REPORTS

Guidelines for phototherapy of mycosis fungoides and Sézary syndrome: A consensus statement of the United States Cutaneous Lymphoma Consortium

Elise A. Olsen, MD,[a] Emilia Hodak, MD,[b] Thomas Anderson, MD,[c] Joi B. Carter, MD,[d] Marsha Henderson, MD,[e] Kevin Cooper, MD,[f] and Henry W. Lim, MD[e]
Durham, North Carolina; Tel Aviv, Israel; Ann Arbor and Detroit, Michigan; Boston, Massachusetts; and Cleveland, Ohio

Background: Ultraviolet light (UVL) is a long established treatment for mycosis fungoides (MF) and Sézary syndrome (SS), subtypes of cutaneous T-cell lymphoma (CTCL). Treatments have traditionally included broadband, narrowband ultraviolet B light (UVB) and psoralen plus ultraviolet A light photochemotherapy (PUVA), but more recently, treatment options have expanded to include UVA1 and excimer laser. UVL is used either as monotherapy or as an adjuvant to systemic therapy, demonstrating efficacy in many cases that equal or surpass systemic medications. Despite its utility and duration of use, the current practice of using UVL guidelines for psoriasis to treat patients with MF/SS is problematic because the goals of prolonging survival and preventing disease progression are unique to CTCL compared to psoriasis.

Objectives: We sought to develop separate guidelines for phototherapy for MF/SS for both clinical practice and for clinical trials.

Methods: Literature review and cutaneous lymphoma expert consensus group recommendations.

Results: This paper reviews the published literature for UVB and UVA/PUVA in MF/SS and suggests practical standardized guidelines for their use.

Limitations: New standardization of phototherapy.

Conclusions: These guidelines should allow the comparison of results with phototherapy in MF/SS across different stages of patients, centers, and in combination with other agents in practice and in clinical trials. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.09.033.)

Key words: cutaneous T-cell lymphoma; phototherapy; PUVA; mycosis fungicides; NB-UVB; Sézary syndrome; UVL.

From the Departments of Dermatology and Medicine,[a] Duke University Medical Center, Durham; Department of Dermatology,[b] Rabin Medical Center, Beilinson Hospital, Sackler Faculty of Medicine, Tel Aviv University; Department of Dermatology,[c] University of Michigan, Ann Arbor; Department of Dermatology,[d] Massachusetts General Hospital, Boston; Department of Dermatology,[e] Henry Ford Hospital, Detroit; and Department of Dermatology,[f] Case Western Reserve University, Cleveland.

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These guidelines were developed specifically by members of the United States Cutaneous Lymphoma Consortium based on the need for education and standardization of phototherapy treatment for mycosis fungoides and Sézary syndrome without relevant conflicts of interest by authors and without outside support. Nonetheless, they should not be considered to be sponsored or endorsed by the American Academy of Dermatology because they were not prepared under the American Academy of Dermatology guidelines.

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Correspondence to: Elise A. Olsen, MD, Box 3294, Duke University Medical Center, Durham, NC 27710. E-mail: elise.olsen@dm.duke.edu.

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INTRODUCTION

Background

Ultraviolet light (UVL)–based therapy, specifically, ultraviolet B light (UVB) phototherapy and psoralen plus ultraviolet A light (PUVA) photochemotherapy, has been a mainstay of treatment of mycosis fungoides (MF) for the past 50 years. Initially, it was used exclusively as monotherapy, but more recently it has been commonly used as part of a multimodality therapeutic regimen. Its efficacy is beyond dispute, but how to best harness this while minimizing side effects has yet to be fully determined.

CAPSULE SUMMARY

- There are no disease-specific guidelines for phototherapy used to treat mycosis fungoides and Sézary syndrome (MF/SS) despite the fact that efficacy in many cases equals or surpasses that of systemic medications.
- This paper reviews the published literature for safety and efficacy of UVB and UVA/PUVA in MF/SS and suggests standardized guidelines for their use.
- These guidelines should enhance patient care and allow the comparison of results with phototherapy in MF/SS across sites and studies.

The United States Cutaneous Lymphoma Consortium (USCLC) is a multidisciplinary group of physicians whose mission is to advance the care of patients with cutaneous lymphoma, either through the establishment of standards for clinical care or clinical research or through collaborative basic or clinical research. This paper reviews the literature on the efficacy and safety of the various types of UVL used to treat MF and its leukemic counterpart, Sézary syndrome (SS), and with the addition of expert opinion, the USCLC hopes to accomplish the following:

a. Develop standardized guidelines for phototherapy, including photochemotherapy, of MF/SS patients seen in practice settings
b. Enable the capture and analysis of accurate efficacy data on phototherapy in MF/SS at multiple sites through standardization of treatment
c. Accurately attribute and track side effects of phototherapy in MF/SS using standardized treatment protocols
d. Narrow the variables of phototherapy used in clinical trials of MF to allow collation of results between centers and comparison of results across sites and studies
e. Assist in the development of clinical performance measures in MF/SS

Types of UVL

The International Congress on Light in 1932 defined the components of UVL as follows: ultraviolet A (UVA) as 315 to 400 nm, UVB as 280 to 315 nm, and ultraviolet C (UVC) as 10 to 280 nm.[1] However, the convention in photobiology has been to divide UVL into subcategories based on biologic effect (ie, UVA, 320-400 nm; UVB, 290-320 nm; and UVC, 200-290 nm).[2-4] Because UVC is absorbed in the atmosphere, the clinically relevant electromagnetic radiation emitted by the sun as it reaches the surface of the earth consists of UVB (5%) and UVA (95%).[3] Because of its biologic properties, UVA is further subdivided into UVA1 (340-400 nm) and UVA2 (320-340 nm). The biologic effect of shorter wavelength UVA2 is closer to UVB (ie, it is more likely to induce erythema than tanning). UVA1 is now used to treat various skin conditions, including MF.[5]

Broadband UVB (BB-UVB) units available in clinical practice emit broadly between 270 and 390 nm, with a peak at 313 nm. Narrowband UVB (NB-UVB) refers to a radiation source with a sharp emission peak between 311 and 312 nm. Although BB-UVB therapy was widely used in the past, currently the vast majority of UVB therapy delivered around the world is in the form of NB-UVB.

There are other forms of phototherapy. The excimer xenon chloride laser emits at 308 nm.[6] In addition, the combination of psoralen, which sensitizes the patient to UVA, followed by UVA exposure is a form of photochemotherapy referred to by the acronym PUVA. For the purposes of our discussion, we will include photochemotherapy under the umbrella of the term phototherapy. Phototherapy with BB-UVB, NB-UVB, UVA1, PUVA, BB-UVA, and the excimer laser have all demonstrated efficacy in the treatment of MF.

The effect of UVL, either as monotherapy or adjuvant therapy, on the various stages of MF/SS, is multifactorial and is different for UVB and UVA. For a given dose, UVB at 300 nm is approximately 1000-fold more erythemogenic compared to UVA at 360 nm.[4] However, because of its shorter wavelength, UVB is primarily absorbed in the epidermis with less ability to penetrate beyond it compared to UVA.[4,7] Therefore, the primary direct effects of UVB are on the epidermal keratinocytes, Langerhans cells (LCs), follicular infundibulum, and any cells in the upper dermis, including lymphocytes. In contradistinction, UVA, particularly UVA1, is able to