MELANOMA CARE
OPTIONS

ISSUE NO. 6 JULY 2005

FOSTERING AN INTERDISCIPLINARY APPROACH TO MELANOMA CARE

WAIT!
Don't open this newsletter yet!

Before breaking the seal, see how your melanoma management style compares to the styles of experts in the field by following these simple instructions:

- Read the case presentation below
- Circle your answers to the multiple-choice questions on the back cover
- Detach the perforated back page and fax your answers to 973-682-9077

Or, if you prefer, you can answer the questions and read the article on our Web site at www.MelanomaCare.org, where you can also complete CME materials and register for electronic delivery of *Melanoma Care Options*.

A 53-Year-Old Man With Melanoma on the Back

Peter K. Lee, MD, PhD and Jeffrey J. Sussman, MD, FACS

A 53-year-old white man presented with a changing pigmented lesion on his right upper back. As often happens with lesions on the posterior of the body, its abnormal appearance was first noted by the patient's spouse 3 months prior. The patient complained of mild pruritus in the affected area and no other local symptoms. Otherwise, he appeared generally healthy, with mild hypertension. At the time of the initial visit, the patient was taking low-dose aspirin and a beta-blocker. Although the patient denied a family history of melanoma, his personal history revealed 2 previous atypical nevi biopsies. He did not use tanning booths but had many severe sunburns in the past. Physical examination revealed a 1.8-cm by 1.6-cm, slightly elevated, pigmented lesion with irregular borders and variegated pigmentation. No lymphadenopathy was noted in potential draining basins nor were there any other suspicious lesions on full body skin survey or contributory findings.

Subsequent biopsy and pathologic analysis revealed superficial spreading melanoma with the following features:

- Breslow depth of 0.79 mm
- Clark level III/IV (later verified as level IV)
- No ulceration
- No regression
- Mitotic rate: 0

Before continuing, please answer the questions on the back cover and fax to 973-682-9077.

Editorial

Dear Reader,

Welcome to ***Melanoma Care Options,*** an interactive newsletter that will put you in the driver's seat. In this newsletter, we describe a case presentation and you will tell us how you would handle it, using the fax-back form on the back of the newsletter. Then read the newsletter to see what the experts from the **Melanoma Care Consortium** had to say. In a future issue we'll present an analysis of what physicians like you decided and how your answers compared to the opinions of our faculty. The cases will come every month for 8 months, so you will have ample opportunity to cast your vote on melanoma cases across the disease spectrum.

Thank you for taking part in this vital and innovative program. We look forward to your input regarding this and the cases to come.

Sincerely,

John M. Kirkwood, MD
Chairman, **Melanoma Care Consortium** Steering Committee

Editorial

The case presented in this issue of ***Melanoma Care Options*** focuses on a 53-year-old man with a thin primary cutaneous melanoma. Although appearing simple and straightforward, this case raises care issues that are important to dermatologists, family practitioners, and other primary care physicians who are often the initial and only physicians treating patients with thin melanoma. In particular, this case presents key decision points that clinicians face when managing the variety of patients with thin melanoma. As part of the management process, physicians must decide on the type of diagnostic and therapeutic biopsies, relative value of sentinel lymph node biopsy (SLNB), suitability of post-staging follow-up studies, necessity or not of adjuvant therapy, and appropriate follow-up. This newsletter discusses the factors that influence these choices, many of which surround the risk of relapse, metastasis, and mortality following surgical excision as well as novel patient- and tumor-related factors that may negatively impact a patient's prognosis. As the number of patients with thin melanomas continues to rise, physicians will increasingly require a thorough understanding of the management of this important disease. We look forward to hearing your thoughts as you consider this case.

Peter K. Lee, MD, PhD

This newsletter is published by PharmAdura, LLC, Pearl River, NY.

STEERING COMMITTEE

Publisher
PharmAdura, LLC
170 Fairview Avenue
Pearl River, NY 10965
845-641-3859
publisher@pharmadura.com

Editor
Andrea Dolce-Singer

Scientific Director
Lisa Faltyn, PhD

Art Director
Meridith Feldman

The Melanoma Care Consortium

The Steering Committee and Content Committee. Pictured from left to right: Rebecca Ferrini, MD; Douglas S. Reintgen, MD; Rosemary Giuliano, ARNP, MSN; John M. Kirkwood, MD; Merrick I. Ross, MD; Ashfaq A. Marghoob, MD, FAAD. Not shown: Susan M. Swetter, MD.

Faculty

Bruce J. Averbook, MD
Associate Professor of Surgery
Metro Health Medical Center
Case Western Reserve University
Cleveland, Ohio
**Speakers' Bureau, Schering Oncology Biotech*

Matthew T. Ballo, MD
Associate Professor of Radiation Oncology
University of Texas
M.D. Anderson Cancer Center
Houston, Texas
**Consultant, IMPAC Medical Systems*

Kathleen A. Bixby, RN, BSN, OCN
Oncology Nurse Care Coordinator
Melanoma Center
Washington Cancer Institute
Washington Hospital Center
Washington, DC
**Speakers' Bureau, Schering Oncology*

Heather Blair, RN, BSN
Clinical Research Coordinator
University of Pittsburgh
Pittsburgh, Pennsylvania
**No financial relationships to disclose*

Ernest C. Borden, MD
Director
Center for Cancer Drug Discovery & Development
Cleveland Clinic Cancer Center and Lerner Research Institute
The Cleveland Clinic Foundation
Cleveland, Ohio
**Grant/Research Support, Immunicon, Igencon, Med, Amgen and Consultant, Coley Pharmaceuticals*

Tania Bridgeman, RN, PhD
Director of Clinical Path Development
University of California
Irvine Medical Center
Orange, California
**No financial relationships to disclose*

John Carucci, MD, PhD
Director
Mohs Micrographic and Dermatologic Surgery
Weill Medical College
Cornell University
New York, New York
**No financial relationships to disclose*

Marc S. Ernstoff, MD
Professor of Medicine
Dartmouth-Hitchcock Medical Center
Lebanon, New Hampshire
**Grant/Research Support, Chiron Inc., Point Therapeutics, Pfizer, Inc.*

Peggy S. Esper, MSN, RN, CS,AOCN
Oncology Nurse Practitioner
University of Michigan
Ann Arbor, Michigan
**Speakers' Bureau, Genentech, Schering-Plough Corporation, Merck, MGI Pharmaceuticals*

Richard Essner, MD
Director of Molecular Therapeutics
Assistant Director of Surgical Oncology
John Wayne Cancer Institute
Santa Monica, California
**No financial relationships to disclose*

Lawrence E. Flaherty, MD
Professor of Medicine and Oncology
Karmanos Cancer Institute
Wayne State University
Detroit, Michigan
**Grant/Research Support, Schering-Plough Corporation, Chiron Therapeutics, Celgene, Bristol-Myers Squibb; Speakers' Bureau, Schering-Plough Corporation*

Larisa J. Geskin, MD
Assistant Professor of Dermatology
Director, Cutaneous Oncology Center
University of Pittsburgh
Pittsburgh, Pennsylvania
**No financial relationships to disclose*

James S. Goydos, MD, FACS
Associate Professor of Surgical Oncology
Robert Wood Johnson Medical School
Cancer Institute of New Jersey
New Brunswick, New Jersey
**Speakers' Bureau, Schering-Plough Corporation*

Caron M. Grin, MD
Professor of Dermatology
University of Connecticut Health Center
Farmington, Connecticut
**Speakers' Bureau, Schering-Plough Corporation*

Denise L. Johnson, MD
Associate Professor of Surgery
Stanford University Medical Center
Stanford, California
**No financial relationships to disclose*

Mohammed Kashani-Sabet, MD
Associate Professor of Dermatology
Director, Melanoma Center
UCSF Cancer Center
University of California
San Francisco School of Medicine
San Francisco, California
**Consultant, CancerVax Corporation; Speakers' Bureau, Schering-Plough Corporation*

Peter K. Lee, MD, PhD
Assistant Professor of Dermatology
University of Minnesota
Minneapolis, Minnesota
**Grant/Research Support, 3M Pharmaceuticals; Consultant, 3M Pharmaceuticals; Speakers' Bureau, Schering Oncology*

Patricia K. Long, MSN, FNP-C
Nurse Practitioner, Surgical Oncology
University of North Carolina
Chapel Hill, North Carolina
**No financial relationships to disclose*

Charlene Love, RN, BSN
Melanoma Research Nurse Coordinator
Wagner & Associates Plastic and Reconstructive Surgery Consultants of Indiana
Indianapolis, Indiana
**No financial relationships to disclose*

Maryellen Maguire-Eisen, RN, CS, MSN, OCN
Executive Director
Sun Protection Foundation
Hingham, Massachusetts
**No financial relationships to disclose*

Jennifer Maitlen, RN, BSN, CCRP
Clinical Research Coordinator
University of Colorado Cancer Center
Aurora, Colorado
**No financial relationships to disclose*

Linda Moors, PA-C
Physician Assistant
Arizona Oncology Associates
Tucson, Arizona
**No financial relationships to disclose*

R. Dirk Noyes, MD
Professor of Surgery
University of Utah
Co-Director, Melanoma Multidisciplinary Clinic
Huntsman Cancer Institute
Salt Lake City, Utah
**Speakers' Bureau, Schering-Plough Corporation*

Steven J. O'Day, MD
Chief of Research
Director of Melanoma Program
The Angeles Clinic and Research Institute
Associate Professor of Medicine
Keck School of Medicine
University of Southern California
Santa Monica, California
**Grant/Research Support, Berlex, Chiron, Schering-Plough Corporation; Consultant, Synta Pharmaceuticals*

Thomas E. Olencki, DO
Clinical Professor
Division of Hematology/Oncology
James Cancer Hospital and Solove Research Institute
Ohio State University
Columbus, Ohio
**Speaker's Bureau: Schering-Plough Corporation, Celgene Corporation*

David W. Ollila, MD
Associate Professor of Surgery
Director, Multidisciplinary Melanoma Program
University of North Carolina
Chapel Hill, North Carolina
**No financial relationships to disclose*

Gary L. Peck, MD
Director, Melanoma Center
Washington Cancer Institute
Washington Hospital Center
Washington, DC
**No financial relationships to disclose*

Douglas S. Reintgen, MD
Director, Lakeland Regional Cancer Center
Lakeland, Florida
**No financial relationships to disclose*

Jon M. Richards, MD, PhD
Director
Biologics Program
Oncology Specialists, SC
Park Ridge, Illinois
**No financial relationships to disclose*

Karen A. Skalla, MSN, ARNP, AOCN
Oncology Nurse Practitioner
Dartmouth-Hitchcock Medical Center
Lebanon, New Hampshire
**No financial relationships to disclose*

Jon D. Smith, RN
Clinical Nurse Coordinator
Seattle Cancer Care Alliance
Seattle, Washington
**No financial relationships to disclose*

John W. Smith II, MD
Member
Northwest Cancer Specialists
Portland, Oregon
**Speakers' Bureau, Astra Zeneca, Amgen*

Bruce Smoller, MD
Interim Chair Department of Pathology
University of Arkansas for Medical Sciences
College of Medicine
Little Rock, Arkansas
**No financial relationships to disclose*

Vernon K. Sondak, MD
Program Leader, Cutaneous Oncology
Director of Surgical Education
H. Lee Moffitt Cancer Center
Tampa, Florida
**Speakers' Bureau, Schering Oncology Biotech*

Laura L. Stover, RN, BSN
Program Leader
Clinical Research Services
University of Pittsburgh
Pittsburgh, Pennsylvania
**Speakers' Bureau, Schering-Plough Corporation, Chiron*

Jeffrey J. Sussman, MD, FACS
Assistant Professor of Surgery
Division of Surgical Oncology
University of Cincinnati
Cincinnati, Ohio
**Speakers' Bureau, Schering-Plough Corporation*

Kenneth K. Tanabe, MD
Chief, Division of Surgical Oncology
Massachusetts General Hospital
Associate Professor of Surgery
Harvard Medical School
Boston, Massachusetts
**No financial relationships to disclose*

John A.Thompson, MD
Professor of Medicine
Co-Director, Melanoma Clinic
Seattle Cancer Care Alliance
Seattle, Washington
**Grant/Research Support, Schering-Plough Corporation, Chiron, Coley, Novartis, Abgenix, Fujis, Zymogenetics, Pfizer, Wyeth; Consultant, Coley Pharmaceuticals; Speakers' Bureau, Schering-Plough Corporation*

Robert W.Weber, MD
Associate Director
Northern California Melanoma Center
San Francisco, California
**No financial relationships to disclose*

Stacie Wenck, MSN, RN, ANP, CCRP
Nurse Practitioner/Clinical Research Coordinator
Wagner & Associates
Indianapolis, Indiana
**No financial relationships to disclose*

Continuing Medical Education Information

Instructions for Participation

To receive up to 1.5 AMA PRA category 1 credits for this activity:

- Read the case summary on the front of the newsletter
- Answer and fax back the questions on the back cover
- Read the remainder of the case study inside the newsletter
- Complete the CME post-test answer and evaluation form at the end of the newsletter and fax or mail these back to the address listed by July 1, 2006
- Within 4 weeks of successful completion, you may access your credit transcript at http://ccehs.upmc.edu/
- 70% of your posttest answers must be correct for you to receive a certificate of credit

Target Audience:

Dermatologists, dermatologic surgeons, surgical and medical oncologists, oncology nurses, primary care physicians, and other health care professionals who treat or screen for melanoma.

Learning Objectives:

After completing this activity, the participant will be better able to:

- Compare and contrast types of initial biopsy for thin melanoma
- List the tumor- and patient-related risk factors that guide the decision to perform SLNB in patients with thin melanoma
- Describe factors that influence disease recurrence and survival in patients initially diagnosed with thin melanoma
- List the minimum follow-up measures that should be taken following staging and for long-term follow-up

Accreditation and Credit Designation:

The University of Pittsburgh School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The University of Pittsburgh School of Medicine designates this continuing medical education activity for a maximum of 1.5 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the educational activity.

**Other healthcare professionals are awarded 0.15 continuing education units (CEUs), which are equal to 1.5 contact hours.*

We gratefully acknowledge an educational grant from Schering-Plough in support of this program.

Faculty and Disclosure:

Peter K. Lee, MD, PhD
Assistant Professor of Dermatology
University of Minnesota, Minneapolis, Minnesota
**Grant/Research Support, 3M Pharmaceuticals; Consultant, 3M Pharmaceuticals; Speakers' Bureau, Schering Oncology*

Jeffrey J. Sussman, MD, FACS
Assistant Professor of Surgery, Division of Surgical Oncology
University of Cincinnati, Cincinnati, Ohio
**Speakers' Bureau, Schering-Plough Corporation*

Faculty for this activity have been required to disclose all financial or other relationships with pharmaceutical companies, biomedical device manufacturers, and other healthcare-related for-profit entities.

The faculty acknowledges the discussion of off-label use of pharmaceuticals, specifically regarding high-dose interferon alfa-2B.

Date of Original Release: July 1, 2005
Expiration Date: July 1, 2006
Date of Last Review: July 1, 2005

Schering-Plough

A 53-Year-Old Man With Melanoma on the Back

Peter K. Lee, MD, PhD

Jeffrey J. Sussman, MD, FACS

CASE PRESENTATION

As noted on the front cover, a 53-year-old white man presented with a changing pigmented lesion located on the right upper back. The lesion was first noted by his spouse 3 months prior, which is a frequent occurrence with posteriorly located abnormalities. The patient complained of mild pruritus in the affected area and no other local symptoms, but was otherwise healthy, with mild hypertension, for which he was taking low-dose aspirin and a beta-blocker. Although he denied a family history of melanoma, he had a personal history of 2 previous atypical nevi biopsies. He did not use tanning booths but had many severe sunburns in the past. Physical examination revealed a 1.8-cm by 1.6-cm, slightly elevated, pigmented lesion with irregular borders and variegated pigmentation. No lymphadenopathy in potential draining basins in the affected area was noted nor were there any other suspicious lesions on full body skin survey or contributory findings.

Figure 1 presents a photograph and dermatoscopic image of the lesion. The clinical image clearly depicts the irregular borders of the lesion as well as its variable pigmentation and darkened center. The dermatoscopic image enhances these features and provides further information about skin structure (see Sidebar 1). As shown in the right panel of Figure 1, the lesion has dark pigmentation in the center, with the presence of a blue-white veil, globules, pseudopods, and pigment dropout. These features are suggestive of melanoma, which prompted the decision to perform a biopsy.

Choice of the Initial Biopsy

Given the findings of the initial exam and the clinical and dermatoscopic images, the expert panel was asked what type of diagnostic biopsy would be best for this patient. The overwhelming majority (86%) voted for an excisional biopsy with a 1-mm or 2-mm margin. The dissenting 13% chose a 2-mm punch biopsy of the center of the lesion where it was darkest. No panel members selected shave biopsy or wide local excision with a 1-cm margin.

Dr Peter Lee, one of the panel moderators, noted that this is often a difficult decision for primary care physicians, who may be tempted either to take only a small sample or, at the other extreme, remove the entire lesion with extensive margins. While a small biopsy could miss the malignant portion of the lesion and lead to an incorrect diagnosis,[1] a very large biopsy holds the potential for scarring or wounding that could interfere with the accuracy of subsequent lymph node mapping, if needed. The goal of the diagnostic biopsy is to remove the atypical pigmented lesion with minimal surgical margins because this approach ensures the proper sampling of the lesion and preserves the local lymphatic drainage patterns for lymphoscintigraphy and SLNB.[2] Thus, the potential for scarring or wounding that could interfere with the accuracy of subsequent lymph node mapping and biopsy precludes the recommendation of a wide local excision with a 1-cm margin. Moreover, if the lesion is benign, then an unnecessarily wide margin is not obtained.

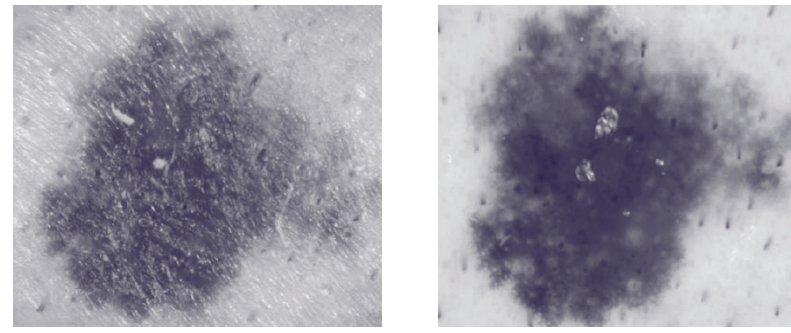
Although a superficial shave biopsy would not disrupt lymphatic drainage, this type of biopsy could transect the lesion and not allow proper evaluation of Breslow depth.[1] A deep shave biopsy that extended into the subcutaneous fat could provide sufficient pathologic information and is the method preferred by many dermatologists as it does not require skin closure; however, this procedure requires substantial expertise and skill to be performed correctly. In addition, approximately 5% of deep shave biopsies underestimate true Breslow depth.[1]

Some panel participants selected the punch biopsy option. Because of the size of the lesion, a 2-mm punch biopsy in its center might miss the diagnostically relevant portion. A larger (8-mm or 10-mm) punch biopsy could be considered in this case; however, up to 20% of punch biopsies underestimate Breslow depth.[1]

Thus, the panel deemed the excisional biopsy with narrow margins as the best choice. When performing an excisional biopsy with narrow margins, it is important not to remove the redundant cutaneous cones or "dog ears" to limit the size of the scar. Prior to undergoing this type of diagnostic biopsy, patients should receive counseling about the potential necessity for a second wide local excision once the pathologic results are known, as well as the chance that SLNB would be required should invasive melanoma be diagnosed.

In this case, the lesion was excised with narrow margins, and the initial pathologic analysis of the biopsy revealed superficial

Figure 1



Clinical Image

Dermatoscopic Image

Clinical and dermatoscopic images of the lesion. The clinical image on the left clearly shows irregularities in pigment and border of the lesion. The dermatoscopic image on the right enhances these observations by revealing the structures of the epidermis and dermal-epidermal junction. Photography courtesy of Peter K. Lee, MD.

Sidebar 1

Dermatoscopy

Dermatoscopy, also known as epiluminescence microscopy (ELM), encompasses a group of noninvasive diagnostic techniques that allow microscopic examination of skin lesions. The procedure permits clinicians to visualize the skin substructures in order to help distinguish between benign and malignant pigmented skin lesions. To perform the procedure, the physician applies immersion oil to the skin, which reduces light reflection from the skin surface and renders the outermost layer of the epidermis (stratum corneum) transparent. The clinician then examines the pigmented lesion using a dermatoscope—a handheld device that provides 10 to 20 times magnification and allows visualization of the structures of the epidermis and epidermal-dermal junction. A variety of structural features suggest malignancy, including pseudopods (fingerlike projections of dark pigment at the periphery of the lesion), radial streaming (radially and asymmetrically arranged, parallel linear extensions at the periphery of the lesion), the pattern of the pigment network, black dots, globules, and blue-white veil (irregular, indistinct, confluent blue pigmentation with an overlying white, ground-glass haze).[19] These features, along with other standard assessment criteria, have been organized into algorithms to clarify the differential diagnosis of pigmented skin lesions.[20]

Sidebar 2

Lentigo Maligna

Lentigo malignas account for 4% to 10% of all melanomas. Commonly occurring in the sun-exposed areas of the face and neck, lentigo maligna are usually very thin lesions with a low propensity to metastasize. These tan-colored lesions typically occur on the face in older white women and rarely appear before age 50. Relatively large (>3 cm), these flat lesions persist for 5 to 15 years. As lesions enlarge, irregular mottling or flecking may arise, with very dark areas interspersed with areas of regression.[14]

As with any melanoma, excisional biopsy is the ideal biopsy to perform; however, the relatively large size and facial location typical of lentigo maligna often make this choice impractical. Dermoscopy can be used as a guide to show potentially malignant portions of the lesion as well as confirm the diagnosis.[21] Definitive diagnosis is made on the basis of the presence of sun-related abnormalities in the dermis and epidermis, particularly asymmetric pigmented follicular openings, dark rhomboidal structures, slate-gray globules, and slate-gray dots.[14,21] New imaging modalities such as confocal laser may assist in deciding where to biopsy and in checking or mapping margins.

Treatment options include surgery, Mohs micrographic surgery, or radiation therapy. Currently, NCCN Clinical Practice Guidelines recommend wide excision of melanoma in situ, such as lentigo maligna.[4] However, adjacent vital structures on the face, such as the eyes and ears, and concerns about cosmesis often limit margins. In addition, recommended margins are often inadequate at completely excising lentigo maligna.[22] Mohs micrographic surgery may precisely map margins, allowing for maximum tumor removal and minimal damage to normal tissues. In this procedure, a specially trained dermatologist or surgeon obtains a beveled specimen with a margin of normal-appearing tissue, which is mapped, immediately processed by frozen section, and examined by microscopy. Optimal use of the technique relies on the ability of the surgeon to detect cancer on the frozen sections.[23] In cases where surgery is not an option, radiation therapy or off-label medications (imiquimod) have been shown to provide some benefit.[24,25] However, radiation scarring and other adverse effects of radiation may limit the use of radiation therapy for treatment of lentigo maligna. Imiquimod is an immune response modifier thought to promote inflammatory responses that kill cancer cells.[26] While topical imiquimod induced complete responses in 93% of patients tested in a small open-label study,[25] imiquimod lacks the validation achieved by large-scale, well-controlled clinical trials.

spreading melanoma with the following features:

- Breslow depth of 0.79 mm
- Clark level III/IV
- No ulceration
- No regression
- Mitotic rate: 0

Subsequent Biopsy

Given this pathologic information, the panel was queried about the appropriate type of therapeutic excision. The majority of the panel (66%) opted for a wide local excision with 1-cm margins down to the fascia. A substantial proportion (39%) voted for SLNB and wide local excision with 1-cm margins down to the fascia, while 4% chose a wide local excision with 5-mm margins.

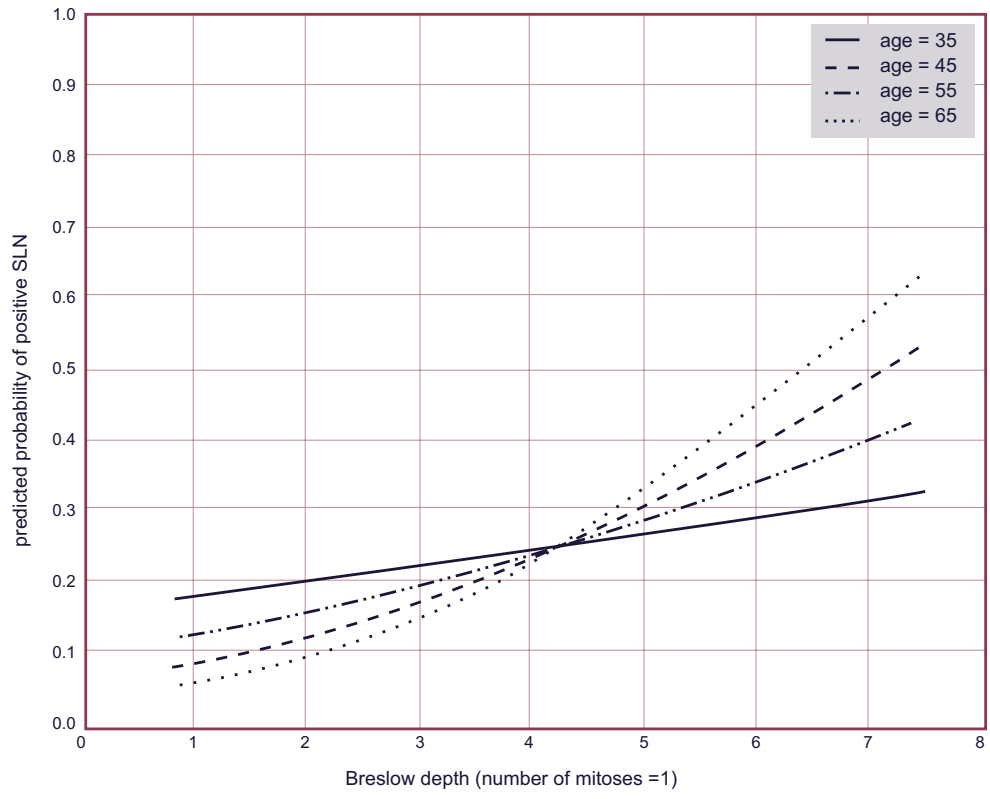
The moderators and most of the panel deemed that the choice of a wide local excision with 5-mm margins was not supported by the current literature, although they indicated that this choice might be appropriate for melanoma in situ or for patients with particular anatomical or cosmetic constraints. Likewise, none of the panel selected Mohs micrographic surgery, considered a good option for nonmelanoma skin cancers and lentigo malignas (see Sidebar 2).

Essentially the major split in the panel surrounded the appropriateness of SLNB for this patient. Panel co-moderator Dr Jeffrey Sussman noted that the literature regarding this subject is evolving; therefore, the decision must be individualized on a case-by-case basis. Because several parameters have been shown to negatively impact prognosis for patients with thin melanomas, the panel agreed that SLNB might be considered for thin melanomas with any of the following characteristics:

- Breslow depth greater than 1 mm[3]
- Stage IB classification by the American Joint Committee on Cancer (AJCC) staging system, reflecting the presence of ulceration or Clark level IV or V in tumors less than 1 mm thick[3]
- High-risk histologic features such as vascular invasion, extensive regression, and high tumor mitotic rate[4-6]
- Vertical growth phase[7]
- Young patient age[8]
- Truncal location[9]
- Male gender when tumor mitotic rate is >0[7]
- Lesions close to but less than 1 mm thick[10]

Defining an approach for treating thin melanomas is emerging as an important goal because melanomas that are 1-mm thick or less now account for the majority of all newly diagnosed invasive melanomas.[7] While the outcome for patients with thin melanomas is generally excellent, some populations of patients do poorly. Because of the disproportional distribution of thin melanomas to thick melanomas, an increasing percentage of melanoma deaths are attributed to "low-risk" primary melanomas. This rising incidence of thin melanomas underscores the importance of elucidating the prognostic factors that relate to recurrence and

Figure 2



The impact of tumor thickness (Breslow depth) on sentinel lymph node positivity is diminished at younger ages. Probability plots for positive SLN at a constant number of mitoses (1/mm^2) show steeper slopes for curves at older ages, indicative of a more significant thickness effect than at younger ages.[6] Reprinted from Sondak VK. *Ann Surg Oncol.* 2004. Reprinted with permission from the Society of Surgical Oncology.

mortality and to the need for a staging SLNB. Unfortunately, the knowledge base regarding prognostic factors for thin melanomas remains deficient.

Impact of Thickness

A known negative prognostic factor for melanoma, tumor thickness, is a central component of the AJCC Melanoma Staging System.[3] By this account, thin melanomas carry very low risk for relapse and mortality, making it difficult to determine the need for SLNB on the basis of this parameter alone. Further complicating the decision are the disparate results of studies evaluating the incidence of SLN positivity in patients with thinner melanomas. A study conducted at the John Wayne Cancer Institute found that nearly 3% of patients with primary melanomas of 1 mm or less had positive lymph nodes.[8] However, a study conducted at Ohio State University reported a substantially lower rate of lymph node positivity (1.4%) for patients with primary melanomas of less than 1.2 mm thick.[11]

The latter study argued against the appropriateness of SLNB for thin melanomas, contending that the cost of SLNB superseded the potential benefit of identifying only a very small proportion of lymph node–positive patients for whom the treatment plan might be amended. The investigators compared the cost of an SLNB, which ranged from $10,000 to $15,000, with the cost for wide excision, which was under $2000, and reasoned that the cost to identify a single positive lymph node in the study population would be between $696,000 and $1,051,100.[11] However, as Dr Sussman indicated, this study did not do careful step-sectioning and immunohistochemistry in the SLN analysis, which potentially diminished the true rate of SLN positivity in patients with thin primary melanomas. Moreover, the denominator used in that study is too large, as no one is arguing that extremely low-risk patients such as melonoma in situ patients, which were included in the study, should undergo SLNB. If the rate of positive SLN is actually higher in appropriately selected patients with thin melanomas, which many other studies suggest, the benefit of SLNB may outweigh the cost.

Indeed, the John Wayne Cancer Institute experience suggests that the true rate of SLN positivity is higher than that reported by the Ohio State series. In this retrospective review of 512 patients with melanomas of 1.5 mm or less who underwent SLNB, the rate of posi-

Table 1

Categorization of Metastasis Risk According to Prognostic Features in Patients with Thin (≤1 mm) Melanoma[7]

Prognostic Features	Metastasis Rate	Risk Group
Male Vertical growth phase lesion Mitotic rate >0	31%	High
Women Vertical growth phase lesion Mitotic rate >0	13%	Moderate
Either gender Vertical growth phase lesion Mitotic rate = 0	4%	Low
Either gender No vertical growth phase Mitotic rate = 0	0.5%	Minimal

Significance between the 4 groups ($P < .001$). N=884

tivity ranged from 1.7% in patients with the thinnest melanomas (≤0.75 mm) to 2.9% in patients with melanomas of 0.75 mm to 1 mm in thickness, and 7.1% in patients with primaries 1.01 mm to 1.05 mm thick.[8] While these arbitrary cut-offs generate specific rates according to thickness, the reality is that there is no specific threshold for higher risk of positivity and that the risk gradually increases over the continuum of tumor thickness. In addition, the results suggest that a very thin melanoma retains the potential to metastasize. The future goal is to identify additional factors that may better identify which patient subsets do not need SLNB.

Impact of Age

Data emerging from various studies suggest that age also influences the risk of lymph node positivity in patients with thin melanomas. The John Wayne Cancer Institute dataset found that patients under the age of 44 who had melanomas of less than 1.5 mm were significantly more likely to have positive lymph nodes (P=.005).[8] Another study of 419 patients with tumors of all thicknesses confirms the impact of age on the probability of finding a positive sentinel lymph node. More than one quarter of patients younger than age 35 had positive SLNs (26.3%). The rate of SLN positivity progressively declined with age, so that 18.6% of patients aged 35 to 60 years and 11.8% of patients over age 60 exhibited positive nodes.[6]

This multivariate analysis also demonstrated an interaction between age and tumor thickness. As shown in Figure 2, the relatively flat curve obtained from plotting the chance of lymph node positivity versus the Breslow depth (at a constant mitotic rate) reflects the relative insensitivity of tumor thickness on the probability of having a positive SLN in patients younger than 35 years. Thus, in younger patients, tumor thickness does not appear to play a large role in predicting SLN status, and the trend of this curve suggests young patients who have tumors thinner than 1 mm may still carry a substantial risk of lymph node positivity despite having a thin lesion.[6] In contrast, the progressively steeper slopes of the same curves in patients aged 45, 55, and 65 years demonstrate a likelihood of positive biopsy that is more dependent on tumor thickness in older patients than it does for younger patients.[6]

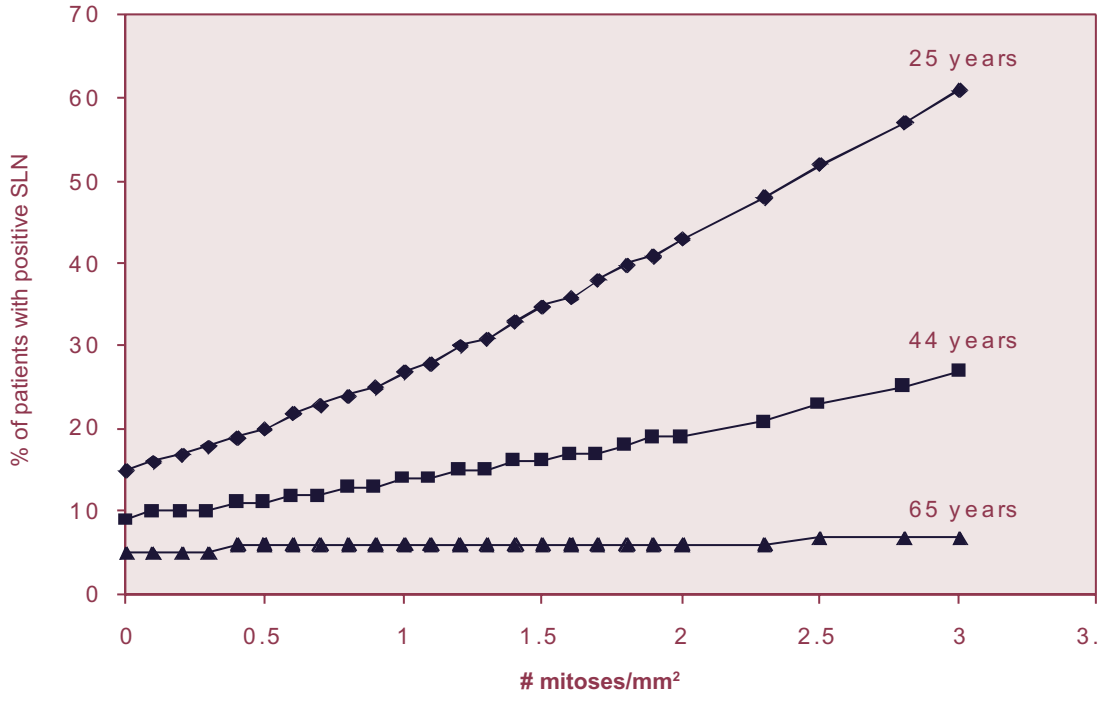
Emerging Factors

These data suggest that tumor characteristics other than thickness may substantially influence the chance of lymph node positivity in younger patients. Although it is not currently incorporated into the AJCC/AIC Melanoma Staging System,[3] tumor mitotic rate appears to play a greater role in determining SLN positivity than Breslow depth in younger patients. In patients aged 35 or younger, a high mitotic rate increased the probability of finding a positive SLN at all tumor thicknesses from 1 mm to 7 mm.[6] In contrast, tumor mitotic rate appears to have almost no effect on the likelihood of finding a positive SLN in patients over age 65 years at any tumor thickness (Figure 3).[6]

The observation that tumor mitotic rate is an important prognostic factor in thin melanoma was corroborated by a retrospective tree analysis of 884 patients with melanomas of 1 mm or less.[7] While the 10-year metastasis rate for patients with thin melanoma observed in this study was 6.5% overall, the rate differed substantially when the data were stratified by gender, vertical growth phase, and tumor mitotic rate. According to the prognostic tree (Table 1), men with lesions demonstrating a vertical growth phase and a mitotic rate >0 were at greatest risk of metastasis (31%). The risk diminished to less than 4% for patients of either gender when the mitotic rate was zero and further to 0.5% if the lesion lacked a vertical growth phase as well.[7]

The expert panel felt that consistency of methods used to assess these novel prognostic factors

Figure 3



The impact of mitotic rate on SLN positivity is diminished at older ages. A probability plot for a positive SLN with tumor mitotic rate at various ages reveals a steeper slope to the curves at younger ages, indicative of a more significant effect of this tumor mitotic rate at younger ages. The relatively flat curve for patients aged 65 years suggests little impact of tumor mitotic rate on SLN positivity in older patients.[6] Adapted from Sondak VK. *Ann Surg Oncol.* 2004. Adapted with permission from the Society of Surgical Oncology.

remained a challenge. Dr Sussman pointed out that vertical growth phase is not always reliably reported by dermatopathologists, which may complicate the use of this tumor feature in determining the need for SLNB in thin melanoma patients. Dr Averbook suggested that the same is true for tumor mitotic rate, highlighting the need for consistent protocols. However, once application of these novel prognostic factors is standardized, studies such as these support incorporating vertical growth phase and tumor mitotic rate into the decision process for the optimal selection of patients for SLNB.

While the panel agreed that no specific guidelines for SLNB in patients with thin melanoma can be proposed at this time, a number of factors are emerging as risk factors for SLN positivity, metastasis, and mortality. Therefore, presence of these aforementioned features could serve to flag a patient as an appropriate candidate for SLNB. In addition, other patient-related factors, including comorbidities and comfort level with the risks and potential results of the procedure, should guide a clinician when recommending SLNB. The large number of contributory features reflects the current situation in which the management strategy must be tailored for individual patients with thin melanoma rather than adopting a one-size-fits-all approach.

Current Practice

Panel members discussed the different parameters that guided the choice to perform SLNB at their institutions. According to Dr Lee, the University of Minnesota does not recommend SLNB for any trunk or extremity lesion less than 1 mm and with less than a Clark level IV, unless there are other negative prognostic factors such as regression, high mitotic rate, vascular invasion, or ulceration. However, the thickness cut-off for recommending SLNB is reduced to 0.75 mm if the lesion is located on the head and neck region or acral sites. Dr David Ollila countered that recently published data suggest not using Clark level as a determining factor in the appropriateness for SLNB.[12] He emphasized that Breslow thickness in combination with ulceration and/or regression should guide the use of SLNB in thin melanoma patients. Dr Sussman noted that the AJCC incorporates Clark level into its staging system for thin melanomas[3] and this level is routinely reported. Therefore, he recommended weighing Clark level as a positive factor that would push the recommendation

Sidebar 3

Dysplastic Nevus Syndrome

Dysplastic nevus syndrome refers to the heritable condition in which patients have between 10 and 1000 pigmented lesions located on the trunk, buttocks, or lower extremities.[14] People exhibiting this syndrome are at greater risk of developing melanoma than the population at large. Despite a recommendation by the National Institutes of Health (NIH) that the term dysplastic nevus be replaced with atypical moles and the syndrome for melanoma-prone families be called familial atypical mole and melanoma (FAMM) syndrome, the medical community continues to use the older terminology.

Not all patients with dysplastic nevus syndrome develop melanoma, and the risk of melanoma development within the syndrome varies, with specific cellular and histologic features increasing the risk. Nevertheless, patients with dysplastic nevus syndrome should be followed regularly, with negative prognostic factors such as a family history of melanoma dictating a shorter, 3- to 6-month interval between evaluations. Other patients may be followed with longer intervals between visits.[27]

toward SLNB but not as a negative factor that would exclude the need for biopsy at present.

Dr Sussman continued with the observation that the University of Cincinnati uses no specific thickness cut-offs and SLNB is discussed in detail with all melanoma patients. In general and in the absence of other negative prognostic features, they encourage younger patients with lesions greater than 0.75 mm to undergo SLNB; they typically treat those with lesions less than 0.5 mm with wide excision only and evaluate patients with lesions falling between 0.5 mm and 0.75 mm on a case-by-case basis. If negative prognostic factors are present, they encourage patients to undergo SLNB regardless of tumor thickness, particularly if they are younger and in otherwise good health. University of North Carolina uses a similar approach, said Dr Ollila. Patients there with tumors falling in the gray zone between 0.5 mm and 1 mm receive a balanced discussion regarding SLNB, unless the lesion has ulceration or regression, in which case clinicians tend to favor SLNB.

In this particular case, the pathology report described the Clark level as III/IV. This represents an ambiguous result that crosses substages within stage I. As such, the clinician requested a reanalysis of the specimen, and the Clark level was verified as level IV. The patient was counseled regarding the benefits and risks of SLNB and elected to undergo the procedure. The lesion was excised with a 1-cm margin down to the fascia and one lymph node was removed. Conventional (H & E) and immunohistochemical staining did not reveal any evidence of metastatic disease. Thus, under the current AJCC Melanoma Staging System, the patient was classified as having Stage IB disease.[3]

Post-Staging Follow-Up

When polled about the key post-staging follow-up tests for this patient, more than half of the expert panel (52%) opted for no laboratory or imaging tests. Half as many (26%) voted for a baseline chest x-ray; 17% chose lactate dehydrogenase (LDH), liver function tests, and a complete blood count (CBC). Four percent of the panel supported the use of CT scans of the chest, abdomen, and pelvis. No participant thought this patient required PET scanning.

The majority of the expert panel agreed with panel moderators and the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for Melanoma.[4] None of the listed laboratory or imaging tests have been shown to improve survival or to be of benefit for detecting metastasis in patients with Stage IB disease. However, as the diversity of panel responses reflects, there is wide variability in the post-baseline follow-up in this patient population, with many oncologists, primary care physicians, and dermatologists ordering baseline chest x-rays, liver function tests, and LDH assessment.

The Approach to Treatment

The panel was then asked about the role of adjuvant therapy for this patient. While 8% of the panel said they would consider interferon (IFN) alfa-2b and 4% might consider radiation therapy, the vast majority of the panel (88%) did not feel that adjuvant therapy was warranted for the patient with very early–stage melanoma. This philosophy mirrors the NCCN Clinical Practice Guidelines, whereby no adjuvant treatment option is recommended for Stage I melanoma.[4]

In part, the lack of enthusiasm for adjuvant therapy for the Stage IB patient stems from the high survival rate among patients with early-stage disease. A retrospective analysis of 17,600 patients with melanoma revealed a 5-year survival rate that exceeded 90% for patients with Stage IB disease.[3]

Long-Term Follow-Up

While the panel agreed that the patient must be followed regularly, there was some disagreement about the relative value of the various types of follow-up measures available for Stage I patients. Nearly two thirds of the panel (64%) deemed periodic skin examination with a dermatologist sufficient for follow-up in the absence of recurrence, but 24% thought optimal follow-up re-quired regular skin examinations, annual chest x-ray and LDH level testing, initial oncology consult, and recommendation of skin examination for

first-degree relatives. The rest of the panel was split, voting for annual chest x-ray and LDH level (4%), initial consultation with a medical oncologist (4%), and recommendation of skin examination for close relatives (4%). Dr Lee suggested that the structure of the question may not accurately reflect the follow-up decisions made by the panel, conceding that there were some options that some practitioners would not recommend while other answers might have been too limited. Nevertheless, the moderators felt that all of the listed follow-up measures could be considered appropriate. In particular, the panel felt that many patients are unnerved by the diagnosis of cancer and are reassured by the feeling that something is being done to manage their disease, even if the measures may not be completely necessary or validated.

This particular patient's history of atypical nevi supported frequent follow-up. In this case, the patient was advised to return to the Melanoma and Pigmented Lesion Clinic every 3 months for 2 years, followed by every 6 months for 3 more years. During a typical visit to this clinic, the patient would undergo a complete head-to-toe skin examination and complete clinical lymph node evaluation and asked questions to elicit symptoms of potential metastatic disease. Dr Lee noted that other institutions may opt to follow this type of patient less frequently or may include different elements as part of the examination. This observation prompted a panel discussion of the wide variability in practices for the full-skin examination. While some clinics always employ dermatoscopy to reveal malignant lesions and carry out lymph node assessments, examinations in other clinics and practices may be less stringent. According to Dr Lee, the inconsistency of methods used for skin examinations across the country prompts many specialists to specify complete skin and lymph node examination when making referrals for their melanoma patients who must switch practices due to a change in residence.

Although an annual chest x-ray and LDH-level testing are not necessary, institutional protocols frequently dictate follow-up regimens in which these tests may be performed. An initial medical oncology consult is not an absolute requirement following the diagnosis of Stage I disease, and the decision to refer should be made on an individual basis. The panel did not feel that this particular patient needed to visit a medical oncologist at this point.

Importantly, the faculty agreed that the parents, siblings, and offspring should be counseled about their increased risk of melanoma. First-degree family members of a patient with melanoma have more than double the risk of developing melanoma; therefore, relatives need to be particularly vigilant in melanoma screening.[13] In part, the increased risk lies in shared genes and phenotypic traits, involving factors as diverse as human leukocyte antigen haplotype (HLA), hair color, fair skin, and nevus count.[14] At particular risk are families categorized as having dysplastic nevus syndrome (see Sidebar 3).

In addition to genotypic and phenotypic traits, family members frequently share environmental factors such as geographic location and propensity to suntan, which also increases exposure to ultraviolet light that contributes to the development of melanoma.[15] Therefore, the patient and family members should be advised about the importance of photo-protection through sun avoidance and use of long-sleeved clothing and sunscreens, although available data conflict about the ability of sunscreens to influence the development and progression of melanoma.[16]

The patient should also be counseled that a previous melanoma increases the risk of developing subsequent skin cancers. Approximately 5% of patients with melanoma develop additional primary melanoma—a rate that translates to a 900-fold greater risk than the general population in developing the disease.[17, 18]

Conclusions

The panel discussion and review of the literature provide the following recommendations for the patient with Stage IB melanoma:

- Adequate biopsy requires full-thickness excision with narrow margins to preserve accuracy of subsequent SLNB, if needed
- Appropriate surgical treatment involves wide local excision with 1-cm margins down to the fascia, with or without SLNB
- The choice to perform SLNB must be tailored to the patient and involve assessment of potential tumor- and patient-related risk factors
- Novel factors such as vertical growth phase and tumor mitotic rate may be more predictive of lymph node positivity and metastasis in thin melanomas than Breslow thickness
- Following staging, no laboratory or imaging tests have been shown to benefit survival rates or detect metastases in Stage IB patients
- No adjuvant treatment option is currently recommended for Stage IB melanoma
- Recommended long-term follow-up measures vary from institution to institution and may include chest x-rays and LDH testing
- At a minimum, follow-up should include recommendations for regular skin examination of themselves and for family members and counseling on the importance of sun protection.

References

1. Ng PC, Barzilai DA, Ismail SA, Averitte RL, Jr., Gilliam AC. Evaluating invasive cutaneous melanoma: is the initial biopsy representative of the final depth? *J Am Acad Dermatol.* 2003;48:420-424.

2. Leong SP, Thelmo MC, Kim RP, et al. Delayed harvesting of sentinel lymph nodes after previous wide local excision of extremity melanoma. *Ann Surg Oncol.* 2003;10:196-200.

3. Balch CM, Buzaid AC, Soong SJ, et al. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. *J Clin Oncol.* 2001;19:3635-3648.

4. National Comprehensive Cancer Care Network. Clinical practice guidelines in oncology-v.1.2004: *Melanoma.* National Comprehensive Care Network, Inc. 2004.

5. Zettersten E, Shaikh L, Ramirez R, Kashani-Sabet M. Prognostic factors in primary cutaneous melanoma. *Surg Clin North Am.* 2003;83:61-75.

6. Sondak VK, Taylor JM, Sabel MS, et al. Mitotic rate and younger age are predictors of sentinel lymph node positivity: lessons learned from the generation of a probabilistic model. *Ann Surg Oncol.* 2004;11:247-258.

7. Gimotty PA, Guerry D, Ming ME, et al. Thin primary cutaneous malignant melanoma: a prognostic tree for 10-year metastasis is more accurate than American Joint Committee on Cancer staging. *J Clin Oncol.* 2004;22:3668-3676.

8. Bleicher RJ, Essner R, Foshag LJ, Wanek LA, Morton DL. Role of sentinel lymphadenectomy in thin invasive cutaneous melanomas. *J Clin Oncol.* 2003;21:1326-1331.

9. Lindholm C, Andersson R, Dufmats M, et al. Invasive cutaneous malignant melanoma in Sweden, 1990-1999. A prospective, population-based study of survival and prognostic factors. *Cancer.* 2004;101:2067-2078.

10. Kalady M, White RR, Johnson JL et al. Thin melanomas: predictive lethal characteristics from a 30-year clinical experience. *Ann Surg.* 2003; 238:528-535.

11. Agnese DM, Abdessalam SF, Burak WE, Jr., Magro CM, Pozderac RV, Walker MJ. Cost-effectiveness of sentinel lymph node biopsy in thin melanomas. *Surgery.* 2003;134:542-547.

12. Stitzenberg KB, Groben PA, Stern SL, et al. Indications for lymphatic mapping and sentinel lymphadenectomy in patients with thin melanoma (Breslow thickness < or =1.0 mm). *Ann Surg Oncol.* 2004;11:900-906.

13. Ford D, Bliss JM, Swerdlow AJ, et al. Risk of cutaneous melanoma associated with a family history of the disease. The International Melanoma Analysis Group (IMAGE). *Int J Cancer.* 1995;62:377-381.

14. Balch C, Houghton AN, Peters LJ. Cutaneous melanoma. In: DeVita VT, editor. In: *Cancer: Principles and Practice of Oncology.* 4th ed. Philadelphia: J.B. Lippincott, 1993; 1612-1661.

15. Whiteman DC, Parsons PG, Green AC. p53 expression and risk factors for cutaneous melanoma: a case-control study. *Int J Cancer.* 1998;77:843-848.

16. Dennis LK, Beane Freeman LE, VanBeek MJ. Sunscreen use and the risk for melanoma: a quantitative review. *Ann Intern Med.* 2003;139:966-978.

17. Blackwood MA, Holmes R, Synnestvedt M, et al. Multiple primary melanoma revisited. *Cancer.* 2002;94:2248-2255.

18. Veronesi U, Cascinelli N, Bufalino R. Evaluation of the risk of multiple primaries in malignant cutaneous melanoma. *Tumori.* 1976;62:127-130.

19. Braun RP, Rabinovitz HS, Oliviero M, Kopf AW, Saurat JH. Dermoscopy of pigmented skin lesions. *J Am Acad Dermatol.* 2005;52:109-121.

20. Argenziano G, Soyer HP, Chimenti S, et al. Dermoscopy of pigmented skin lesions: results of a consensus meeting via the Internet. *J Am Acad Dermatol.* 2003;48:679-693.

21. Schiffner R, Schiffner-Rohe J, Vogt T, et al. Improvement of early recognition of lentigo maligna using dermatoscopy. *J Am Acad Dermatol.* 2000;42:25-32.

22. Huilgol SC, Selva D, Chen C, et al. Surgical margins for lentigo maligna and lentigo maligna melanoma: the technique of mapped serial excision. *Arch Dermatol.* 2004;140:1087-1092.

23. Carucci JA. Mohs' micrographic surgery for the treatment of melanoma. *Dermatol Clin.* 2002;20:701-708.

24. Schmid-Wendtner MH, Brunner B, Konz B, et al. Fractionated radiotherapy of lentigo maligna and lentigo maligna melanoma in 64 patients. *J Am Acad Dermatol.* 2000;43:477-482.

25. Naylor MF, Crowson N, Kuwahara R, et al. Treatment of lentigo maligna with topical imiquimod. *Br J Dermatol.* 2003;149 Suppl 66:66-70.

26. Aldara™. Prescribing information. St. Paul, Mn. 3M Pharmaceuticals;2004.

27. Salopek TG. The dilemma of the dysplastic nevus. *Dermatol Clin.* 2002;20:617-28, viii.

We'll bring the World Congress to you…

Insights in Melanoma:
Highlights From the 6th Annual World Congress on Melanoma

(Held September 6–10, 2005) • Vancouver, British Columbia

- **Read viewpoints on the congress from the medical oncology, surgical oncology, and dermatology perspective**
- **Receive CME credits for the congress proceedings**

To participate:
1) Fill out the form to the right and fax it in
2) Download the form from our Web site
3) Receive the publications in approximately 2 months

Name _____ Degree _____
Specialty _____
Address _____
City, State, ZIP _____
Phone _____
Fax _____
Email _____

Fax back this form to: 845-398-5108 or mail to:
World Congress on Melanoma, c/o PharmAdura, LLC
523 Route 303, Orangeburg, NY 10962

Schering-Plough

This CME activity is supported by an educational grant from Schering-Plough Corporation

MelanomaCare.org

Your FREE online resource.

Keep up to date on Melanoma Care Options by:

Searching our LINKS to find the latest information as close as your keyboard — **LINKS**

Taking CME tests and comparing answers to other Melanoma Care professionals — **CME ONLINE**

Finding out first about upcoming EVENTS designed for you — **EVENTS**

Accessing this article and others in our archive in one place — **ARCHIVES**

Reviewing our Information Resource Center — **MELANOMA CARE CENTERS**

Reading about the Melanoma Care Consortium — **MEMBERS**

CME Evaluation Form

Please use the scale below to answer these questions.
Fill in the circle completely. You may use pen or pencil to fill in the circles.

Very Low Low Moderate High Very High

1. To what extent were the objectives of the educational activity achieved?
   O O O O O
2. To what extent were you satisfied with the overall quality of the educational activity?
   O O O O O
3. To what extent was the content of the program relevant to your practice?
   O O O O O
4. To what extent did the activity enhance your knowledge of the subject area?
   O O O O O
5. To what extent did the activity change the way you think about clinical care/professional responsibilities?
   O O O O O
6. To what extent will you make a change in your practice/professional responsibilities as a result of your participation in this educational activity?
   O O O O O
7. Which of the following best describes the impact of this activity on your performance? **(Please use the scale below in answering this question.)**
   - O This program will not change my behavior because I am already currently conducting my professional responsibilities in a manner consistent with the information presented in this educational activity.
   - O This activity will not change my behavior because I do not agree with the information presented.
   - O I need more information before I can change my practice behavior.
   - O I will immediately implement the information into my practice.
8. What action(s) will you take as a result of participating in this activity?
   (Please use the scale below in answering these questions.)
   - O None.
   - O Discuss new information with other professionals.
   - O Discuss with industry representative.
   - O Participate in another educational activity.
9. To what extent did the activity present scientifically rigorous, unbiased, and balanced information?
   O O O O O
10. To what extent was the presentation free of commercial bias?
    O O O O O
11. Please indicate your degree:
    O MD/DO O Physician Assistant
    O Nurse O Nurse Practitioner O Other
12. Was there any particular content that was irrelevant to your practice? If yes, why? _____
13. What types of information should be used to determine topics for this activity if repeated? _____
14. Would you prefer a different learning format (discussions, skills training, formal course)? _____
15. In the event that content exhibited commercial bias, please describe the specifics. _____
16. Do you have any other comments or suggestions for improving this education activity? Please discuss. _____

Answer CME Questions Here

1. ☐ 2. ☐ 3. ☐ 4. ☐ 5. ☐ 6. ☐ 7. ☐ 8. ☐ 9. ☐ 10. ☐

If you wish to receive credit for this activity, please fill in your name and address and send to:

PharmAdura, LLC, 170 Fairview Avenue, Pearl River, NY 10965 Fax: (973) 682-9077

❑ I have completed the activity and claim _____ credit hours

Request for Credit

Name: Degree:

Address: City, State, ZIP:

Organization: Specialty: Last 5 Digits of SSN:

Telephone: Fax: E-mail:

Case Re-evaluation Questions

Please circle the answer that best describes your current view of the case.

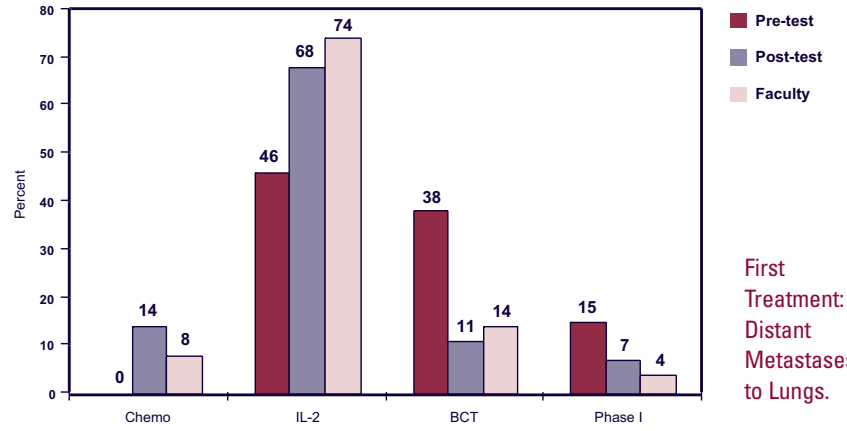
1. Did your opinion on patient management change after you completed this exercise?
   A. Yes B. No
2. What type of diagnostic biopsy would you perform on this patient?
   A. Deep shave biopsy
   B. Excisional biopsy with narrow margins
   C. Large punch biopsy (8mm–10 mm)
   D. Superficial shave biopsy
3. Would you recommend SLNB to this patient?
   A. Yes B. No
4. What follow-up measures would you recommend for a Stage IB patient?
   A. Annual chest x-ray and LDH level
   B. Initial consultation with oncologist
   C. Advise first-degree family members to receive skin examinations
   D. All of the above
5. Do you have any additional comments, questions, or observations about how your management strategy changed?

_____
_____
_____
_____
_____

Feedback on Case 3: Metastatic Melanoma

Case 3 (March issue) concerned a patient with distant melanoma metastases (ie, bilateral pulmonary nodules). All readers (pre-case reading) and an overwhelming majority of faculty recommended a biopsy of one of the pulmonary nodules (100% vs 80%, respectively). The largest proportion of both readers and faculty chose the FDA-approved treatment high-dose interleukin-2 (IL-2) as the appropriate therapy at this stage. A far higher percentage of faculty than readers chose IL-2 (46% of readers, 74% of faculty). A larger proportion of readers than faculty opted for biochemotherapy (BCT) (38% of readers, 14% of faculty). No readers, but 8% of faculty, recommended chemotherapy (DTIC-based single-agent or multi-agent regimen).

Two-thirds of participants said that their management approach changed after reading the newsletter. Larger proportions of participants chose IL-2 or chemotherapy after reading the case (46% pre-test vs 68% post-test for IL-2; 0% pre-test vs 14% post-test for chemotherapy). Fewer opted for BCT (38% pre-test vs 11% post-test). These changes are consistent with faculty case presenters' recommendation that chemotherapy is a valid choice if IL-2 is unavailable, and that BCT is appropriate only in the context of a clinical trial. Survival and response rates for BCT have been disappointing. Post-test opinions about management after confirmation of pulmonary nodules thus reflected closer alignment with those of the faculty, as the graphic illustrates.



First Treatment: Distant Metastases to Lungs.

What led to the shift? Readers indicated they changed their view based on clinical data regarding response and durable response rates (3.7% and 14.81% of readers, respectively). Toxicity also played a role, cited by 7.4%. A sizable proportion of readers cited all 3 factors as affecting their judgment (44.44%).

Faculty and participants largely agreed about when to recommend hospice care for the patient. Faculty presenters said that hospice was a reasonable option after progression of liver disease following chemotherapy, though they did recommend enrolling the patient in a clinical trial. About 7% of faculty and 8% of participants (pre-reading) would advise hospice care upon development of brain metastases. More than three-quarters of faculty (78%) viewed hospice care as appropriate after progression following whole brain radiotherapy and stereotactic radiosurgery, at a point when the patient's Karnofsky performance status was 60% and declining. Similarly, about 85% of readers would advise hospice in the face of disease progression and declining functional score. Another 8% of readers would recommend hospice when discussing therapy after detection of distant metastatic disease.

After reading the case, nearly 40% of readers said that they would introduce the topics of hospice and palliative care with the patient after first detection of distant metastatic disease. Another third (32%) would first discuss these issues at progression of metastatic disease after therapy. About 7% would raise these matters for the first time at development of brain metastases, and 18% would use disease progression and declining functional score as the impetus for bringing up these topics. About 4% would introduce discussion of hospice and palliative care at initial suspicion of melanoma. These findings are consistent with direction to discuss hospice and palliative care well before they are needed.

CME Post-test Questions

Please answer each question on the space provided on page 14.

1. Dermoscopy allows for:
   A. Calculation of the tumor mitotic rate
   B. More accurate staging of thin melanomas
   C. Visualization of skin structures that suggest melanoma
   D. All of the above

2. The best diagnostic biopsy for a changing pigmented lesion is:
   A. Excisional biopsy with narrow margins
   B. Excisional biopsy with wide margins
   C. Sentinel lymph node biopsy
   D. Small (2-mm) punch biopsy in the center of the lesion
   E. Superficial shave biopsy

3. How wide of an excision is needed for a diagnosed thin melanoma?
   A. 1 cm on both sides of the prior local excision and down to muscle fascia
   B. 3 cm on both sides of the prior local excision and down to muscle fascia
   C. No further excision necessary if negative margins obtained on initial excision
   D. Excision such that the total width of the excised specimen is 1 cm and down to muscle fascia

4. The majority of all new invasive melanomas have a(n):
   A. Age of onset of greater than 65 years
   B. Thickness of 1 mm or less
   C. Tumor mitotic rate of 4 mitoses/mm^2
   D. Vertical growth phase

5. In which of the following age groups is tumor thickness less likely to impact SLN positivity?
   A. Under age 35 B. Age 36–50
   C. Age 51–64 D. Over age 65

6. Which of the following is true?
   A. An increase in deaths due to melanoma is being seen due to thin lesions
   B. Tanning booths provide a "safe" form of U.V. light
   C. Melanomas cannot metastasize until they reach 0.7 mm in thickness
   D. Adjuvant systemic therapy is indicated in Stage IB patients due to their low but real risk of metastasis

7. Which of the following prognostic features for thin melanomas is currently not part of the AJCC Melanoma Staging System?
   A. Clark level
   B. Thickness
   C. Tumor mitotic rate
   D. Ulceration

8. Post-staging tests shown to improve survival in patients with Stage IB disease include:
   A. Baseline chest x-ray
   B. CT scans
   C. LDH testing
   D. PET scan
   E. None of the above

9. A patient with Stage IB melanoma has a 5-year survival rate of:
   A. 60%
   B. 70%
   C. 80%
   D. > 90%

10. The risk of melanoma doubles in:
    A. All relatives of the melanoma patient
    B. First-degree family members of the melanoma patient
    C. The patient who previously had melanoma
    D. All of the above

Please answer these questions BEFORE OPENING this newsletter.

The following questions refer to the case study of a 53-year-old man with a changing pigmented lesion, outlined on the front cover. Please circle the answer that most represents your opinion, detach this perforated page, and fax to 973-682-9077. Or, if you prefer, you can visit the Melanoma Care Consortium at www.MelanomaCare.org.

1. What type of initial biopsy is appropriate for this changing pigmented lesion?
A. 2-mm punch biopsy
B. Shave biopsy
C. Excisional biopsy with narrow margins
D. Excisional biopsy with wide margins

2. Given the final pathology report, what is the next step for this patient?
A. Wide excision
B. Mohs micrographic surgery
C. Wide excision and SLNB
D. No further treatment

3. Does the expense of SLNB outweigh the potential benefit of finding a positive SLN in patients with thin melanoma?
A. Yes
B. No

4. At baseline, what medical tests are appropriate for a Stage IB melanoma patient?
A. CT of chest, abdomen, and pelvis
B. Baseline chest x-ray
C. LDH, liver function tests, and CBC
D. PET scan
E. None of the above

5. What follow-up measures would you recommend for a Stage IB patient?
A. Annual chest x-ray and LDH level
B. Initial consultation with oncologist
C. Advise first-degree family members to receive skin examinations
D. All of the above

Please retain this sheet because it includes the CME post-test questions on page 15.

MELANOMA CARE OPTIONS

JULY 2005

FOSTERING AN INTERDISCIPLINARY APPROACH TO MELANOMA CARE

PharmAdura, LLC
523 Route 303
Orangeburg, NY 10962

PRSRT STD
U.S. POSTAGE
PAID
Permit No. 664
S.HACKENSACK,NJ

7/05