (FDA) approved and there is no consensus on the optimal approach, mainly owing to a lack of high-level data. Physical modalities are widely used, but require repeated outpatient visits for administration, are painful and difficult to perform in children, and are associated with the possibility of residual scarring and post-inflammatory hypo- or hyperpigmentation. Two experimental topical drugs, a new standardized preparation of

topical cantharidin, called VP-102, and a topical nitric oxide (NO)-releasing product containing berdazimer, called SB206, represent promising products that have been designed to overcome the limitations of current treatments. They have recently shown good results in terms of safety and efficacy in large cohorts of patients in phase III studies and have the potential to be the first FDA-approved therapies for the treatment of MC.

Keywords: Molluscum contagiosum; Treatment; Cantharidin; Berdazimer; Nitric oxide

F. Lacarrubba (✉) · G. Micali · A. C. Trecarichi ·
A. E. Verzi
Dermatology Clinic, University of Catania, Via S.
Sofia 78, 95123 Catania, Italy
e-mail: franclacarrubba@gmail.com

E. Quattrocchi
Dermatology Department, Mayo Clinic Rochester,
Rochester, MN, USA

G. Monfrecola
Section of Dermatology, Department of Clinical
Medicine and Surgery, University of Naples Federico
II, Naples, Italy

Key Summary Points

A safe and effective treatment for molluscum contagiosum (MC) still represents an unmet need.

VP-102 is a proprietary drug-delivery device combination containing cantharidin 0.7% [w/v] in a film-forming topical solution designed to overcome compounded cantharidin formulation limitations and application concerns.

SB206 is a new nitric oxide (NO)-releasing topical drug consisting of a gel containing berdazimer sodium and a carboxymethyl cellulose hydrogel that acts as a proton donor.

Robust phase III trials are available for both drugs, showing complete clearance in 50% of patients treated with VP-102 and 32% of patients treated with SB206, with mild to moderate local skin reactions.

It is still unclear whether VP-102 and SB206 are superior or not in terms of efficacy to the currently adopted MC treatments as in the clinical trials they were compared with vehicle.

Based on good results in terms of safety and efficacy, VP-102 and SB2016 have the potential to be the first FDA-approved MC therapies.

INTRODUCTION

Molluscum contagiosum (MC) is a common cutaneous infection caused by a DNA poxvirus that mainly affects children, sexually active adults, and immunocompromised patients [1]. There are four known types of MC virus (MCV1–4), with MCV1 and MCV2 being the most common. MC is one of the five most prevalent skin diseases in the world and the



Fig. 1 Molluscum contagiosum: multiple, typical umbilicated papules of the pubis

third most common viral skin infection in children, with a reported prevalence of 5.1–11.5% [2, 3]. There is no gender predilection, but there is a different prevalence depending on the geographical areas, with greater frequency in regions with warm climates [3, 4]. Children affected by atopic dermatitis represent a risk group. MC virus replicates in epidermal keratinocytes, leading to focal hyperplasia. It is mainly transmitted by skin-to-skin contact, and the incubation period is estimated to be 2–8 weeks [5, 6].

The diagnosis of MC is generally clinical due to its typical presentation. It is characterized by single or multiple, small (2–5 mm), pink or skin-colored papules with a typical central umbilication [7] (Fig. 1). They generally occur on the face, trunk, and extremities in children and on the genitals in young adults as a sexually transmitted disease and can be associated with itching, eczema, and secondary bacterial infections. Dermoscopy can help in doubtful cases by showing a central area with white and/or yellow amorphous structures and a peripheral crown of linear or branched vessels [8, 9]. Other emerging diagnostic techniques that can aid in the diagnosis of MC include reflectance confocal microscopy (RCM) and line-field confocal optical coherence tomography (LC-OCT) [10–12]. Biopsy for histopathological evaluation is limited to atypical cases: the characteristic microscopic findings are represented by a crateriform invagination of hyperplastic

epithelium composed of enlarged keratinocytes containing inclusion bodies known as Henderson–Patterson bodies [13].

MC is a self-limiting condition that usually resolves spontaneously within 6–9 months in immunocompetent individuals [14]. In a retrospective study [15] on treated and untreated MC lesions, a 12-month resolution rate of 45.6% and 48.8%, respectively, was observed. After 18 months, the resolution rate was 69.5% in the treated versus 72.6% in the untreated group [15]. For this reason, the decision to treat or not is made on a case-by-case basis, and some clinicians suggest a wait-and-see approach to avoid painful, time-consuming, and costly therapies that may result in skin discoloration and/or scarring [16]. However, in some cases, the lesions can spread and persist for several months to years. In a study on 306 children affected by MC, 30% of the cases persisted at 1.5 years, and 13% at 2 years [17].

Treatment of MC is especially indicated in patients with extensive disease, for esthetic reasons, or in case of secondary complications (bacterial superinfection, molluscum dermatitis, or conjunctivitis) [18]. Other reasons for treating MC include relieving discomfort, reducing the risk of autoinoculation and spread to others, and eliminating social stigma [16, 18, 19].

A wide variety of treatments with different levels of evidence are available for the management of MC [14, 20, 21]. They can be classified as physical, chemical, immunomodulatory, and antiviral (Table 1) [20, 22–24]. This large number of approaches suggests that a method that is unanimously recognized to be better than others does not exist, as confirmed by the 2020 European guideline on the management of genital MC (25) and the 2017 Cochrane review on the interventions for MC [16]. Several studies have been conducted on different treatments, with conflicting results [15, 16, 20, 23, 26]. The choice to adopt one approach or another depends on different factors, including the number/localization of lesions, the clinician's experience, and the patient's characteristics and compliance [16, 20, 22–24]. According to some authors [20, 22, 23, 25], surgical/physical approaches represent the first-line treatments. In some

Table 1 Reported treatments for molluscum contagiosum

Physical/mechanical
Cryotherapy
Curettage
Duct tape occlusion
Squeezing/extraction
Laser therapy
Photodynamic therapy
Chemical (topical)
5-Fluorouracil
Benzoyl peroxide
Cantharidin
Glycolic acid
Lactic acid
Podophyllotoxin
Potassium hydroxide
Retinoids (tretinoin, adapalene)
Salicylic acid
Silver nitrate
Trichloroacetic acid
Immunomodulatory
Imiquimod (topical)
Cimetidine (oral)
Interferon alfa (subcutaneous/intralesional)
Intralesional immunotherapy (<i>Candida</i> antigen, combined measles, mumps, rubella vaccine, tuberculin purified protein derivative, vitamin D3)
Diphencyprone (topical)
Autoinoculation
Antiviral
Cidofovir (topical/intravenous)

clinical trials, clearance rates ranged from 71% to 100% for cryotherapy and from 70% to 80% for curettage [27, 28]. However, these procedures

require repeated in-office visits for administration, and are painful and difficult to perform in children, who account for the majority of MC patients, owing to fear and the discomfort of the treatment. Other disadvantages are the possibility of residual scarring and post-inflammatory hypo- or hyperpigmentation, which may be not accepted, especially in the case of lesions localized on the face. As regards topical approaches, a systematic review conducted in 2018 identified eight studies (with a total of 991 MC patients) evaluating different cantharidin strengths (from 0.7% to 0.9%) [29]. Clearance rates were variable, ranging from 15.4% to 100% depending on the variability of the concentration, treatment interval, procedure, demographics, and rates of concurrent dermatitis [29]. However, an overall low level of evidence of the included studies was evidenced [29]. In a randomized clinical trial on 53 children, 10% and 15% potassium hydroxide formulations were demonstrated to clear MC lesions in 58.8% and 64.3% of the patients, respectively [30]. In a 2010 study conducted on 37 patients, imiquimod 5% cream resulted in complete MC clearance in 92% of cases [27], but the 2017 Cochrane review concluded that it is not better than placebo and may produce adverse effects at the application site such as pain, blistering, scars, and/or pigmentary changes [16].

For the above reasons, the development and assessment of efficacious, painless, and safe topical treatments for MC are desirable. From a literature search, two experimental topical medications, a novel standardized preparation of topical cantharidin, called VP-102 (Verrica Pharmaceuticals), and a topical nitric oxide (NO)-releasing product containing berdazimer, called SB206 (Novan), have recently shown promising results in phase II and III studies and will be the object of the present review. This article is based on previously conducted studies and does not contain any new studies with human participants or animals.

VP-102

Cantharidin is a naturally occurring terpenoid compound derived from the alimentary tract of beetles belonging to the order Coleoptera,

family Meloidae, otherwise known as blister beetles, which has a long history of use for MC [24, 31]. Compounded cantharidin formulations in different strengths (usually from 0.7% to 0.9%) have been used for the topical treatment of MC with or without occlusion for more than 60 years [32, 33]. The mechanism of action includes weakening and degradation of keratinocyte desmosomes, localized blister formation within a few hours with shedding of infected keratinocytes, and viral clearance [33]. As already reported in the “Introduction,” although some studies evaluating different compounded formulations of cantharidin in small cohorts of MC patients showed good results, the safety and efficacy of doses, regimens, and application methods have not been assessed in large-scale controlled trials [6, 29, 33–36]. In addition, cantharidin is usually applied by the physician using nonstandardized tools, such as cotton-tipped wooden swabs or toothpicks, which can cause unwanted side effects, unaffected skin treatment, and/or cross-contamination [37]. Common reported adverse events (AEs) associated with topical cantharidin are discomfort/pain and dyschromia, which are directly related to its vesicant mode of action [24]. Another important limitation regarding the use of cantharidin in treating MC is that, currently, there is no Food and Drug Administration (FDA)-approved and/or European Medicines Agency (EMA)-approved formulation of this molecule, as well as no uniform manufacturing processes in accordance with Good Manufacturing Practices [2, 24]. Cantharidin can be difficult to obtain in compounding pharmacies due to local guidance, with uncertainties regarding formulation stability and concentration of the active ingredient [2, 38].

VP-102 is a proprietary drug-delivery device combination containing cantharidin 0.7% weight/volume [w/v] in a film-forming topical solution. It consists of a glass ampule of 450 μ L of solution within a single-use applicator and contains cantharidin that is more than 99% pure [14]. When the ampule is crushed, the solution is released to flow through a filter and into the tip of the applicator [33]. This commercially manufactured cantharidin

formulation also includes gentian violet, a surgical dye that should facilitate the distinction between treated and untreated lesions during application, and denatonium benzoate, a bittering agent to deter potential oral ingestion. The standardized drug formulation and precision applicator combination of VP-102 are designed to overcome the compounded cantharidin formulation limitations and application concerns [37]. In particular, the small tip of the applicator has been designed to improve safety and efficacy by targeting MC lesions and sparing surrounding healthy skin, while the presence of gentian violet dye avoids overtreatment of each lesion. The single-use applicator may also reduce the potential for cross-contamination [37].

The first clinical evaluation of VP-102 was obtained by a phase II, open-label study assessing systemic exposure, safety, efficacy, and impact on quality of life (QoL) of VP-102 treatment in 33 immunocompetent children aged 2–15 years affected by MC [37]. Treatment was administered every 21 days until clinical clearance (maximum four cycles). At the end of the study, negligible systemic cantharidin exposure was observed. Adverse effects were mild to moderate in severity and did not lead to treatment discontinuation (pain in 57.6% of subjects). Complete clearance was observed in 48.5% of cases, with an overall reduction from baseline in MC number of 90.4%. Finally, an improvement in QoL from a mild disease effect at baseline to no effect at the end of the study was recorded [37].

To determine the safety and efficacy of VP-102 in MC versus vehicle in a larger population, two phase III, randomized, double-blind, vehicle-controlled trials of identical design [Cantharidin Application in Molluscum Patients (CAMP-1 and CAMP-2)] were conducted on a total of 528 individuals with MC aged 2 years and older in 31 centers across the USA [33]. Participants were randomized to topical application of VP-102 ($n = 310$) or vehicle ($n = 218$) to all treatable lesions every 21 days until complete lesion clearance, or up to four treatments. Mean age was 7.5 years (range 2–60 years) for VP-102 and 6.8 years (2–54 years) for vehicle, and patients presented at baseline a mean lesion

count of 20.5 ± 23.1 (range 1–184) in the VP-102 group and 22.5 ± 22.3 (range 1–110) in the vehicle group. At the end of the study, VP-102 was statistically significantly superior to vehicle in achieving complete clearance of MC lesions in both trials [33]. In the pooled analysis of the two trials, the percentage of subjects with complete clearance (primary endpoint) at day 84 was 50% compared with 15% in the vehicle group [39]. As regards the secondary outcome, significant differences in favor of VP-102 in the percentage of participants achieving complete lesion clearance were observed after a single treatment at day 21 for CAMP-1 and for all subsequent time points for CAMP-1 and CAMP-2. Moreover, at the end of treatment, VP-102-treated participants had experienced a mean percent decrease in lesions from baseline of 69% for CAMP-1 and 83% for CAMP-2 (versus 20% increase and 19% decrease in lesions from baseline for vehicle for each trial) [33]. Application site pain, pruritus, erythema, and blistering, mild or moderate in severity, were the most commonly reported AEs, which were expected due to the pharmacodynamic action of cantharidin on the skin. The AE-related discontinuation rate was 1.9% (compared with 0.5% for the vehicle). There was no evidence of AEs suggestive of systemic absorption. Finally, post hoc analyses of pooled data from the two trials showed consistent safety and efficacy of VP-102 across each affected body region (head/neck, chest/abdomen, back/buttocks, groin, upper and lower extremities) [38]. VP-102 is still in preregistration phase in the USA for the treatment of MC.

SB206

Nitric oxide is an endogenous molecule that provides localized immunity against foreign organisms by acting as both a short-lived immune modulator and a direct broad-spectrum antimicrobial agent against bacteria, yeast, fungi, and viruses including human Herpesviridae, human papillomavirus, and MC [40–47].

SB206 is a novel topical NO-releasing medication consisting of two components: a gel

containing berdazimer sodium, a macromolecule with a polysiloxane backbone covalently bound to *N*-diazoniumdiolate NO donors, coadministered with a carboxymethyl cellulose hydrogel functioning as a proton donor [40, 48]. This combination promotes NO release from the macromolecule at the time and site of application, thus minimizing systemic exposure [41]. SB206 likely exerts its antiviral effects on MC through protein nitrosylation and NF- κ B modulation [49].

A phase II, multicenter, randomized, double-blind, vehicle-controlled, dose-finding trial evaluated the efficacy and tolerability of three concentrations and two dosing regimens of topical SB206 (4%, 8%, and 12% twice daily and 12% once daily) used for up to 12 weeks in patients at least 2 years of age with 3–70 MC lesions at baseline [41]. In patients who completed 12 weeks of treatment ($n = 217$), all MC lesions cleared in 20.0% of those who received vehicle compared with 13.2%, 41.0%, and 35.1% of those treated with twice daily SB206 4%, 8%, and 12%, respectively, and 41.9% of patients treated with once daily SB206 12%. The most common AEs were application-site reactions (erythema, dryness, eczema, and edema) that led to treatment discontinuation in two patients in each of the SB206 4%, 8%, and 12% twice daily groups and zero patients in the vehicle or SB206 12% once daily group. This study identified berdazimer sodium 12%, equivalent to berdazimer free base 10.3%, applied once daily as a suitable candidate for phase III development, providing the best balance between lesion clearance and drug tolerability [41, 49].

The results of the phase III multicenter, randomized, vehicle-controlled study evaluating the efficacy and safety of SB206 10.3% (called in the trial “berdazimer 10.3% gel”) in the treatment of MC (B-SIMPLE4 study) were published in July 2022 [49]. The trial included 891 patients at least 6 months of age with 3–70 MC lesions from 31 centers across the USA [49]. Patients were randomized to once-daily treatment with SB206 (444) or vehicle gel (447) for 12 weeks. Mean ages were 6.6 years for the SB206 group and 6.5 years for the vehicle group. At the end of the study, 32.4% of patients in the

SB206 group achieved complete clearance, compared with 19.7% of patients in the vehicle group ($P < 0.0001$). Moreover, 43.5% of the SB206 group achieved a lesion count of 0 or 1 compared with 24.6% of the vehicle group, and 43.0% of the SB206 group achieved a reduction of 90% or greater from baseline of MC lesion number compared with 23.9% of the vehicle group. Overall, SB206 treatment was well tolerated, as demonstrated by low AE-related discontinuation rates (4% compared with 0.7% for the vehicle group). The most common AEs were application site pain and erythema, mostly mild in severity and reversible [49]. They were common in the first 2 weeks of application but improved with time [49].

There is also evidence that SB206 may trigger the beginning of the end (BOTE) sign, a clinical sign of inflammation (including erythema, induration, and scale) that predicts imminent resolution of MC lesions [40]. In an integrated analysis of two prospective, 12-week, randomized, double-blind clinical trials on 707 patients, those treated with SB206 and BOTE+ experienced the greatest reduction in MC lesion count [40].

SB206 has not yet been approved by the FDA, but the developer announced their intention to submit a new drug application (NDA) to the US FDA for MC in Q4 of 2022.

DISCUSSION

Currently, a safe and effective treatment for MC represents an unmet need. Although several approaches are used by clinicians for this widespread skin infection, there are no FDA-approved treatments and there is no consensus on the optimal approach, mainly because of the lack of high-level data.

VP-102 and SB206 are new promising topical products that have been designed to overcome the limitations of current treatments (Table 2). Robust phase III trials are available for both drugs, where the timing of administration was different: a single application (to be repeated every 21 days in case of persistence) for VP-102 and once daily (self or caregiver administered) for SB206 [33, 49]. Complete clearance was

Table 2 New developing drugs with phase III study for molluscum contagiosum

Drug name	VP-102	SB206
Formulation	Topical solution	Topical gel
Schedule	Single application to be repeated every 3 weeks until complete lesion clearance (up to four treatments)	Once daily for up to 12 weeks
Modality of administration	Physician administered	Self or caregiver administered
Number of subjects enrolled in the study	528 aged 2 years or older	891 aged 6 months or older
Complete clearance	50% at day 84 (versus 20% vehicle)	32.4% at day 84 (versus 19.7% vehicle)
Common adverse events	Application site pain, pruritus, erythema, and blistering, mild or moderate in severity	Application site pain and erythema, mild in severity
AE-related discontinuation rates	1.9% (versus 0.5% vehicle)	4% (versus 0.7% vehicle)

observed after 3 months in 50% of patients treated with VP-102 and 32% of patients treated with SB206, and in both studies a significant reduction in lesion count was recorded [33, 49]. AEs were mild to moderate for both treatments, although comparing the results of the two studies, they appear to be milder for SB206. A common issue is that MC lesions located near mucosal sites were excluded in both trials, and this could represent a limitation in clinical practice for the management of periorificial and sexually transmitted MC [50].

The good results in terms of safety and efficacy obtained for VP-102 and SB206 in large cohorts of patients suggest that they have the potential to be the first FDA-approved MC therapies [50]. It is unclear whether they are superior or not in terms of efficacy to the currently adopted treatments as in the clinical trials they were compared with vehicle. Previous studies showed that surgical/physical approaches show higher clearance rates (70–100%) [27, 28], but these represent invasive procedures burdened by possible side effects. Based on the available clinical data, the new treatments could be particularly suitable for children and other sensitive subjects because they are relatively painless in contrast to destructive techniques. Moreover, unlike cryotherapy and aggressive curettage, the risk of scarring is negligible.

Based on the clinical trials, the treatment schedules of the two new products, if approved, will likely consist of a single application to be repeated after 21 days (VP-102), and one application per day for home use for up to 3 months (SB206), respectively. Such treatments, when combined with teledermatology consultations for follow-up, can reduce the number of visits, which is particularly important during pandemic times or in any other environmental limitation that could impair access to medical care services [51].

ACKNOWLEDGEMENTS

Funding. No funding or sponsorship was received for this study or publication of this article.

Author Contributions. Concept and design: FL, GMi, AEV; Literature review: FL, GMi, ACT, AEV; Drafting the manuscript: FL, GMi, ACT, EQ, GMo, AEV; Review and Editing: FL, GMi, ACT, EQ, GMo, AEV.

Disclosures. Authors have nothing to disclose.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- Chen X, Anstey AV, Bugert JJ. Molluscum contagiosum virus infection. *Lancet Infect Dis*. 2013;13(10):877–88.
- Eichenfield L, Hebert A, Mancini A, Rosen T, Weiss J. Therapeutic approaches and special considerations for treating molluscum contagiosum. *J Drugs Dermatol*. 2021;20(11):1185–90.
- Olsen JR, Gallacher J, Piguet V, Francis NA. Epidemiology of molluscum contagiosum in children: a systematic review. *Fam Pract*. 2014;31(2):130–6.
- Rogers M, Barnetson RSC, et al. Diseases of the skin. In: Campbell AGM, McIntosh N, et al., editors. *Forfar and Arneil's textbook of pediatrics*. 5th ed. New York: Churchill Livingstone; 1998. p. 1633–5.
- Bugert J. Genus molluscipoxvirus. *Poxviruses Birkhäuser advances in infectious diseases*. Basel: Birkauser; 2007. p. 89–112.
- Hanna D, Hatami A, Powell J, et al. A prospective randomized trial comparing the efficacy and adverse effects of four recognized treatments of molluscum contagiosum in children. *Pediatr Dermatol*. 2006;23(6):574–9.
- Leung AKC, Barankin B, Hon KLE. Molluscum contagiosum: an update. *Recent Pat Inflamm Allergy Drug Discov*. 2017;11(1):22–31.
- Ku SH, Cho EB, Park EJ, Kim KH, Kim KJ. Dermoscopic features of molluscum contagiosum based on white structures and their correlation with histopathological findings. *Clin Exp Dermatol*. 2015;40:208–10.
- Lacarrubba F, Verzi AE, Dinotta F, Scavo S, Micali G. Dermatoscopy in inflammatory and infectious skin disorders. *G Ital Dermatol Venereol*. 2015;150(5): 521–31.
- Lacarrubba F, Verzi AE, Ardigo M, Micali G. Hand-held reflectance confocal microscopy for the diagnosis of molluscum contagiosum: histopathology and dermoscopy correlation. *Australas J Dermatol*. 2017;58(3):e123–5.
- Scope A, Benvenuto-Andrade C, Gill M, Ardigo M, Gonzalez S, Marghoob AA. Reflectance confocal microscopy of molluscum contagiosum. *Arch Dermatol*. 2008;144(1):134.
- Verzi AE, Micali G, Lacarrubba F. Line-field confocal optical coherence tomography in molluscum contagiosum: a case series. *J Eur Acad Dermatol Venereol*. 2021;35(12):e934–6.
- Broggi G, Verzi AE, Micali G, Caltabiano R, Lacarrubba F. Horizontal histopathology correlates with in vivo reflectance confocal microscopy features of molluscum contagiosum: a case series. *J Cutan Pathol*. 2021;48(11):1430–1.
- Phan S, Wyant C, Huynh C, Joaquin C, Hassan O. Efficacy of topical treatments for molluscum contagiosum in randomized controlled trials. *Clin Dermatol*. 2021;39(6):1005–13.
- Basdag H, Rainer BM, Cohen BA. Molluscum contagiosum: to treat or not to treat? Experience with 170 children in an outpatient clinic setting in the northeastern United States. *Pediatr Dermatol*. 2015;32(3):353–7.
- van der Wouden JC, Menke J, Gajadin S, et al. Interventions for cutaneous molluscum contagiosum. *Cochrane Database Syst Rev*. 2017;5: CD004767.

17. Olsen JR, Gallacher J, Finlay AY, Piguat V, Francis NA. Time to resolution and effect on quality of life of molluscum contagiosum in children in the UK: a prospective community cohort study. *Lancet Infect Dis.* 2015;15(2):190–5.
18. Leung AK. The natural history of molluscum contagiosum in children. *Lancet Infect Dis.* 2015;15(2):136–7.
19. Silverberg N. Pediatric molluscum contagiosum: optimal treatment strategies. *Paediatr Drugs.* 2003;5(8):505–12.
20. Javed A, Coulson I. Molluscum contagiosum. In: Lebwohl MG, Berth-Jones J, Heymann WR, Coulson I, editors. *Treatment of skin disease: comprehensive therapeutic strategies.* 4th ed. Philadelphia: Elsevier-Saunders USA; 2014. p. 460–3.
21. Gerlero P, Hernandez-Martin A. Update on the treatment of molluscum contagiosum in children. *Actas Dermosifiliogr.* 2018;109(5):408–15.
22. Meza-Romero R, Navarrete-Dechent C, Downey C. Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment. *Clin Cosmet Investig Dermatol.* 2019;12:373–81.
23. Sheth PB, Landis MN. Topical and intralesional antiviral agents. In: Wolverson SE, editor. *Comprehensive dermatologic drug therapy.* 3rd ed. Philadelphia: Saunders-Elsevier; 2012. p. 479.
24. Del Rosso JQ, Kircik L. Topical cantharidin in the management of molluscum contagiosum: preliminary assessment of an ether-free, pharmaceutical-grade formulation. *J Clin Aesthet Dermatol.* 2019;12(2):27–30.
25. Edwards S, Boffa MJ, Janier M, et al. 2020 European guideline on the management of genital molluscum contagiosum. *J Eur Acad Dermatol Venereol.* 2021;35(1):17–26.
26. Hughes CM, Damon IK, Reynolds MG. Understanding US healthcare providers' practices and experiences with molluscum contagiosum. *PLoS ONE.* 2013;8(10): e76948.
27. Al-Mutairi N, Al-Doukhi A, Al-Farag S, Al-Haddad A. Comparative study on the efficacy, safety, and acceptability of imiquimod 5% cream versus cryotherapy for molluscum contagiosum in children. *Pediatr Dermatol.* 2010;27(4):388–94.
28. Qureshi A, Zeb M, Jalal-Ud-Din M, Sheikh ZI, Alam MA, Anwar SA. Comparison of efficacy of 10% potassium hydroxide solution versus cryotherapy in treatment of molluscum contagiosum. *J Ayub Med Coll Abbottabad.* 2016;28(2):382–5.
29. Vakharia PP, Chopra R, Silverberg NB, Silverberg JJ. Efficacy and safety of topical cantharidin treatment for molluscum contagiosum and warts: a systematic review. *Am J Clin Dermatol.* 2018;19(6):791–803.
30. Teixido C, Diez O, Marsal JR, et al. Efficacy and safety of topical application of 15% and 10% potassium hydroxide for the treatment of molluscum contagiosum. *Pediatr Dermatol.* 2018;35(3):336–42.
31. Ogilvie-Turner K, Goldman RD. Cantharidin for molluscum contagiosum. *Can Fam Physician.* 2020;66(6):419–20.
32. Forbat E, Al-Niimi F, Ali FR. Molluscum contagiosum: review and update on management. *Pediatr Dermatol.* 2017;34(5):504–15.
33. Eichenfield LF, McFalda W, Brabec B, et al. Safety and efficacy of VP-102, a proprietary, drug-device combination product containing cantharidin, 0.7% (w/v), in children and adults with molluscum contagiosum: two phase 3 randomized clinical trials. *JAMA Dermatol.* 2020;156(12):1315–23.
34. Moye VA, Cathcart S, Morrell DS. Safety of cantharidin: a retrospective review of cantharidin treatment in 405 children with molluscum contagiosum. *Pediatr Dermatol.* 2014;31(4):450–4.
35. Guzman AK, Schairer DO, Garelik JL, Cohen SR. Safety and efficacy of topical cantharidin for the treatment of pediatric molluscum contagiosum: a prospective, randomized, double-blind, placebo-controlled pilot trial. *Int J Dermatol.* 2018;57(8):1001–6.
36. Silverberg NB, Sidbury R, Mancini AJ. Childhood molluscum contagiosum: experience with cantharidin therapy in 300 patients. *J Am Acad Dermatol.* 2000;43(3):503–7.
37. Niazi S, Brabec B, Anschutz L, Willson C, Davidson M, Burnett P. A phase 2 open-label study to evaluate VP-102 for the treatment of molluscum contagiosum. *J Drugs Dermatol.* 2021;20(1):70–5.
38. Eichenfield LF, Kwong P, Gonzalez ME, et al. Safety and efficacy of VP-102 (Cantharidin, 0.7% w/v) in molluscum contagiosum by body region: post hoc pooled analyses from two phase III randomized trials. *J Clin Aesthet Dermatol.* 2021;14(10):42–7.
39. Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two randomized phase III trials evaluating VP-102, a drug-device combination product containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Am J Clin Dermatol.* 2021;22(2):257–65.

40. Maeda-Chubachi T, Hebert D, Messersmith E, Siegfried EC. SB206, a nitric oxide-releasing topical medication, induces the beginning of the end sign and molluscum clearance. *JID Innov.* 2021;1(3): 100019.
41. Hebert AA, Siegfried EC, Durham T, et al. Efficacy and tolerability of an investigational nitric oxide-releasing topical gel in patients with molluscum contagiosum: a randomized clinical trial. *J Am Acad Dermatol.* 2020;82(4):887–94.
42. DeGroot MA, Fang FC. NO inhibitions: antimicrobial properties of nitric oxide. *Clin Infect Dis.* 1995;21(Suppl. 2):S162–5.
43. Miller C, McMullin B, Ghaffari A, et al. Gaseous nitric oxide bactericidal activity retained during intermittent high-dose short duration exposure. *Nitric Oxide.* 2009;20:16–23.
44. Weller R, Price RJ, Ormerod AD, Benjamin N, Leifert C. Antimicrobial effect of acidified nitrite on dermatophyte fungi, *Candida*, and bacterial skin pathogens. *J Appl Microbiol.* 2001;90:648–52.
45. Tyring SK, Rosen T, Berman B, Stasko N, Durham T, Maeda- CT. A phase 2 controlled study of SB206, a topical nitric oxide-releasing drug for extragenital wart treatment. *J Drugs Dermatol.* 2018;17(10): 1100–5.
46. Fang FC. Mechanisms of nitric oxide-related antimicrobial activity. *J Clin Invest.* 1997;99: 2818–25.
47. Belmesk L, Litvinov IV, Netchiporouk E. SB206, a new topical nitric oxide-releasing drug on the horizon for the treatment of molluscum contagiosum and external anogenital warts. *J Cutan Med Surg.* 2020;24(4):412–3.
48. Stasko N, McHale K, Hollenbach SJ, Martin M, Doxey R. Nitric oxide-releasing macromolecule exhibits broad-spectrum antifungal activity and utility as a topical treatment for superficial fungal infections. *Antimicrob Agents Chemother.* 2018;62(7):e01026-17.
49. Browning JC, Enloe C, Cartwright M, et al. Efficacy and safety of topical nitric oxide-releasing berdazimer gel in patients with molluscum contagiosum: a phase 3 randomized clinical trial. *JAMA Dermatol.* 2022. (**Epub ahead of print**).
50. Oza VS. Molluscum contagiosum therapeutics-new options may be around the corner. *JAMA Dermatol.* 2022. (**Epub ahead of print**).
51. Micali G, Dall'Oglio F, Verzi AE, Platania H, Lacarubba F. Home treatment of single cutaneous warts combining face-to-face and teledermatology consultation: a new perspective. *Dermatol Ther.* 2022;35(7): e15528.