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ASCO SPECIAL ARTICLE

Sentinel Lymph Node Biopsy for Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Joint Clinical Practice Guideline

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This guideline was developed through collaboration between the American Society of Clinical Oncology and Society of Surgical Oncology and has been published jointly by invitation and consent in both *Journal of Clinical Oncology* and *Annals of Surgical Oncology*.

Editor's note: This represents a brief summary overview of the complete "Sentinel Lymph Node Biopsy for Melanoma: American Society of Clinical Oncology and Society of Surgical Oncology Joint Clinical Practice Guideline" and provides the recommendations with brief discussions of the relevant literature for each. The complete guideline, which includes comprehensive discussions of the literature, methodologic information, and additional citations, along with an Appendix and Data Supplement, is available on the American Society of Clinical Oncology Web site (http://www.asco.org/guidelines/snbmelanoma) and Society of Surgical Oncology Web site (http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx).

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

Purpose
The American Society of Clinical Oncology (ASCO) and Society of Surgical Oncology (SSO) sought to provide an evidence-based guideline on the use of lymphatic mapping and sentinel lymph node (SLN) biopsy in staging patients with newly diagnosed melanoma.

Methods
A comprehensive systematic review of the literature published from January 1990 through August 2011 was completed using MEDLINE and EMBASE. Abstracts from ASCO and SSO annual meetings were included in the evidence review. An Expert Panel was convened to review the evidence and develop guideline recommendations.

Results
Seventy-three studies met full eligibility criteria. The evidence review demonstrated that SLN biopsy is an acceptable method for lymph node staging of most patients with newly diagnosed melanoma.

Recommendations
SLN biopsy is recommended for patients with intermediate-thickness melanomas (Breslow thickness, 1 to 4 mm) of any anatomic site; use of SLN biopsy in this population provides accurate staging. Although there are few studies focusing on patients with thick melanomas (T4; Breslow thickness, $>$ 4 mm), SLN biopsy may be recommended for staging purposes and to facilitate regional disease control. There is insufficient evidence to support routine SLN biopsy for patients with thin melanomas (T1; Breslow thickness, $<$ 1 mm), although it may be considered in selected patients with high-risk features when staging benefits outweigh risks of the procedure. Completion lymph node dissection (CLND) is recommended for all patients with a positive SLN biopsy and achieves good regional disease control. Whether CLND after a positive SLN biopsy improves survival is the subject of the ongoing Multicenter Selective Lymphadenectomy Trial II.

INTRODUCTION

Metastasis to regional nodes is the most important prognostic factor in patients with early-stage melanoma and has been shown to occur in approximately 20% of patients with intermediate-thickness tumors.[1,2] As such, it is critically important to identify those patients for whom the expected benefits of resecting regional lymph nodes outweigh the risks of surgical morbidity.

Sentinel lymph node (SLN) biopsy is commonly used by surgeons who treat melanoma in the United States, Canada, Australia, and Western Europe and has been endorsed by the American Joint Committee on Cancer (AJCC) as a valuable staging procedure for patients with melanoma who are at risk of clinically occult nodal metastases. This highly accurate and low-morbidity staging procedure should be used to guide treatment decisions (ie, completion lymph node dissection [CLND] and adjuvant therapy) as well as entry into clinical trials.[3]

To develop and formalize guideline recommendations for the use of SLN biopsy in oncology practice, the American Society of Clinical Oncology (ASCO) and Society of Surgical Oncology (SSO)

convened a joint Expert Panel. This guideline addresses two overarching clinical questions:

What are the indications for SLN biopsy?

What is the role of CLND?

This article represents a brief summary overview of the full guideline. Table 1 provides the recommendations. The full guideline, which includes comprehensive discussions of the literature, methodologic information, and additional citations, can be found online on the ASCO Web site (http://www.asco.org/guidelines/snbmelanoma) and SSO Web site (http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx). An Appendix providing a discussion of some of the key technical considerations for SLN biopsy, a Data Supplement, and clinical tools and resources are also available on the Web sites.

METHODS

ASCO and SSO convened an Expert Panel (members listed in Appendix Table A1, online only) to develop guideline recommendations based on its assessment of evidence from a comprehensive systematic review and meta-analysis of the literature.[4]

Literature Review and Analysis

Literature search strategy. A comprehensive systematic review of the literature published between January 1990 and August 2011 was completed using MEDLINE and EMBASE. Abstracts from ASCO and SSO annual meetings were also included in the evidence review. A detailed description of the systematic review methodology has been published elsewhere.[4]

Inclusion and exclusion criteria. Studies were required to report the number of patients in whom SLN biopsy was attempted, the number who had successful identification and removal of an SLN, and continuous follow-up for the group of patients who had a negative SLN biopsy. No exclusion was made based on Breslow thickness, type of study, or whether the study was retrospective or prospective in nature. However, the population reported had to be original. When a single institution had multiple reports on its populations, the report that had the largest population, longest follow-up, and/or more appropriate outcomes was selected. Studies were excluded if they reported only patients with positive SLN biopsy, referred only to a highly specific population or location, and/or involved ≤ 50 patients.

Meta-analysis. A meta-analysis was the evidentiary base for the guideline recommendations. The meta-analysis was conducted based on the results of an initial systematic review of the literature and included literature published from January 1990 through December 2009. Valsecchi et al[4] provide a detailed description of the methods and findings from the meta-analysis. Primary outcomes consisted of measures of test performance, including: the proportion

THE BOTTOM LINE

Sentinel Lymph Node Biopsy for Melanoma: ASCO and SSO Joint Clinical Practice Guideline

Intervention

- Sentinel lymph node (SLN) biopsy for patients with newly diagnosed melanoma

Target Audience

- Surgical oncologists, medical oncologists, dermatologists, primary care physicians, pathologists, nuclear medicine specialists

Key Recommendations

- Intermediate-thickness melanomas: SLN biopsy is recommended for patients with cutaneous melanomas with Breslow thickness of 1 to 4 mm at any anatomic site
- Thick melanomas: SLN biopsy may be recommended for staging purposes and to facilitate regional disease control for patients with melanomas that are T4 or $>$ 4 mm in Breslow thickness
- Thin melanomas: There is insufficient evidence to support routine SLN biopsy for patients with melanomas that are T1 or $<$ 1 mm in Breslow thickness, although it may be considered in selected high-risk patients
- Completion lymph node dissection is recommended for all patients with a positive SLN biopsy

Methods

- An Expert Panel was convened to develop clinical practice guideline recommendations based on a review of evidence from a systematic review of the medical literature

Additional Information

- This Executive Summary of the full guideline includes the clinical questions, recommendations, a brief summary of the literature, and discussions.

The full guideline (which includes a comprehensive discussion of the literature, description of the methodology, and complete reference list), along with an Appendix, a Data Supplement, and clinical tools and resources, can be found on the ASCO Web site (http://www.asco.org/guidelines/snbmelanoma) and SSO Web site (http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx).

Table 1. Summary of Clinical Practice Guideline Recommendations

Clinical Question	Recommendation
What are the indications for SLN biopsy?	
Intermediate-thickness melanomas	SLN biopsy is recommended for patients with intermediate-thickness cutaneous melanomas (Breslow thickness, 1 to 4 mm) of any anatomic site. Routine use of SLN biopsy in this population provides accurate staging, with high estimates for PSM and acceptable estimates for FNR, PTPN, and PVP
Thick melanomas	Although there are few studies focusing specifically on patients with thick melanomas (T4; Breslow thickness, > 4 mm), use of SLN biopsy in this population may be recommended for staging purposes and to facilitate regional disease control
Thin melanomas	There is insufficient evidence to support routine SLN biopsy for patients with thin melanomas (T1; Breslow thickness, < 1 mm), although it may be considered in selected patients with high-risk features when the benefits of pathologic staging may outweigh the potential risks of the procedure. Such risk factors may include ulceration or mitotic rate $\geq 1/mm^2$, especially in the subgroup of patients with melanomas 0.75 to 0.99 mm in Breslow thickness
What is the role of CLND?	CLND is recommended for all patients with positive SLN biopsy. CLND achieves regional disease control, although whether CLND after a positive SLN biopsy improves survival is the subject of the ongoing MSLT II

Abbreviations: CLND, completion lymph node dissection; FNR, false-negative rate; MSLT II, Multicenter Selective Lymphadenectomy Trial II; PSM, proportion successfully mapped; PTPN, post-test probability negative; PVP, positive predictive value; SLN, sentinel lymph node.

successfully mapped (PSM), false-negative rate (FNR), post-test probability negative (PTPN), and predictive value positive (PVP) using same nodal basin recurrence as the outcome of interest. The PSM was defined as the ratio between the number of patients who had at least one SLN excised and the total number of patients included in the study. Specifically, for the calculation of the FNR, the following formula was used: FN/(TP + FN), where FNR = patients with regional recurrence after negative SLN biopsy/(patients with positive SLN biopsy regardless of recurrence + patients with regional recurrence after negative SLN biopsy). PTPN was calculated as the ratio of patients with negative SLN biopsy who recurred to all patients with negative SLN biopsy. This is equivalent to 1 − predictive value negative of the test. PVP was calculated as the ratio of patients with positive SLN biopsy with recurrence, divided by all patients with positive SLN biopsy. Secondary outcomes included the results of CLND and the same measurements of test performance as for primary outcomes, focusing on regional recurrences with or without distant metastases.

Study quality and limitations of the literature. There is currently only one randomized controlled trial (Multicenter Selective Lymphadenectomy Trial I [MSLT I]) that addresses whether patients with melanoma managed using SLN biopsy have better clinical outcomes than those whose disease is managed with nodal observation.[5] Hence, observational studies were included in the systematic review of the literature.

Two reviewers independently assessed the quality of the selected studies using the criteria from the Methodological Index for Non-Randomized Studies.[4,6] The methods and results of the quality assessment have been reported elsewhere.[4]

Guideline Policy

This Executive Summary for clinicians is an abridged version of the ASCO and SSO clinical practice guideline. Neither the practice guideline nor this summary is intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This summary does not recommend any particular product or course of medical treatment. Use of the practice guideline and this summary is voluntary. The full practice guideline and additional information are available on the ASCO Web site (http://www.asco.org/guidelines/snbmelanoma) and SSO Web site (http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx).

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the ASCO Conflict of Interest Management Procedures for Clinical Practice Guidelines (summarized at http://www.asco.org/guidelinescoi). Members of the Panel completed a disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline.

Table A1. Expert Panel Members

Panel Member	Affiliation
Sandra L. Wong, MD, Co-Chair	University of Michigan, Ann Arbor, MI
Gary H. Lyman, MD, MPH, Co-Chair	Duke University, Durham, NC
Sanjiv S. Agarwala, MD	St Luke's Cancer Center, Bethlehem, PA
Timothy J. Akhurst, MD	Peter MacCallum Cancer Institute, Melbourne, Victoria, Australia
Charles M. Balch, MD	University of Texas Southwestern, Dallas, TX
Alistair Cochran, MD	University of California at Los Angeles Center for Health Services, Los Angeles, CA
Janice N. Cormier, MD, MPH	University of Texas MD Anderson Cancer Center, Houston, TX
Mark Gorman	National Coalition for Cancer Survivorship, Silver Spring, MD
Theodore Y. Kim, DO, MS	Skagit Valley Regional Cancer Center, Mount Vernon, WA
Kelly M. McMasters, MD, PhD	University of Louisville, Louisville, KY
R. Dirk Noyes, MD	Huntsman Cancer Institute, Salt Lake City, UT
Lynn M. Schuchter, MD	University of Pennsylvania, Philadelphia, PA
Matias E. Valsecchi, MD	Thomas Jefferson University, Philadelphia, PA
Donald L. Weaver, MD	University of Vermont College of Medicine, Burlington, VT

Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with the Procedures, the majority of the members of the Panel did not disclose any such relationships.

RESULTS

There were 73 studies, including more than 25,000 patients, that met full eligibility criteria. A QUOROM diagram is available in the online Data Supplement, along with a table that summarizes the characteristics and outcomes of studies included in the systematic review and meta-analysis (refer to the ASCO Web site [http://www.asco.org/guidelines/snbmelanoma] or SSO Web site [http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx]). Valsecchi et al[4] provide detailed findings from the systematic review and meta-analysis.

GUIDELINE RECOMMENDATIONS

CLINICAL QUESTION 1

What are the indications for SLN biopsy?

Recommendation

Intermediate-thickness melanomas. SLN biopsy is recommended for patients with intermediate-thickness cutaneous melanomas (Breslow thickness, 1 to 4 mm) of any anatomic site. Routine use of SLN biopsy in this population provides accurate staging, with high estimates for PSM and acceptable estimates for FNR, PTPN, and PVP.

Thick melanomas. Although there are few studies focusing specifically on patients with thick melanomas (T4; Breslow thickness, >4 mm), use of SLN biopsy in this population may be recommended for staging purposes and to facilitate regional disease control.

Thin melanomas. There is insufficient evidence to support routine SLN biopsy for patients with thin melanomas (T1; Breslow thickness, <1 mm), although it may be considered in selected patients with high-risk features when the benefits of pathologic staging may outweigh the potential risks of the procedure. Such risk factors may include ulceration or mitotic rate $\geq 1/mm^2$, especially in the subgroup of patients with melanomas 0.75 to 0.99 mm in Breslow thickness.

Literature Review and Analysis

The systematic review of the literature and meta-analysis demonstrate that SLN biopsy is a feasible and accurate technique, with PSM estimates ranging from 97.3% to 98.6% in the meta-analysis.[4] Across studies, weighted summary estimates of 12.5% and 3.4% for FNR and PTPN, respectively, support the reliability of this minimally invasive staging technique.[3,4] After a positive SLN biopsy, 97.5% of patients underwent CLND, and 20.1% were found to have additional positive lymph nodes. Overall, the recurrence rate in the same nodal basin after a positive SLN biopsy was 7.5%, despite CLND in nearly all patients.[4]

More recent articles tended to report even higher PSM estimates, demonstrating improvements in technical performance with more experience. Because of the stringency of the criteria for inclusion in this systematic review of the literature, many SLN biopsy studies representing large single-institution experiences and reporting outcomes such as PSM and FNR could not be included. Cited FNRs have been as low as 0% to 2%,[7-10] although the meta-analysis found that FNR tended to be higher with longer follow-up. Overall, the SLN biopsy procedure is well tolerated and associated with low complication rates.[11]

Intermediate-thickness melanomas. Although clinical variables such as older age have been variably reported as lower risk factors,[12-14] there are no specific variables that can reliably identify patients with intermediate-thickness melanomas at low risk for metastases. The definition of intermediate-thickness melanoma varied by study. Nevertheless, it is clinically consistent with contemporary staging systems to define intermediate-thickness melanomas as those measuring 1 to 4 mm.[15]

Comorbid conditions. Clinical judgment must be used when considering SLN biopsy in patients with comorbid medical conditions. The individual risks and benefits of the procedure should be weighed against the operative and anesthetic risks as well as potential competing causes of mortality.

Complications. Complications after SLN biopsy are uncommon. The overall complication rate reported in MSLT I was 10.1% after SLN biopsy compared with 32.7% after CLND.[16] The most common complications after SLN removal documented in MSLT I included seroma (5.5%), infection (4.6%), and wound separation (1.2%). The Sunbelt Melanoma Trial (also a prospective randomized trial) similarly showed a low overall rate of complications from SLN biopsy (4.6%) compared with CLND (23.2%).[11,12] Most complications were noted to be short-term issues that resolved over time with wound care and selective use of antibiotics.

Staging. Accurate identification of patients with node-negative (stage I or II) or node-positive (stage III) disease improves staging and may facilitate regional disease control and decision making for treatment with adjuvant therapy.[3,17] With substantive changes in the melanoma staging guidelines in 2002, the AJCC staging system effectively linked disease stage and prognosis.[18,19] At that time, the number of nodal metastases and whether nodal disease was occult or clinically apparent (ie, how the N category was defined with regard to burden of disease) were noted to be the most significant independent predictors of survival in patients with stage III melanomas. With later iterations of the AJCC staging system (2009), additional refinements were made in the N category based on the prognostic value of distinguishing micrometastases (as would be diagnosed after SLN biopsy) from macrometastases.[20,21] A melanoma macrometastasis is detected by clinical examination (not by size criteria) and confirmed pathologically, whereas a melanoma micrometastasis is a clinically occult nodal metastasis that is detected by a pathologist on microscopic examination of lymph nodes, with or without immunohistochemistry, and is not limited by any minimum or maximum size threshold. Recognizing the value of examining SLNs to detect low volumes of metastatic disease (aggregates of only a few cells), the current staging system[1,22] incorporates the use of immunohistochemistry and eliminates any minimum size threshold for defining nodal metastases. Molecular diagnostics, such as reverse transcriptase-polymerase chain reaction, have unproven prognostic significance, and these results are not used to define positive nodes. As a result, more refined definitions of the N category are now used for classification. Distinct differences in classifications have validated prognostic significance. For example, 5-year survival ranges from 70% for patients with one SLN positive with micrometastatic disease to 39% for patients with $>$ four involved nodes or with nodes that are extensively involved (eg, matted nodes).[1]

Thick melanomas. Although SLN biopsy has been widely accepted for the pathologic staging of patients with intermediate-thickness melanomas, somewhat more controversy exists regarding the value of this procedure for patients with thick primary tumors (T4; Breslow thickness, > 4 mm). Conventional wisdom asserts that patients with thick melanomas have a high risk of systemic disease at the time of diagnosis and that no survival benefit can be derived from removal of regional lymph nodes. However, among patients without distant disease, it can be argued that those with thick melanomas have indications for SLN biopsy similar to those of patients with intermediate-thickness melanomas and derive the same benefits from SLN biopsy as a pathologic staging procedure. One of the main advantages of SLN biopsy in patients with thick melanomas is better regional disease control, which is especially important in a population with > 30% chance of lymph node involvement.[20,21,23]

Evidence from multiple retrospective studies has demonstrated that SLN biopsy provides important staging and prognostic information for patients with thick melanomas. Seven of eight published studies—each evaluating SLN biopsy in > 100 patients with T4 melanomas—have shown that SLN biopsy is a significant predictor of overall survival.[2,20,21,23-28] The one study that did not show a significant difference in overall survival demonstrated a significant difference in disease-free survival.[24]

Thin melanomas. A majority (70%) of melanomas diagnosed in the United States are thin melanomas (T1; Breslow thickness, < 1 mm).[29] In general, the routine use of SLN biopsy in patients with thin melanomas has not been advocated, because the overall risk of nodal involvement is estimated to be only approximately 5.1%,[30] although there are reports of positive SLNs in up to 20% of patients in subsets with thin melanomas (especially those that are 0.75 to 0.99 mm in thickness with ulceration and/or mitotic rate $\geq 1/mm^2$).[22]

An individualized approach to SLN biopsy for patients with thin melanomas has been advocated in many treatment centers based on risk factors that have been shown to be associated with SLN metastasis. Use of SLN biopsy in patients with thin melanomas must consider the low rate of positivity in the context of a known FNR. Further investigation is also needed to better identify the subgroups of patients with thin melanomas with a greater risk of nodal metastasis.

CLINICAL QUESTION 2

What is the role of CLND?

Recommendation

CLND is recommended for all patients with a positive SLN biopsy. CLND achieves regional disease control, although whether CLND after a positive SLN biopsy improves survival is the subject of the ongoing Multicenter Selective Lymphadenectomy Trial II (MSLT II).

Literature Review and Analysis

Patients with tumor-positive SLNs. Currently, CLND is the standard recommendation for patients with tumor-positive SLNs. The goals of CLND are to improve survival rates, maximize regional disease control, and minimize operative morbidity. Whether CLND improves survival is the subject of the ongoing prospective randomized MSLT II study.[31] The main objective of MSLT II is to determine if there is a therapeutic benefit to removing any non-SLNs in patients who have already had their tumor-positive SLN removed. In MSLT I, patients with demonstrated nodal metastases had a survival advantage with early intervention compared with those who had a delayed lymphadenectomy when they presented with clinically evident nodal metastases.[5] Hence, although two goals of CLND are regional disease control and cure, there is currently insufficient evidence to determine whether omission of CLND is safe.

Risk of regional nodal recurrence if CLND is not performed. In the two large prospective randomized trials (ie, the Sunbelt Melanoma Trial[12] and MSLT I[5]), the rate of positive non-SLNs among patients who underwent CLND for a tumor-positive SLN was 16%. In a retrospective multi-institutional study by Wong et al,[32] which included 134 highly selected patients with positive SLNs who did not undergo CLND, regional nodal metastasis was a component of first recurrence in 15% of these patients. Therefore, it is reasonable to conclude from these data that the risk of developing regional nodal metastasis as a first site of recurrence, if no CLND is performed, is at least 15% to 20%.[33,34]

Effect of CLND on regional disease control. In MSLT I, the rate of regional nodal recurrence after CLND was 4.2%[5]; in the Sunbelt Melanoma Trial, it was 4.9% (unpublished data). These rates are much lower than the 15% rate of regional nodal recurrence as a site of first metastasis and the 41% overall regional nodal recurrence rate when CLND was not performed, reported in the study by Wong et al.[35]

Until final results of MSLT II are available, we will not be able to determine, with higher-level evidence, the impact of CLND on regional disease control. Until that time, the best available evidence suggests that CLND is effective at achieving regional disease control in the majority of patients with positive SLNs.

Impact of CLND on overall survival. MSLT I showed no benefit of CLND with regard to overall survival, likely because only a minority of patients (16%) had tumor-positive SLNs, and the majority of the patients in the study would not have been helped by removal of regional lymph nodes.[5] However, the 5-year survival rate for patients with tumor-positive SLNs who underwent CLND was 72.3% compared with 52.4% for patients who did not undergo SLN biopsy and developed palpable nodal disease (hazard ratio, 0.51; 95% CI, 0.32 to 0.81; $P = .004$). CLND should be performed until there is convincing evidence that it does not improve regional disease control or survival.

Risk of morbidity. CLND is associated with risks of long-term morbidity, especially lymphedema. However, morbidity with CLND may be considerably worse when it is delayed until there is clinically evident disease. The observed increases in morbidity for patients who have undergone therapeutic lymphadenectomy for palpable disease and the increased morbidity associated with radiation therapy support the continued use of CLND for patients with a positive SLN biopsy rather than delayed CLND for palpable disease.

PATIENT AND CLINICIAN COMMUNICATION

Discussion with a patient about SLN biopsy for melanoma should be part of a comprehensive treatment planning process. Patient counseling regarding individual risks and benefits of SLN biopsy is essential to ensure that patients are making informed decisions. The Panel encourages health care providers to have an open dialogue with their patients to help them make informed decisions. An open dialogue

should include consideration of scientific evidence, weighing individual risks with potential harms and benefits, and consideration of patient values and preferences.

HEALTH DISPARITIES

This guideline represents expert recommendations on the best practices in disease management, aimed at providing the highest level of cancer care for all patients diagnosed with cutaneous melanoma. However, racial, ethnic, and socioeconomic disparities in the quality of health care provided are realities that exist and persist in the United States. Members of racial and ethnic minorities, in general, tend to be diagnosed with cancer at more advanced stages and have worse outcomes.[36] This is because of complex and diverse reasons, which include but are not limited to: financial and insurance status, access to medical attention, language-related barriers, education, culture, and religious beliefs. These disparities seem to be constants in most cancers, and melanoma is not an exception. Moreover, disparities in the use of SLN biopsy have been noted,[37] despite the fact that cutaneous melanoma is largely (> 90%) diagnosed in white non-Hispanic populations, with middle to high levels of income.

Awareness of disparities in quality of care and access to care should be considered in the context of these clinical practice guideline recommendations. Health care providers should strive to deliver the highest level of care to all patients.

FUTURE DIRECTIONS

There is a need for future clinical trials to address many unresolved research questions related to the use of SLN biopsy in patients with melanoma. These include: determining precise criteria for selecting which patients should undergo SLN biopsy, determining whether early identification of metastases in the SLN truly improves survival or merely represents lead-time bias, identifying which criteria for individualized risks best inform appropriate risk stratification for patients at high risk for relapse and those for whom CLND and/or adjuvant therapy are suitable, and establishing the role of prognostic markers from the primary melanoma and SLN to help assign appropriate risk stratification. Results from MSLT II, in which patients were randomly assigned to CLND or observation, will help determine whether there is any benefit to CLND after a positive sentinel node in patients with melanoma.

Answers to questions like these will assist clinicians and patients with making decisions and ultimately help to identify patients who may avoid expensive and intrusive procedures in staging and follow-up.

ADDITIONAL RESOURCES

The full guideline (which includes a comprehensive discussion of the literature, description of the methodology, and complete reference list), along with an Appendix, a Data Supplement, and clinical tools and resources, can be found on the ASCO Web site (http://www.asco.org/guidelines/snbmelanoma) and SSO Web site (http://www.surgonc.org/practice--policy/practice-management/clinical-guidelines/snbmelanoma.aspx). Patient information is also available at http://www.asco.org/guidelines/snbmelanoma and http://www.cancer.net.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Administrative support: Patricia Hurley
Manuscript writing: All authors
Final approval of manuscript: All authors

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