Topical pharmacotherapy for skin cancer

Part II. Clinical applications

Giuseppe Micali, MD,[a] Francesco Lacarrubba, MD,[a] Maria Rita Nasca, MD, PhD,[a] Salvatore Ferraro, MD,[a] and Robert A. Schwartz, MD, MPH[b]
Catania, Italy, and Newark, New Jersey

CME INSTRUCTIONS

The following is a journal-based CME activity presented by the American Academy of Dermatology and is made up of four phases:

1. Reading of the CME Information (delineated below)
2. Reading of the Source Article
3. Achievement of a 70% or higher on the online Case-based Post Test
4. Completion of the Journal CME Evaluation

CME INFORMATION AND DISCLOSURES

Statement of Need:
The American Academy of Dermatology bases its CME activities on the Academy's core curriculum, identified professional practice gaps, the educational needs which underlie these gaps, and emerging clinical research findings. Learners should reflect upon clinical and scientific information presented in the article and determine the need for further study.

Target Audience:
Dermatologists and others involved in the delivery of dermatologic care.

Accreditation
The American Academy of Dermatology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AMA PRA Credit Designation
The American Academy of Dermatology designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AAD Recognized Credit
This journal-based CME activity is recognized by the American Academy of Dermatology for 1 AAD Credit and may be used toward the American Academy of Dermatology's Continuing Medical Education Award.

Disclaimer:
The American Academy of Dermatology is not responsible for statements made by the author(s). Statements or opinions expressed in this activity reflect the views of the author(s) and do not reflect the official policy of the American Academy of Dermatology. The information provided in this CME activity is for continuing education purposes only and is not meant to substitute for the independent medical judgment of a healthcare provider relative to the diagnostic, management and treatment options of a specific patient's medical condition.

Disclosures

Editors
The editors involved with this CME activity and all content validation/peer reviewers of this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors
The authors of this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Planners
The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Resolution of Conflicts of Interest
In accordance with the ACCME Standards for Commercial Support of CME, the American Academy of Dermatology has implemented mechanisms, prior to the planning and implementation of this Journal-based CME activity, to identify and mitigate conflicts of interest for all individuals in a position to control the content of this Journal-based CME activity.

Learning Objectives
After completing this learning activity, participants should be able to describe the evidence supporting the use of topical therapies in the treatment of skin cancers, including actinic keratosis, basal cell carcinoma, Bowen disease, erytroplasia of Queyrat, extramammary Paget disease, lentigo maligna and melanoma metastases and identify topical skin cancer therapies that are appropriate for specific clinical indications.

Date of release: June 2014
Expiration date: June 2017

http://dx.doi.org/10.1016/j.jaad.2013.12.037

Technical requirements:

American Academy of Dermatology:
- Supported browsers: FireFox (3 and higher), Google Chrome (5 and higher), Internet Explorer (7 and higher), Safari (5 and higher), Opera (10 and higher).
- JavaScript needs to be enabled.

Elsevier:
Technical Requirements
This website can be viewed on a PC or Mac. We recommend a minimum of:
- PC: Windows NT, Windows 2000, Windows ME, or Windows XP
- Mac: OS X
- 128MB RAM
- Processor speed of 500MHz or higher
- 800x600 color monitor
- Video or graphics card
- Sound card and speakers

Provider Contact Information:
American Academy of Dermatology
Phone: Toll-free: (866) 503-SKIN (7546); International: (847) 240-1280
Fax: (847) 240-1859
Mail: P.O. Box 4014; Schaumburg, IL 60168

Confidentiality Statement:

American Academy of Dermatology: POLICY ON PRIVACY AND CONFIDENTIALITY

Privacy Policy - The American Academy of Dermatology (the Academy) is committed to maintaining the privacy of the personal information of visitors to its sites. Our policies are designed to disclose the information collected and how it will be used. This policy applies solely to the information provided while visiting this website. The terms of the privacy policy do not govern personal information furnished through any means other than this website (such as by telephone or mail).

E-mail Addresses and Other Personal Information - Personal information such as postal and e-mail address may be used internally for maintaining member records, marketing purposes, and alerting customers or members of additional services available. Phone numbers may also be used by the Academy when questions about products or services ordered arise. The Academy will not reveal any information about an individual user to third parties except to comply with applicable laws or valid legal processes.

Cookies - A cookie is a small file stored on the site user's computer or Web server and is used to aid Web navigation. Session cookies are temporary files created when a user signs in on the website or uses the personalized features (such as keeping track of items in the shopping cart). Session cookies are removed when a user logs off or when the browser is closed. Persistent cookies are permanent files and must be deleted manually. Tracking or other information collected from persistent cookies or any session cookie is used strictly for the user's efficient navigation of the site.

Links - This site may contain links to other sites. The Academy is not responsible for the privacy practices or the content of such websites.

Children - This website is not designed or intended to attract children under the age of 13. The Academy does not collect personal information from anyone it knows is under the age of 13.

Elsevier: http://www.elsevier.com/wps/find/privacypolicy.cws_home/privacypolicy

The purpose of the paper is to provide an in-depth, evidence-based analysis of the clinical use of topical treatments for skin cancer. A comprehensive review of topical drugs has been performed, including 5-fluorouracil, imiquimod, diclofenac, ingenol mebutate, retinoids, resiquimod, piroxicam, dobesilate, and betulinic acid. The evaluated studies were rated according to their level of evidence level (I-V), as indicated by recent guidelines for evidence-based medicine, *The Oxford 2011 Levels of Evidence*. Therapeutic response is generally related to tumor type, extent, and localization, and also to patient compliance. Careful patient selection is required in order to achieve the desired goal of complete tumor clearance. (J Am Acad Dermatol 2014;70:979.e1-12.)

Key words: actinic keratosis; basal cell carcinoma; Bowen disease; erythroplasia of Queyrat; lentigo maligna; melanoma; Paget disease; skin cancer; squamous cell carcinoma; topical treatment.

INTRODUCTION

The incidence of skin cancer is increasing worldwide, with >2 million cases diagnosed in the United States per year.[1] Surgical or invasive procedures represent the main approach, but noninvasive, tissue-sparing, topical self-administered treatments may be a highly desirable alternative, both in aged and unhealthy patients (who may be poor surgical candidates) and in relatively young subjects with lesions located on cosmetically sensitive areas and who wish to avoid disfiguring scars.[2]

The purpose of this review is to evaluate the effectiveness of topical treatments of skin cancer according to evidence-based medicine guidelines. The mechanism of action, formulations, indications, side effects, and contraindications of these drugs were analyzed in part I of this continuing medical education article.

All studies evaluating topical treatments for skin cancer published in the English literature between January 1960 and June 2013 were analyzed. To accomplish this, an electronic search was performed using the National Library of Medicine PubMed database of the National Institutes of Health and the Ovid MEDLINE database using the phrase "topical treatment" in combination with 1 of the following terms: "skin cancer," "actinic keratosis," "basal cell carcinoma," "squamous cell carcinoma," "Bowen disease," "erythroplasia of Queyrat," "Paget disease," and "melanoma." In addition, pertinent references not identified by search engines and retrieved from articles and books were also considered. All studies identified as relevant were analyzed, including metaanalyses, systematic reviews, clinical trials, controlled studies, and case reports. Evaluated studies were rated according to recent modified guidelines for evidence-based medicine, *The Oxford 2011 Levels of Evidence*,[3] as follows: level of evidence I, systematic review of randomized trials; II, randomized trial or observational study with dramatic effect; III, nonrandomized controlled cohort/follow-up study; IV, case series, case control studies, or historically controlled studies; and V, mechanism-based reasoning.

Abbreviations used:

5-FU:	5-fluorouracil
AK:	actinic keratosis
BCC:	basal cell carcinoma
BD:	Bowen disease
DHA:	diclofenac 3% gel in 2.5% hyaluronic acid
EPD:	extramammary Paget disease
EQ:	erythroplasia of Queyrat
IM:	ingenol mebutate
IQ:	imiquimod
LM:	lentigo maligna
RQ:	resiquimod
SC:	solar cheilosis

ACTINIC KERATOSES

Key points

- **In the management of multiple actinic keratoses, topical therapy should be preferred to more destructive and/or invasive treatments in consideration of the field effect, which allows treatment of both visible and subclinical lesions**
- **A Cochrane review concluded that, among field-directed treatments, 5-fluorouracil, imiquimod, diclofenac 3% gel in 2.5% hyaluronic acid, and ingenol mebutate showed similar efficacy with different adverse events and cosmetic outcomes, and more direct comparisons between these treatments are needed to determine the best efficacy profile**

From the Dermatology Clinic,[a] University of Catania, Italy, and the Department of Dermatology,[b] Rutgers University, New Jersey Medical School, Newark.

Funding sources: None.
Conflicts of interest: None declared.

Reprint requests: Giuseppe Micali, MD, Dermatology Clinic, University of Catania, A.O.U. Policlinico-Vittorio Emanuele, Via Santa Sofia, 78 - 95123, Catania, Italy. E-mail: cldermct@nti.it.

0190-9622/$36.00