Nonmelanoma Skin Cancer and Cutaneous Viral Diseases: An Update

Cutaneous Cancer: Combination Treatment Strategies

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Cutaneous Oncology and Immunomodulator Therapy: From Warts to Skin Cancers

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Molluscum Contagiosum: An Evidence-Based Review

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CME

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TARGET AUDIENCE
This activity was developed for dermatologists and other health care providers who diagnose and treat patients with nonmelanoma skin cancers, molluscum contagiosum, and warts.

EDUCATIONAL NEEDS
Research focusing on the functioning of the immune system at the molecular level continues to provide support for ongoing work in the further development of immune-modifying agents. Among these are biologic agents that block tumor necrosis factor in diseases such as rheumatoid arthritis and psoriasis, as well as immune response modifiers such as systemic interferons and topical imiquimod. This last agent has been approved for the treatment of several cutaneous diseases and is being studied worldwide for its potential applications in a number of others. Dermatologists need to remain up-to-date as the results of both basic research and clinical studies are published. This supplement provides current information about immunomodulators in several viral and malignant skin diseases.
LEARNING OBJECTIVES
By reading and studying this supplement, participants should be able to:
• Name at least three types of immunomodulators and explain the basic mechanisms by which they work to treat diseases.
• Describe the results of studies demonstrating the benefits of immunomodulator therapy in the treatment of nonmelanoma skin cancers and cutaneous viral diseases.
• Discuss the emerging role of topical medical therapy in the treatment of nonmelanoma skin cancers.
• List and describe the treatment options available for molluscum contagiosum.

ACCREDITATION STATEMENT
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Dr Del Rosso has received grant support from Allergan Inc., Amgen Inc., Connetics Corporation, Coria Laboratories Ltd., Doak Dermatologics, Galderma Laboratories, L.P., Graceway Pharmaceuticals, LLC, Medicis Pharmaceutical Corporation, OrthoNeutrogena, Stiefel Laboratories, Inc., and Warner Chilcott. He is a consultant and on the speaker’s bureau of Coria, Doak, Galderma, Graceway, Intendis, OrthoNeutrogena, and Stiefel; he is a consultant to Novartis Pharmaceuticals Corporation and Astellas Pharma Inc. Dr Del Rosso discusses the off-label/investigational uses of imiquimod, 5-fluorouracil, diclofenac, and interferon. Dr Kress is a consultant to and on the speaker’s bureau of Amgen, Connetics, Galderma, Graceway, Novartis, PharmaDerm, and Stiefel. Dr Spencer is on the speaker’s bureau of Graceway. He discusses the off-label/investigational use of imiquimod 5% cream.

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Combination treatments with surgery, radiation, and medical modalities are typically used by oncologists when treating patients with malignancies in general. In the past, dermatologic oncologists have been limited to surgery and radiation as modalities to treat skin cancers. Within the last decade, medical treatments, including topical immunomodulator therapy, have been developed that offer new options for the management of patients with skin cancer. Although each of these three modalities has a role in skin cancer, they are not usually used in combination. This article focuses on the potential for including medical therapy in combination with surgery and radiation therapy.

Presurgical Medical Therapy
When surgery is the definitive treatment of choice for a particular patient, the use of medical therapy first to reduce the size of the tumor may have several advantages; for example, it is possible that the surgery might be more limited than it would otherwise be, and surgical intervention might be more effective.

Theoretically, this would be particularly helpful with nonmelanoma skin cancer, in which postsurgical recurrence is local, not metastatic. This is thought to be the result of subclinical peripheral extensions that are not excised during surgery. A topical medical therapy such as imiquimod, because of its mechanism of action, may eliminate such cancerous areas prior to surgical excision of the tumor. The patient whose photos are shown and described below (Figure 1) is an individual who was treated in our practice, using preoperative topical chemotherapy with imiquimod.

The argument has been made that topical immunomodulator therapy prior to surgery could treat areas in the center of the tumor, thus generating histologic “skip areas.” If a tumor were discontinuous, histologic control would be mitigated or lost because histologically clear margins would not have the same meaning as they would in a continuous lesion.

The counterargument is that any topical antitumor therapy can be expected to work from the periphery of a tumor toward its center, rather than working from the center toward the periphery. Experimental exploration is necessary to resolve this issue.

Postsurgical Medical Therapy
A second scenario in which medical therapy may be helpful to reduce the risk of tumor recurrence is its use following surgical excision. Curettage and desiccation (C&D) is commonly used in the United States for treating nonmelanoma skin cancer. The recurrence rates of basal cell carcinoma (BCC) after

![Figure 1. Postradiation Basal Cell Carcinoma of the Cheek](image)

As an adolescent, this patient had undergone radiation therapy for acne. In subsequent years, she developed a number of skin cancers, including the basal cell tumor shown here on her cheek (left). Surgery was needed to excise a large area, and a rotation graft from her neck was required for wound closure.

For 1 month prior to surgery, this patient used topical imiquimod nightly. A brisk reaction to imiquimod resulted in erosion (2nd from left), which resolved prior to surgery. The area of the tumor that required excision was smaller than it had been before imiquimod therapy (3rd from left). The final photograph (4th from left) shows the area postsurgery.

Source: Courtesy of James M. Spencer, MD, MS.
C&D procedures vary widely according to a tumor’s size, histology, and anatomic location, ranging from 1% to 30%.1,2

For the type of nonmelanoma cancer lesions usually seen in dermatologic practices—that is, uncomplicated BCC 1 cm in diameter, located in low-risk sites such as the shoulder or forehead—the rate of recurrence is estimated to be 5% to 10% at 5 years posttherapy.1,2 Yet, histologic studies have shown that residual tumor is present in 21% to 37% of cases immediately following C&D.3-5 The explanation for this discrepancy has not been determined, but a proposed mechanism is that inflammation from the wound healing process destroys residual cancer cells remaining after mechanical removal of the tumor.

Study of Postsurgical Imiquimod
The possible role of inflammation in the 5-year efficacy of C&D suggested a study of postsurgical imiquimod use. Topical imiquimod’s mechanism of action is the induction of a cascade of cytokines and other inflammatory molecules resulting from a local immune response.

We performed a small randomized, double-blind study of 20 patients with primary nodular BCC of areas on the face and ears. The patients each received three cycles of C&D and were assigned to receive either topical imiquimod (n=10) or placebo (n=10), to be applied nightly for 1 month, beginning the same night after surgery.

The area of tumor was excised 2 months after C&D (thus, 1 month after completion of daily imiquimod or placebo use). Histologic specimens showed that the frequency of residual tumor was dramatically less in the group of patients who received imiquimod than in the control group: only one patient in the active-treatment group had residual tumor cells, whereas residual cells were seen in 4 of 10 patients who received placebo.

Figures 2 and 3 are photographs taken of patients before and after 1-month applications of either imiquimod or placebo.

Additional Observations
In addition to the primary end point of histologic evidence of residual tumor cells, secondary observations were made concerning time to heal and cosmetic appearance.

At the end of 1 month of nightly applications of either imiquimod or placebo (and 2 months postsurgery), all patients were assessed for degree of wound healing. All patients in the control group had complete wound closure, whereas wound healing was delayed in 60% of patients in the imiquimod group. Within a month after cessation of imiquimod applications, all of the patients in the imiquimod group had complete wound closure.

An assessment of cosmetic appearance showed that the surgical sites in the majority of patients in the imiquimod group were flat and slightly pink. In contrast, the majority of patients in the control group had atrophy and hypopigmentation of the wound area. Measurement of the wound areas in the active-treatment group also demonstrated that wound contracture was much less in these patients compared to controls.

Potential Applications
Topical imiquimod following surgery may be helpful for skin cancers associated with a high risk for recurrence. These include morpheaform BCC, squamous cell carcinoma.
The therapeutic benefits of immune modulation treatment in dermatologic diseases derive from either of two basic mechanisms. The first involves inhibiting or downregulating undesirable immune responses—for example, topical calcineurin inhibitors for atopic dermatitis and the tumor necrosis factor-alpha inhibitors, such as etanercept, infliximab, and adalimumab, for psoriasis. The second involves upregulating desirable immune responses—such as systemic therapy with interferon (IFN), or, for anogenital human papillomavirus infections, actinic keratosis (AK), and superficial basal cell carcinoma (BCC), topical therapy with imiquimod.

**Immunomodulator Therapy Overview**

Damage to DNA by ultraviolet (UV) radiation from the sun is a mechanism that has been well studied and well described. The UV-associated carcinogenic changes in the skin include mutations and alterations in the p53 gene, affecting the normal process of apoptosis. Additionally, p16, ras, and a number of other oncogenes also may be involved in cutaneous carcinogenesis resulting from UV radiation exposure.

The most fundamental topical immunomodulator agents are sunscreens and sunblocks. These agents are immune response modifiers in that they protect epidermal cells, including dendritic cells and keratinocytes. Consistent photoprotection has been shown to decrease p53 mutation by 88% to 92%, thus preventing genetic reprogramming of the protected cells.

IFNs, members of a family of naturally occurring glycoproteins, are immunomodulators that also have antiproliferative and antiviral activity. IFN alfa-2b is approved by the US Food and Drug Administration (FDA) for the treatment of high-risk melanoma, and IFN alfa-2a and alfa-2b have been FDA approved for the treatment of Kaposi’s sarcoma associated with human immunodeficiency virus infection and acquired immune deficiency syndrome. In addition, IFN has been used to treat BCC.

Imiquimod, the first topical immune response modifier, is FDA approved for the treatment of anogenital warts, AK, and superficial BCC. When certain conditions exist, this agent upregulates T helper (Th1) type 1 cells, while mediating the innate immune response. First, plasmacytoid dendritic cells must be present. These are usually found in small numbers in normal skin but are upregulated in response to certain disease states. These dendritic cells express toll-like receptor 7, which is the molecule to which imiquimod binds. In addition, a predominant lymphocytic infiltrate must be present that is rich in CD4+ cells and in which natural killer cells make up approximately 25% of the infiltrate. When application of topical imiquimod results in the creation of this milieu (referred to as the “interferon signature”), it works by producing the same immune response that is seen with natural regression of the disease from the host.

**Immunomodulation in BCC**

Studies on the immunopathology of BCC have shown that, untreated, the tumor evades the host response. Histopathologic examinations of BCC tumor samples have demonstrated an insufficient number of Th1 cells at the margins and the absence of lymphocyte-binding receptors on the surface of the tumor. Gaspari and Sauder have shown that the intraleisonal injection of IFN and the topical application of imiquimod both result in the production of the missing lymphocyte-binding receptors, allowing tumor cell apoptosis to occur.

**Imiquimod Treatment Regimens**

The recommended regimens for topical imiquimod—the frequency of application and the duration of the course of therapy—vary according to disease state (Table).

In the treatment of either clinical or subclinical AK, the goal of therapy is to prevent progression of the lesions to squamous cell carcinoma (SCC) in situ or invasive SCC. The regimen approved for the treatment of AK is twice-weekly applications for 16 weeks. However, other regimens have been studied and have been shown to be effective.

**Actinic Keratosis**

In one of the earliest studies of imiquimod therapy in AK, Salasche and colleagues used “cycle therapy.” Areas of treatment were divided into cosmetic units; 33 units were treated in 25 patients: 4 weeks of thrice-weekly imiquimod application.

**TABLE. Suggested Regimens for Use of Topical Imiquimod 5% Cream in Cutaneous Epithelial Malignancy**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinic keratosis</td>
<td>2x/wk</td>
<td>16 wk‡</td>
</tr>
<tr>
<td></td>
<td>3x/wk</td>
<td>6-8 wk†</td>
</tr>
<tr>
<td></td>
<td>3x/wk</td>
<td>Cycle therapy†</td>
</tr>
<tr>
<td>Superficial BCC</td>
<td>5x/wk</td>
<td>6 wk†</td>
</tr>
<tr>
<td>SCC in situ</td>
<td>3x/wk</td>
<td>≤6 wk†</td>
</tr>
</tbody>
</table>

BCC = basal cell carcinoma; SCC = squamous cell carcinoma.
*Regimen approved by US Food and Drug Administration.
†Further study is under way to evaluate regimens/durations of therapy.
‡May extend or repeat therapy.

Source: Courtesy of James Q. Del Rosso, DO.
tions, followed by 4 weeks with no applications. After completion of two cycles of therapy, complete clearance was seen in 82% of cosmetic units. In another study, follow-up 2 years later showed that complete clearance had been maintained in 80% of patients treated with topical imiquimod three times weekly for 12 weeks. These findings support the observation of many authors that imiquimod therapy provides a field effect by treating both visible and subclinical AK lesions, and that, unlike cytotoxic or ablative treatments, imiquimod may stimulate immunologic memory.

**Superficial BCC**

Double-blind clinical trials have been done to evaluate a variety of frequencies of imiquimod application in patients with superficial BCC. Marks and colleagues in Australia and Salasche in the United States evaluated treatment durations of 6 and 12 weeks, respectively. The best results—87.9% clearance in the Australian study and 87.1% clearance in the American study—were obtained with once-daily applications for either 6 or 12 weeks.

Marks et al. and Sterry and colleagues showed that comparable results—that is, a clearance rate of approximately 85%—can be achieved with imiquimod applications five times weekly for 6 weeks. The efficacy of this strategy was demonstrated histologically by excision of treatment sites and careful step sectioning of the specimens, typically performed at 6 weeks posttherapy.

**SCC In Situ**

The potential benefit of imiquimod therapy for SCC in situ was first demonstrated by MacKenzie-Wood et al. in patients with large leg lesions, ranging from 1 to 5.4 cm in diameter. Once-daily applications for 16 weeks resulted in a 93% clearance rate, confirmed by biopsy at 6 weeks post-treatment. In addition, a number of case reports have been published suggesting that topical immunomodulator therapy may be beneficial for SCC in situ at other anatomic sites, including the penis.

Overall, data suggest that every-other-day application over a duration of 6 to 8 weeks often is sufficient. Clinical assessments to determine visible clearance after completion of imiquimod therapy and long-term follow-up are important components of the management plan.

**Other Cutaneous Malignancies**

The use of imiquimod in vulvar intraepithelial neoplasia (VIN) is quite reasonable, given the fact that most patients with VIN have multiple foci of involvement, probably resulting from human papillomavirus infection. In one study of 47 patients, imiquimod application one to three times weekly for 3 to 4 months yielded clinical and histologic remission in 42.5% of cases. These results are not as impressive as those seen with immunomodulator therapy in other conditions. However, it may be that the application frequencies were too limited; a daily or alternate-day application regimen may have yielded better results.

Imiquimod has also been studied in nodular BCC, with some success, but it does not appear to be as consistently effective for this condition. More definitive treatment, including surgery, is appropriate therapy for nodular BCC. Nevertheless, imiquimod may be an option for treating tumors at low-risk sites in patients whose general health status makes them poor surgical candidates. In such cases, daily applications for 12 weeks has been recommended.

Case reports have been published on the use of imiquimod in patients with extramammary Paget’s disease. In these cases, imiquimod was applied daily or every other day for 6 to 8 weeks.
Molluscum Contagiosum: An Evidence-Based Review

Douglas W. Kress, MD

Molluscum contagiosum (MC) is a highly infectious poxvirus that infects the skin and, rarely, the mucous membranes. The estimated incidence of MC in the United States has not been well studied, but a study from the Netherlands showed that 17% of children and teenagers less than 15 years of age had the infection. MC is seen in a bimodal distribution, with most cases occurring in childhood, followed by a sharp drop in incidence during adolescence, then a sharp rise in young adulthood.

Transmission of Infection

Transmission is usually by direct contact—young children sharing a bath, youngsters roughhousing in swimming pools, and contact sports such as wrestling are typical examples. Infection with the MC virus can also occur through fomites, such as shared towels, and by autoinoculation, especially when an individual with pruritic MC lesions (molluscum dermatitis) scratches the skin. In young adulthood, MC infection often is sexually transmitted.

Predisposing Diseases and Drugs

A number of diseases predispose patients to developing larger numbers of MC and a more severe infection. Two of the most common are atopic dermatitis and Darier’s disease.

Patients who are immunosuppressed, including those who have received organ transplants or have leukemia, comprise another population at increased risk for more severe cases of MC. Patients with human immunodeficiency virus (HIV) infection are also at greater risk. In fact, the prevalence of MC infection is also higher in this latter group: an estimated 5% to 18% of patients infected with HIV develop MC.

In a paper published in 1971, topical corticosteroids were implicated as agents that increase the risk for MC infection. However, the association was quite tenuous, and those results have never been confirmed. Some clinicians also believe—erroneously—that the same association exists between MC and immunomodulators. In fact, anecdotal, many clinicians have found that treatment of molluscum dermatitis with either a topical corticosteroid or an immunomodulator makes MC infection itself more amenable to treatment as a result of restoration of normal skin barrier function.

Natural History and Reason to Treat

MC is a benign, self-limited infection. All lesions spontaneously clear within 2 to 4 years. However, this does not mean that patients with MC should not be treated.

With proper treatment, complications may be avoided. These include bleeding, the development of secondary infection such as impetigo, and the development of molluscum dermatitis, which is associated with itching and discomfort. As noted above, scratching can cause lesion spread by autoinoculation. When MC lesions develop around the eyes, chronic keratoconjunctivitis is a potential complication.

In addition, the number of MC lesions that develop usually is associated with the duration of the infection. Treatment that shortens the course of MC infection is likely to reduce the number of lesions a patient might otherwise develop. Brown and colleagues reported that treatment can shorten the course of the disease to about 6 to 8 months (down considerably from about 2 to 4 years). An estimated 7% of untreated lesions resolve with some degree of scarring, so a patient with a long-standing infection may develop a large number of scars. MC lesions also may cause or exacerbate an eczematous rash.

Finally, and not least, MC lesions on exposed areas of the skin—and, particularly, on the face—subject a patient to psychosocial consequences, including embarrassment and social exclusion because of fear of contagion.

Diagnosis

MC lesions (Figure 1) typically appear as smooth, dome-shaped papules 1 to 2 mm in diameter. Often, these will have an erythematous base. Central umbilication is the classic sign of MC but usually is clearly seen only in larger lesions. In early lesions, umbilication may not be readily apparent but may be visible with magnification (with dermoscopy, for example).

The trunk, axillae, antecubital and popliteal fossae, and crural folds are the most common anatomic sites for development of lesions, but they may appear anywhere on the body. When MC occurs in the perianal area, the lesions must be distinguished from condylomata acuminata. Lesions around the eyes may be confused with benign appendageal tumors, including chalazion. Giant molluscum—lesions >2 cm in diameter—may resemble deep fungal infections such as cryptococcosis and histoplasmosis.

When MC lesions are characteristic in appearance and are found in the common anatomic locations, the diagnosis can be made with a Tzanck smear. These classic molluscum contagiosum lesions are on the trunk of a young child. Note the clearly umbilicated lesion (arrow). The molluscum poxvirus resides in the volcano-like center, the site from which a sample should be collected for a Tzanck smear.

Source: Courtesy of Douglas W. Kress, MD, and Shay Jones, PA-C, MEd, MPH.

FIGURE 1. Typical Molluscum Contagiosum Lesions
be made based on those clinical findings. To confirm the clinical diagnosis, a Tzanck preparation can be made of a scraping from the central core of an umbilicated lesion. If present, molluscum bodies—the largest viral body seen in dermatology practice—will be clearly identifiable on microscopic examination. If lesions are not characteristic and/or are in uncommon anatomic locations and if a Tzanck preparation fails to demonstrate molluscum bodies, a biopsy may be indicated.

**Treatment Options**

A number of treatments for MC have been discussed in the literature, and 10 of these strategies will be reviewed briefly here (Table). It should be noted that, to date, no treatment currently available for MC is approved for this indication by the US Food and Drug Administration.

**Watchful waiting** is an option. This strategy costs very little, and no office visits are required. However, the potential consequences of not actively treating MC—as discussed above—make watchful waiting an undesirable choice for most patients.

**Curettage** is undoubtedly an effective treatment for MC. In a case series of 110 children, Kakourou and colleagues demonstrated 100% clearance of lesions with three treatments. However, despite its efficacy, curettage is associated with local bleeding and pain, distinct disadvantages in young patients and in patients of any age who have more than just a few lesions.

**Cryotherapy** is an effective and acceptable therapy, especially on the face, in older children with a small number of lesions. However, it is uncomfortable and may not be tolerated by younger children.

**Cantharidin** is a treatment that is both effective and painless when applied appropriately and carefully. In a study conducted at Children’s Memorial Hospital in Chicago, 90% of 300 patients experienced clearing, 8% improved, only 2% had no response. Cantharidin is painless on application and causes an asymptomatic blister. However, the compound is caustic and is not suitable for home application. It must be applied by a clinician, and so this modality requires office visits. Also, the only lesions that clear are the ones to which cantharidin was applied.

The sites of cantharidin application should be chosen carefully. The trunk and extremities are good locations for treatment, but the face, neck, and any intertriginous areas are not because of the risk that cantharidin will spread beyond the center of the treated lesions and cause blistering of noninfected skin.

**Imiquimod 5% cream** as monotherapy for molluscum has yielded promising results in some studies. In a study of 15 patients, 8 (53%) achieved complete clearance of lesions using imiquimod once daily five times per week. Four other patients (27%) had a 50% reduction in lesions. In the subset of children in the study (n=7), six (86%) had complete regression of lesions. In a placebo-controlled study by Theos and colleagues, 33% of patients had complete clearance and 67% had partial response (vs 9% and 18%, respectively, in the control group)—a large, though not statistically significant, difference.

Because of imiquimod’s mechanism of action, which induces local immune responses, local inflammation is an expected reaction. Usually, the resulting erythema is mild and well tolerated. In the study by Hengge and colleagues, almost one third of patients reported erythema, although only one patient withdrew from the study. As a result of its mechanism of action, imiquimod stimulates dendritic cells to produce interferon alpha. Although it is well documented that systemic administration of interferons can cause side effects such as malaise and fever, topical administration of imiquimod has rarely been associated with such side effects. The most recently reported association was a case report of fever in a child treated with imiquimod.

**Tretinoin cream** has been mentioned as potentially useful for treating MC, although no controlled efficacy and safety trials have been done. Nevertheless, tretinoin may be helpful, particularly for treating areas of the body that are cosmetically sensitive—such as the face—where cantharidin use may not be advisable.

**TABLE. Treatment Options for Molluscum Contagiosum**

- Watchful waiting
- Curettage
- Cryotherapy
- Cantharidin
- Imiquimod 5% cream
- Tretinoin cream
- Pulsed dye laser
- Salicylic acid gel
- Cimetidine
- Combination therapy: cantharidin + imiquimod

**FIGURE 2. Severe Cantharidin Reaction**

This baby had multiple molluscum lesions on the neck that were treated with cantharidin. Excessive drooling caused the cantharidin to spread to surrounding tissue, causing a severe reaction.

Source: Courtesy of Douglas W. Kress, MD, and Shay Jones, PA-C, MEd, MPH.
Pulsed dye laser also has been discussed in the literature as an effective therapy for MC. However, this modality is costly, unlikely to be covered by health insurance plans, and, because it can cause some discomfort, may require the use of general anesthesia when being used in pediatric patients. However, pulsed dye laser is dramatically effective for MC, resulting in 100% clearance and no permanent scarring, so it is an option for children with multiple lesions who do not respond to other therapies.

Salicylic acid gel. 12%, was reported as 87% effective within 6 months (that is, complete clearance) in one placebo-controlled trial, although this dramatic result must be considered in relation to the results in the control group: 60% of patients who used vehicle only also had complete clearance. This compound is available over the counter, is reasonably effective, and is well tolerated. However, clearance of lesions may require many months of use.

Cimetidine has been studied in a limited way in MC, and the results of these clinical trials are equivocal. In one of these studies, although this dramatic result must be considered in 6 months (that is, complete clearance) in one placebo-controlled trial, 25 although this dramatic result must be considered in relation to the results in the control group: 60% of patients who used vehicle only also had complete clearance. This compound is available over the counter, is reasonably effective, and is well tolerated. However, clearance of lesions may require many months of use.

Combination therapy with cantharidin plus imiquimod was shown to be effective in a series of 16 pediatric patients with MC. 24 The investigators applied cantharidin once a week, followed by topical imiquimod 5% cream daily for 5 weeks. According to the published study, 73% of patients had at least 90% clearance of MC lesions. These results are encouraging and deserve further study.

Conclusion

A number of treatment strategies have been tried in MC, several with good success and others with varying degrees of limited utility, either because of lack of efficacy or because of other disadvantages, including side effects, high cost, or the need for long duration of treatment. The choice of modality should be age-appropriate; the other main factors to consider are the number of lesions present and their anatomic location. Several of the modalities discussed—in particular, pulsed dye laser and cimetidine—should be reserved for cases in which other therapies have failed.

Acknowledgement

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ma, lentigo maligna of the face (associated with a recurrence rate of 10% to 20% following surgery alone6), and extramammary Paget’s disease (recurrence rate of 40% after surgery alone5). In addition, topical imiquimod may be helpful for reducing the 50% rate of recurrence following surgical excision of keloids. A pilot study by Berman and Kaufman7 in 11 patients with keloids showed no recurrence of keloids when a course of topical imiquimod was used following surgical excision.

Conclusion
Our study of 20 patients with BCC demonstrated that topical imiquimod, applied nightly for 1 month immediately following C&D, resulted in a substantially decreased frequency of residual tumor, a longer healing time, and an improved cosmetic appearance compared with placebo.

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12 weeks. With further study, a role may be established for topical immunomodulator therapy in this condition. Meanwhile, such treatment should be approached cautiously and should be undertaken as part of a multidisciplinary strategy for evaluation and therapy.

Finally, a few studies and case reports discuss the use of imiquimod in patients with lentigo maligna, showing some benefit. However, more data are needed to evaluate the efficacy of topical imiquimod therapy in this condition.

Conclusion
The topical immune response modifier imiquimod has proved to be effective for the treatment of AK and several cutaneous malignancies. To date, imiquimod is FDA approved for the treatment of AK, superficial BCC, and anogenital warts. In addition to a large body of data supporting the approved treatment regimens, a number of studies have been published providing evidence that alternative regimens also may be useful, depending on the condition treated. Further, studies have been published demonstrating the utility of topical immunomodulator therapy in other conditions, including VIN and extramammary Paget’s disease.

References
9. Sterry W, Bichel J, Andres K, Ginkel AM. Imiquimod 5% cream for 6 weeks with occlusion treating superficial BCC. Presented at: 8th World Congress on Cancers of the Skin; July 18-21 2001; Zurich, Switzerland.
**Skin & Allergy News**

**Nonmelanoma Skin Cancer and Cutaneous Viral Diseases: An Update**

**CME POST-TEST and EVALUATION**

**Release Date:** July 2007  
**Expiration Date:** July 31, 2008  
**Estimated Time to Complete This Activity:** 1 hour

This supplement to *Skin & Allergy News* provides 1 free AMA PRA Category 1 Credit.™ To receive credit, log on to www.elseviercmce.com/getcme/2M3MVS7 to print your certificate or forward the Post-Test Answer Sheet and Evaluation Form to: Elsevier Office of Continuing Medical Education (EOCME), Department 2M3MVS7, 685 Route 202/206, Bridgewater, NJ 08807 FAX: (800) 201-7217. Please allow 6 to 8 weeks for processing.

**Instructions:** For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate response. Six of eight responses are required for credit.

1. ________ is an agent that upregulates desirable immune responses.
   a. Adalimumab  
   b. Infliximab  
   c. Imiquimod  
   d. Pimecolimus

2. In “cycle therapy,” as described by Salasche, a cycle is defined as 4 weeks of __________ applications of topical imiquimod followed by a 4-week rest period off therapy.
   a. Once-daily  
   b. Once-weekly  
   c. Thrice-daily  
   d. Thrice-weekly

3. Among other findings, histopathologic examinations of basal cell carcinoma (BCC) tumor specimens have demonstrated the absence of lymphocyte-binding receptors on the surface of the tumor. Intralymphosomal interferon injection and topical imiquimod applications both result in the production of the missing lymphocyte-binding receptors, which:
   a. Allows tumor cell apoptosis to occur  
   b. Causes a systemic immune response  
   c. Increases the number of dendritic cells  
   d. Results in upregulation of tumor necrosis factor

4. All but one of the following statements are true regarding postsurgical recurrence of nonmelanoma skin cancer. The exception is:
   a. Skin cancer is thought to recur because of peripheral extensions that are not excised during surgery.  
   b. Recurrence is always inevitable.  
   c. Recurrence is local.  
   d. Recurrence is the result of metastases.

5. An estimated 7% of untreated molluscum contagiosum (MC) lesions:
   a. Develop secondary infection such as impetigo  
   b. Heal spontaneously  
   c. Heal with scarring  
   d. Persist for longer than 5 years

6. For uncomplicated BCC less than 1 cm in diameter and located in low-risk sites (e.g., the shoulder or forehead), histologic studies have shown that residual tumor is present in 21% to 37% of cases immediately following curettage and desiccation. The rate of recurrence for these lesions is estimated to be ____ at 5 years posttherapy.
   a. 1%–5%  
   b. 5%–10%  
   c. 15%–25%  
   d. 35%–40%

7. In young adults, MC often is ________.
   a. More severe than in younger patients  
   b. Seen in an atypical anatomic distribution  
   c. Sexually transmitted  
   d. Subclinical

8. Good evidence has been published confirming that three of the four following choices are associated with an increased risk for the development of MC, for larger numbers of MC lesions, and/or a more severe case of MC. The exception is:
   a. Atopic dermatitis  
   b. Darier’s disease  
   c. Human immunodeficiency virus  
   d. Topical corticosteroids

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**Objective #4:**
List and describe the treatment options available for molluscum contagiosum.

1  2  3  4  5

How do you rate the overall quality of the activity?  
1  2  3  4  5

How do you rate the educational content of the activity?  
1  2  3  4  5

After participation in this activity, have you decided to change one or more aspects in the treatment of your patients? ____Yes ____ No

If yes, what change(s) will you make?

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Was the presented information fair, objective, balanced, and free of bias in the discussion of any commercial product or service? ____Yes ____ No

If no, please comment:

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Suggested topics for future activities:

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Suggested authors for future activities:

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Would you be willing to participate in post-activity follow-up surveys? ____Yes ____ No

Would you be willing to participate in a phone, e-mail, or in-person discussion exploring ways to improve our CME activities? ____Yes ____ No

The EOCME thanks you for your participation in this CME activity.

All information provided improves the scope and purpose of our programs and your patients’ care.

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