At a symposium conducted in conjunction with the 2008 Annual Meeting of the Society of Surgical Oncology and moderated by Jonathan S. Zager, MD, and Keith A. Delman, MD, four renowned leaders in medical and surgical oncology discussed management of melanoma. They reviewed melanoma staging and predictors of outcome, atypical melanocytic neoplasms and Spitz nevi, an approach to complicated regional disease, and the role of surgery for Stage IV disease.

**Learning Objectives**
Upon completing the review of this symposium, the physician should be able to:
- Understand the role of adjuvant radiation and other treatments in conjunction with surgery in the management of regional nodal disease.
- Discuss the selection criteria for and the results of surgery in the multi-modality approach to the management of stage IV melanoma.
- Know the characteristics of primary and metastatic melanoma that predict metastatic risk and survival outcomes.
- Know the TNM criteria and stage grouping for the melanoma staging system.

**Audience**
Surgical oncologists, medical oncologists, and other physicians who participate in the care of patients with melanoma and researchers who are interested in the investigation of new approaches to the treatment of this disease.

This educational activity and newsletter were supported by an educational grant from Schering-Plough Corporation.

---

**Current Management of Melanoma: From Ambiguous Lesions to Metastatic Disease**

*Highlights from a symposium conducted in conjunction with The Society of Surgical Oncology’s Annual Meeting, held in Chicago, Illinois, on March 13–16, 2008.*

**AJCC Melanoma Staging and Predictors of Melanoma Outcome**

Charles M. Balch, MD, Professor of Surgery, Oncology and Dermatology, Johns Hopkins Medicine, Baltimore, reviewed the current version of the melanoma staging as well as new data on staging and prognosis contained in the 2008 version of the American Joint Committee on Cancer (AJCC) Melanoma Staging Schema. The final version of the melanoma staging criteria are embargoed until May 2009 and implementation of the new version will not take place officially until January 2010. Therefore, this chapter will include the 6th edition version of melanoma staging as the primary reference and also describe those changes recommended by the Melanoma Staging Committee in 2008.

The AJCC Melanoma Task Force used a collaborative database of 17,600 patients to redefine the staging classifications in 2001. During the past two years, 49,487 patients with Stages I, II, and III melanoma have been entered into the database to update the staging schema. Dr. Balch noted that 70% of melanoma patients present with T1 melanomas. In predicting survival by tumor thickness, the database shows that for patients with Stage I/II melanoma, those with T1 melanomas (0.01-0.50 mm) have a 10-year melanoma-specific survival rate of 95%, which goes down to 40% for those with T4 melanomas (> 8 mm).

The updated staging classification data takes into account the impact of ulceration. In the T classification, the “a” category indicates ulcerative melanoma. In the stage groupings, the committee combined thicker, nonulcerative (well-differentiated) melanomas with thinner, ulcerative melanomas. For example, T1b and T2a melanomas, with 10-year survival rates of 87% and 83%, respectively, are both Stage IB. The exception is T4b melanomas, for which there is a separate category—Stage IIC.

“This use of tumor ulceration allows us to take into account more aggressive melanomas that are not as thick but have an increased risk for metastatic disease, similar to those nonulcerated melanomas that are thicker,” said Dr. Balch. He noted that the Melanoma Committee also decided that a localized melanoma is Stage II and all regional disease is Stage III.

New information from a multivariate Cox regression analysis for Stages I and II melanoma indicates the importance of mitotic rate as a predictor of outcome. Among patients in whom mitotic rate was not measured, the most dominant feature predicting outcome was tumor thickness, followed by ulceration and age. However, when tumor thickness was correlated with number of mitoses, as tumor thickness increased the incidence of mitosis more than zero/mm² increased. Among Stage I/II melanoma patients, there was a decrease in 5-year and 10-year survival rate as the number of mitoses/mm² increased, which was a highly significant correlation. These findings are now being reviewed by the Melanoma Staging Committee to determine if mitotic rate should be incorporated into the revised TNM staging system.

A study by Gimotty and colleagues demonstrated the importance of mitotic rate. Among patients with T1 melanomas, the relapse rate fell in a range from 0.5% (for patients with mitotic rate of zero and radial...
Current Management of Melanoma: From Ambiguous Lesions to Metastatic Disease

Needs Assessment
The management of melanoma patients requires a multidisciplinary approach, and the surgical oncologist often plays a central role in guiding therapy. Surgical oncologists must understand surgical approaches to the management of Stage III and IV melanoma. The surgeon should also understand the pathology of the primary lesion and nodal treatment algorithms for lesions with ambiguous metastatic potential.

Although surgery is the mainstay of therapy in melanoma, there is a definitive role for adjuvant systemic therapy as well as radiation. The surgeon should understand other forms of treatment available as well as the risks, benefits and alternatives in using these treatment modalities. Surgical oncologists must stay abreast of the most recent advances in research and treatment including systemic therapy options.

CME Credits
This activity has been planned and implemented in accordance with the Accreditation Council for Continuing Medical Education (ACCME) by the Society of Surgical Oncology.

The Society of Surgical Oncology (SSO) is accredited by the ACCME to provide continuing medical education for physicians. The SSO takes responsibility for the content, quality, and scientific integrity of this CME activity.

SSO designates this educational activity for a maximum of 1.75 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Term of approval is from June 1, 2008 to June 1, 2009

Disclosure Statements
Martin C. Mihm, MD, reports none.
Merrick I. Ross, MD, reports speaker relationship with Schering-Plough and Genentech, and medical advisory board participant for Schering-Plough.
Vernon K. Sondak, MD, reports none.
Charles M. Balch, MD, reports honorarium from Schering Plough.

Discussion of Experimental or Off-label Products or Uses
Martin C. Mihm, MD, reports no discussion of off-label products or uses.
Merrick I. Ross, MD, reports no discussion of off-label products or uses.
Vernon K. Sondak, MD, discusses investigational and off-label uses of interferon alfa-2b, interleukin-2, and granulocyte-macrophage colony-stimulating factor.
Charles M. Balch, MD, reports no discussion of experimental or off-label products or uses.

This newsletter is published jointly by Medical Association Communications, Newtown, Pennsylvania, and the Society of Surgical Oncology, Inc., Arlington Heights, Illinois.

© 2008 Medical Association Communications and the Society of Surgical Oncology, Inc.

No content may be reproduced in any form without the prior written permission of the publishers. The opinions expressed herein are those of the speakers and do not necessarily reflect the opinions or recommendations of their affiliated institutions, the publishers, or any other person or entity.

growth pattern) to 31% (for male patients with > 0 mitotic rate). For example, within T1 melanomas (0.1-1 mm), female patients with a 0.5 mm melanoma and no mitosis have a 10-year survival rate of 97%. “They could safely be treated with conservative therapy and minimum follow-up,” said Dr. Balch.

Dr. Balch explained that age is an important independent factor in predicting 10-year survival. In the 2001 data, the 10-year survival rate for patients ages 10 to 19 with melanoma was 80%, which declined incrementally every decade to 41% for those over age 80 years. While older patients, in general, present with thicker melanomas and more often with ulceration, patient age remains as one of the most powerful predictors of survival outcome in every cohort of patients.

Dr. Balch next presented data on Stage III melanoma patients from the melanoma database. Those with Stage IIIA melanoma have micrometastasis from a nonulcerative primary tumor (T1-4a/N1a or N2a). In the Stage IIIB group, two-thirds of patients have micrometastases arising from an ulcerative primary tumor (T1-4b/N1a or N2a) and one-third have palpable disease arising from a nonulcerative melanoma. Those patients with palpable nodal metastases arising from ulcerative melanomas or those with recurrent regional disease are classified as Stage IIIC (T1-4b/N2c or N3). Among all Stage III patients the range of survival is enormous, from 69% for 1 to 3 microscopic (clinically occult) nodal metastases arising from a nonulcerated melanoma to 25% for >3 macroscopic (clinical detected) nodal metastases arising from ulcerated melanomas.

According to a multivariate Cox regression analysis, for all patients with Stage III melanoma, the most powerful indicators that a nodal metastasis arising from an ulcerative melanoma will spread to distant sites after surgery are number of metastatic lymph nodes, age, and ulceration. When this data is subdivided between patients with micro- and macrometastases, the number of positive lymph nodes is the only predictor of outcome for patients with macrometastases. In contrast, in patients with micrometastases, features of the primary melanoma, including mitotic rate, ulceration, and tumor thickness, also predict outcome.

In conclusion, the AJCC Melanoma Committee is not recommending major changes for the TNM stage grouping criteria for melanoma Stages I, II, and III. However, mitotic rate of primary melanoma is an independent factor and will likely be incorporated into the T1 classification. In addition, the committee will recommend that immunohistochemical detection of nodal metastases is acceptable for staging purposes and that there should be no lower limits of nodal metastasis to designate node-positive disease.
Atypical Melanocytic Neoplasms and Spitz Nevi

Martin C. Mihm, MD, Clinical Professor of Pathology and Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, began his discussion of atypical melanocytic neoplasms and Spitz nevi by describing the classic histology of a Spitz nevus, which is a sharply circumscribed dermoepidermal melanocytic proliferation.

It is an inverted cone with the base parallel to the epidermis and the apex in the reticular dermis. There are large junctional thèques separated by cleft-like spaces from the hyperplastic epidermis and then “raining-down” vertical spindled fascicles that break up into single cells. The cells further down in the dermis go from nests of cells into single cells. The cells diminish in size as the base is approached.

Mitoses are present in 20% of Spitz nevus cases. However, they are superficial and do not lie in the margin. Intravascular proliferations are seen in 14% of childhood Spitz nevi. Pagetoid spread is present to some degree in most cases. It is more prominent in children than adults and also more common in acral than other sites. Stern and colleagues showed that 96% of melanomas have pagetoid spread. “It is only important when the cells are malignant,” said Dr. Mihm.

Desmoplastic Spitz nevi present in adults as a tan or flesh-colored nodule (< 1.0cm). They affect the extremities and trunk and spare the palms and soles. Desmoplastic Spitz nevi are lesions that have spindle cells and epithelioid cells in a dense stroma; they do not have mitotic activity but they do mature. Some pathologists may confuse this with a desmoplastic melanoma, which is composed of hyperchromatic irregular fibroblast-like cells.

The spindle cell nevus is a black or dark dome-shaped lesion or plaque (2-6 mm in diameter) located on proximal extremities or the trunk. It is generally seen in women in their 20’s, but also occurs on the knees and elbows in children. Histologic features include superficial plaque-like growth involving the epidermis and/or the dermis. This lesion is not associated with dermal mitosis.

Another typical Spitz nevus lesion is a deep penetrating nevus. This is a blue to blue-black lesion (4-5 mm diameter), which is often diagnosed as malignant melanoma. It is associated with fascicles of cells that are surrounded by melanophages. It frequently shows a plexiform pattern and it extends in an inverted cone-like manner, often into the subcutaneous fat. Mitoses are rare. However, metastasis to lymph nodes has been reported in mitotically active lesions.

Atypical Spitz Nevi

According to Barnhill and colleagues, atypical Spitz nevi are a subset of Spitzoid melanocytic proliferations with worrisome histology but indeterminate biologic behavior. They have architecture that resembles the vertical growth phase of melanoma and cytology that resembles conventional Spitz nevi. Metastases, when present, tend to be confined to regional lymph nodes. They are usually larger than typical Spitz nevi (> 1 cm).

A group of atypical Spitz nevi tumors were studied by Spatz and coworkers, who found that the only independent prognostic variables were age > 10 years, ulceration, involvement of subcutis, and mitotic rate > 6 per mm². The last three features do not occur in classical Spitz nevi. Dr. Mihm noted that in some rare cases, atypical Spitz nevi can be fatal. “Spitzoid melanoma is a distinctive entity,” he said.

Spitzoid melanoma

The classic Spitzoid melanoma is seen mainly in the pediatric population, most commonly in the head and neck. Its biological behavior is unpredictable. The lesion shows a dominantly dermal-based expansile nodule with variable permeation of the subcutaneous fat.

The classic Spitzoid melanoma is seen mainly in the pediatric population, most commonly in the head and neck. It shows numerous bizarre-appearing giant cells similar to those described in the Spitz nevus but with greater pleomorphism and striking nuclear atypia; the cells assume a confluent sheet-like disposition. Usually there is extension deep, even into the subcutaneous fat.

Bastian and colleagues conducted a study comparing genomic hybridization of 17 Spitz nevi versus melanoma. They found that 13 Spitz nevi had no chromosomal anomalies, 3 had gains of 11p, and 1 had a gain of 7q21. In another study by Bastian et al., 102 Spitz nevi were studied for 11p copy increases by FISH (11p is the site of the hRAS gene). They found that 11.8% had at least three times the copy number of the short arm of chromosome 11, as compared to melanomas, which have variable but numerous chromosomal abnormalities shown by comparative genomic hybridization. “These tests are examples of how genomics can be helpful in understanding lesions with different biological outcomes,” said Dr. Mihm.

Treatment for Spitz nevi and variants is complete excision. Atypical tumors with current melanoma margins (≤ 1cm) are excised. Spitzoid melanoma is treated with conventional melanoma therapy with sentinel node biopsy for lesions > 1 mm. Dr. Mihm recommended sentinel node biopsy in atypical Spitz tumors as a staging procedure. He also recommended it for tumors that meet any two of the following criteria: lesions with large expansile nodules in the base, plexiform lesions that extend throughout the dermis, lesions > 2 mm in depth, lesions with mitoses > 6 mm², and lesions with atypical marginal mitoses.

Childhood Melanoma

Dr. Mihm concluded with a discussion of childhood melanoma, which generally occurs in the head and neck, especially the scalp. The dorsal surface is favored for lesions arising in congenital nevi. However, more recent studies emphasize the more generalized distribution of melanoma on the remainder of the body and especially on extremities.

Features associated with death in children younger than age 13 usually include large bulky lesions that are usually deeply invasive, ulceration, necrosis, severe pleomorphism, numerous dermal and marginal mitoses, intravascular invasion, and multiple positive lymph nodes in the draining basin.

Dr. Mihm next discussed epithelial-mesenchymal transition (EMT), which refers to embryonic development and tumor progression. “You have epithelial cell separation and transformation of the cells into fibroblast-like cells or spindle cells,” he said. This occurs in melanoma through NFkappaB activation of Sna1. This results in repression of E-cadherin and expression of N-cadherin and production of metalloproteinases that allows a tumor to invade. Repression of E-cadherin also leads and activation of WNT5A, which is the factor most associated with cell motility. Epithelioid cells of melanoma are driven by other mechanisms, including cyclin-D or CDK’s.
Stage III melanoma includes both nodal metastases and in-transit disease. Merrick I. Ross, MD, Professor of Surgery, Chief, Melanoma Section, Department of Surgical Oncology, M. D. Anderson Cancer Center, Houston, focused his presentation on the multi-modality management of patients with advanced nodal disease.

Patients with advanced nodal disease are those with multiple palpable involved nodes, large matted lymph nodes with extracapsular extension, nodal disease that is fixed to or ulcerated through the skin or fixed to the underlying structures, associated lymphedema, in-basin recurrence after a previous therapeutic dissection, or marginally resectable or unresectable nodal metastases.

“Stage III melanoma has changed over the past 10 to 15 years because of the use of sentinel node biopsies as a staging procedure for patients with intermediate and high risk primary melanomas,” said Dr. Ross.

“The presentation of nodal disease has changed over the past 10 to 15 years because of the use of sentinel node biopsies as a staging procedure for patients with intermediate and high risk primary melanomas,” said Dr. Ross. Historically, most nodal disease was seen in patients who had a wide excision only and no pathologic assessment of their clinically negative regional lymph node basin(s), who developed clinically apparent nodal disease later. Today, the most common scenarios in which patients develop palpable nodal disease are a false negative sentinel lymph node biopsy, no completion lymph node dissection after a positive sentinel lymph node biopsy, unknown primary melanoma, late recurrence after treatment for thin melanoma, synchronous advanced primary disease and nodal metastases, and in-basin failure after therapeutic dissection.

“These are complicated patients who have competing risks in terms of the patterns of recurrent disease,” said Dr. Ross. At least 50% will develop systemic (Stage IV) disease. There also is a 20% to 50% risk for in-basin failure after a therapeutic dissection, which can be a source of significant morbidity and may be difficult to treat. It is also important to consider the potential toxicity of therapies that are used as adjuvant to surgery, as well as underlying co-morbidities.

The primary management goal in treating patients with advanced Stage III melanoma is durable local/regional disease control, which in turn may achieve long-term survival in addition to durable palliation. “We need to accomplish these goals in a way that minimizes morbidity and functional deficits that may occur from surgery or other therapies,” said Dr. Ross.

**Extent of Surgical Dissection**

For axillary dissection, a formal level I to III node dissection is recommended. This removes the entire lymph node basin. Whether to take down the pectoralis minor muscle is the subject of some debate. Dr. Ross noted that this maneuver results in little morbidity and provides excellent exposure to the level III lymph nodes. For patients with cervical metastases, a comprehensive level II to V neck dissection is standard. Depending on the location of the primary or the location of the nodal disease, level I nodes may be included as well.

The greatest controversy concerns the surgical treatment of metastasis to the groin. Some experts recommend a combined superficial femoral and iliac and obturator node dissection for any patient who has palpable node disease. Others suggest a selective approach, recommending a femoral dissection, but being selective about performing an iliac dissection, depending on the number of positive nodes, whether Cloquet’s node is positive, or if there is disease evident on pelvic CT or PET scan.

Surgical treatment for very advanced disease is an en bloc resection of all involved structures within the nodal basin, keeping in mind the importance of avoiding a negative impact on functional outcome.

Neck dissection is a well-tolerated procedure with little short- or long-term morbidity, particularly if the spinal accessory nerve can be spared if not directly involved. A possible complication of axillary dissection is lymphedema; however, the rate is low in patients who have formal node dissection for melanoma. The rate is lower than would be predicted from the breast cancer experience because the chest wall lymphatics are preserved in melanoma, while they are not in breast cancer (as a result of the mastectomy or the use of XRT in breast conservation patients). Morbidity associated with inguinal dissection includes a high rate of wound infection/dehiscence, lymphedema, and nerve paresthesia.

Concerning the decision about routine or selective iliac and obturator dissection, Dr. Ross noted that there are no prospective, randomized data concerning survival, regional control, morbidity, or quality of life. The data from a few articles in the literature suggest that 10% to 15% of patients with clinically palpable disease in the superficial femoral region will develop pelvic nodal disease after superficial dissection. Among these patients, less than 1% will develop pelvic nodal metastases.

“We need to accomplish these goals in a way that minimizes morbidity and functional deficits that may occur from surgery or other therapies,” said Dr. Ross.

“The presentation of nodal disease has changed over the past 10 to 15 years because of the use of sentinel node biopsies as a staging procedure for patients with intermediate and high risk primary melanomas,” said Dr. Ross.
The risk of failure within the nodal basin increases relative to the size of lymph node involvement, number of nodes involved, and in the presence of extracapsular extension as well as the anatomic basin involved.

All of these patients are also at high risk for subsequent distant metastases. While such events are the ultimate determinants of survival—and therefore adjuvant systemic therapy is a critical component in the management of these patients—durable regional disease control is of great value in terms of quality of life. Therefore, a predicted risk of recurrence is reduced to 5% to 10% with radiation therapy. The most serious side effect of radiation therapy is lymphedema, which is seen more often after multi-modality treatment for inguinal nodal disease than the head/neck or axillary regions. Patients with a body mass index ≥25 kg/m² are at especially high risk for developing lymphedema.

The risk of failure within the nodal basin increases relative to the size of lymph node involvement, number of nodes involved, and in the presence of extracapsular extension as well as the anatomic basin involved. Therefore, the risk of regional post-dissection failure, as well as the risk for postradiation morbidity, must be factored into the decision-making process to use adjuvant irradiation. When considering radiation therapy, we lower the threshold for cervical disease, because the risk for recurrence is high, and raise it for groin/pelvic disease, because the complication rate is higher,” said Dr. Ross.

There has been a resurgence of interest in surgical therapy for metastatic melanoma,” began Vernon K. Sondak, MD, Chief, Division of Cutaneous Oncology, H. Lee Moffitt Cancer Center & Research Institute, and Professor, Departments of Oncologic Sciences and Surgery, University of South Florida College of Medicine, Tampa.

“Reasons for this resurgence include improvements in imaging which allow for better selection of patients, availability of minimally invasive approaches, decreased morbidity and mortality after major surgery, failure of nonsurgical treatments to improve overall survival for patients with metastatic melanoma, and reports of long-term survival after resection.

“The secret to surgical management is selection,” said Dr. Sondak. Whole body PET-CT fusion scans and brain MRI scans should be performed to select patients with isolated tumors that can be resected. In a study by Brady and colleagues, 36 of 103 patients with potentially resectable stage IIC, III, or IV melanoma had their management altered (usually their surgery canceled) by PET/CT findings.” Dr. Sondak noted that false positives are common in melanoma, at around 10% or even higher.

In addition to selecting surgical candidates, it is also important to select the right procedure with the least morbidity necessary. There should also be clear therapeutic goals of the procedure, such as cure, palliation, or symptom prevention.

According to the National Cancer Database, the 5-year survival rate for patients with Stage IV melanoma is 13.8%. “Clearly, there are more Stage IV survivors than most surgeons (or oncologists) would have expected,” said Dr. Sondak. Therefore, long-term survival is not necessarily proof that surgery caused the outcome. Selection bias may play a role; that is, surgeons select patients who would have lived a long time anyway.

Retrospective studies are characterized by significant selection and referral bias, as are prospective randomized trials of adjuvant therapy. For example, in order for patients to be entered into a trial, they must be able to undergo surgery, be able to survive surgery, be rendered disease-free by surgery, be healthy enough to get referred, recover from surgery in time to enroll, be willing to accept randomization, and have no prior treatment for metastatic melanoma.” Prospective randomized trials of adjuvant therapy after resection of metastatic melanoma overestimate the prognosis for patients with resected stage IV melanoma,” said Dr. Sondak.

“The secret to surgical management is selection,” said Dr. Sondak.

To limit the bias, Dr. Sondak and colleagues conducted the Southwest Oncology Group (SWOG)-9430 study, which was a prospective evaluation of surgery for metastatic melanoma. 20 Patients were registered to the study before surgery, once the decision had been made that the patient was potentially resectable. Any site(s) of disease were allowed per physician choice. The investigators evaluated the resectability rate and outcome.

Among 77 patients entered into the study from 18 SWOG institutions, 4 had no evidence of metastatic melanoma at resection, 10 were unresectable, and 63 (82%) were resected free of disease from different—sometimes multiple—sites (61% skin/soft tissue/lymph nodes; 13% lung, 8% liver, 5% central nervous system, 27% other visceral sites).

Most of the patients had a recurrence within 6 months of the resection. Interestingly,
overall survival was much longer. Half the patients survived 21 months, and 15% were still alive at the end of the study, in some cases beyond 5 years. At 24 months, the overall survival rate was twice the progression-free survival rate, meaning half the people who were alive at 2 years were alive with recurrent disease. Median survival was more than 3 times the median time to progression.

Dr. Sondak addressed how this compares to systemic therapy. He reviewed a meta-analysis, in which 2100 patients on 70 cooperative group phase II melanoma trials were evaluated for progression-free and overall survival after systemic therapy. Median progression-free survival was 1.7 months; progression-free survival at 6 months was 14.5%. In contrast, median progression-free survival at 6 months after surgery was 50%. At one year, overall survival for patients on systemic therapy was 25.5%, compared to 71% of patients after surgery. Median survival for surgery patients was 21 months versus 6.2 months for patients receiving systemic therapy. Further analysis revealed that the highest progression-free survival tended to be seen in the smallest studies, while the larger studies came closer to the average.

How does the SWOG trial compare to other prospective trials in resected Stage IV melanoma? A Phase II trial of adjuvant granulocyte-macrophage colony-stimulating factor (GM-CSF) was conducted by Spitzer et al., and a randomized phase III trial of the adjuvant canvaxin allogeneic vaccine was performed by Morton and colleagues. All patients in both studies were resected free of disease and restaged prior to entry.

In the GM-CSF study, progression-free survival was compared to historical controls. At 6 months about half of all patients had a recurrence. However, 64% of patients treated with GM-CSF were alive at 2 years versus 12% of controls. In the randomized prospective trial by Morton, 496 patients were randomized to receive Bacille Calmette-Guerin (BCG) plus either canvaxin allogeneic vaccine or placebo. Reresection was encouraged in case of relapse in potentially resectable sites.

In the Spitzer study, median survival was 37.5 months for resected Stage IV patients receiving GM-CSF (vs. 8.1 months for historical controls). In the Morton study, median survival was 38.7 months for the placebo arm, and there was 5-year overall survival of 45%.

“The long overall survival attributed to the adjuvant therapy in this nonrandomized study (Spitzer) can perhaps be explained by the placebo arm of the Morton study,” said Dr. Sondak. He noted that in the SWOG-9430 trial, median survival was shorter than in these trials, at 21 months; the 5-year overall survival was 15%, likely reflecting the selection bias in prospective trials previously discussed.

Dr. Sondak asserted that surgeons do

References


Dr. Sondak concluded: “The role of neoadjuvant therapy deserves further exploration, but surgery remains the first option for appropriately selected patients with isolated, advanced, or metastatic melanoma regardless of the site, provided that a complete resection can be carried out.”

“Neoadjuvant therapy is an extremely important adjunct in borderline or unresectable patients,” said Dr. Sondak.

1. Patients with T1 melanomas should be categorized as T1b (with higher metastatic risk) with which of the following characteristics of the primary melanoma?
   a. Nodular growth pattern  c. Ulceration
   b. Female gender  d. Level III invasion

2. A patient with a single nodal metastasis by sentinel node biopsy arising from an ulcerative melanoma (T2b) would be staged as:
   a. IIIa  c. IIIC
   b. IIIb

3. Which characteristics of melanoma apply best in patients > 70 years old, compared to younger adults with the same T stage:
   a. Lower incidence of sentinel node +; lower mortality rates  b. Higher incidence of sentinel node +; higher mortality rates
   c. Higher incidence of sentinel node +; lower mortality rates  d. Lower incidence of sentinel node +; higher mortality rates

4. The compound nevus of Spitz is a pre-malignant lesion.
   a. True  b. False

5. Treatment of both severely atypical Spitz nevi and Spitzoid melanoma usually includes sentinel lymph node biopsy.
   a. True  b. False

6. The following information is useful in making recommendations for including a pelvic (deep) node dissection when performing an inguinal dissection except:
   a. Number of positive nodes in the superficial compartment  b. Whether or not Cloquet’s node is involved
   c. The BMI of the patient  d. Whether the disease in the superficial compartment is microscopic or macroscopic  e. Findings on a CT of the pelvis

7. Which of the statements about adjuvant nodal irradiation is (are) true?
   a. It should be offered routinely to patients who have undergone a therapeutic dissection for clinically positive nodes
   b. The number and size of involved nodes influences recommendations for XRT
   c. If extranodal extension is absent, XRT is not necessary
   d. Both basin location and patient BMI influences morbidity of XRT
   e. b and d

8. All of the following are reasons for the resurgence of interest in surgery for stage IV melanoma EXCEPT:
   a. Improvements in imaging to allow for better patient selection
   b. Reports of long-term survival after resection
   c. Decreased morbidity and mortality after major surgery
   d. Availability of anti-CTLA4 (correct?) antibodies to decrease recurrence after surgery
   e. All of the above

9. Which of the following statements best characterizes PET-CT scans in the preoperative evaluation of stage IV melanoma patients?
   a. Allows for imaging of the entire body
   b. Eliminates the need for any other form of imaging to detect metastatic disease
   c. Has a very low rate of false-negative findings (below 1%)  d. Frequently reclassifies patients as “resectable” who were initially thought to have unresectable disease
   e. All of the above

10. According to the National Cancer Data Base, the 5-year survival rate for patients with stage IV melanoma, including all types of treatment approaches, is:
    a. <1%
    b. 4.5%
    c. 13.8%
    d. 24.4%
    e. 33.3%
Objectives
Upon completion of this monograph, participants should be able to:

- Understand the role of adjuvant radiation and other treatments in conjunction with surgery in the management of regional nodal disease.
- Discuss the selection criteria for and the results of surgery in the multi-modality approach to the management of stage IV melanoma.
- Know the characteristics of primary and metastatic melanoma that predict metastatic risk and survival outcomes.
- Know the TNM criteria and stage grouping for the melanoma staging system.

Program Evaluation

1. How well organized was the newsletter? (1 = poor; 2 = fair; 3 = good; 4 = excellent)

2. How would you rate the clarity of the newsletter’s content? (1 = poor; 2 = fair; 3 = good; 4 = excellent)

3. Overall, how would you rate the importance of the newsletter? (4 = very; 3 = moderate; 2 = little; 1 = not at all)

4. Do you intend to make any changes in your practice or patient care as a result of this newsletter?
   Yes _____, No _____
   If Yes, how? Comment

5. Did the newsletter include proper disclosure of speakers’ potential conflict of interest and relationship with industry?
   Yes _____, No _____

6. Did the newsletter include proper disclosure of speakers’ discussion of FDA Off-Label use of medications or products?
   Yes _____, No _____
   If NO, please comment

7. Was this a fair and balanced newsletter? Please comment on the scientific rigor, fairness, and balance of the material.
   Comment

8. What related topics would you find useful for future SSO programs and publications?

Name ________________________________
Address ________________________________
City/State/Zip __________________________
Phone _______________________________
Fax _________________________________
Email ________________________________
Number of credit hours claimed ________
Signature ______________________________

Medical Association Communications
54 Friends Lane, Suite 125
Newtown, Pennsylvania 18940