Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer: ASCO Guideline Update

Ko Un Park, MD[1]; Mark R. Somerfield, PhD[2]; Nirupama Anne, MD[3]; Muriel Brackstone, MD, PhD[4]; Alison K. Conlin, MD[5]; Henrique Lima Couto, MD, PhD[6]; Lynn T. Dengel, MD, MSc[7]; Andrea Eisen, MD[8]; Brittany E. Harvey, BS[2]; Jeffrey Hawley, MD[9]; Janice N. Kim, MD, MS[10]; Nwamaka Lasebikan, MBBS[11]; Elizabeth S. McDonald, MD, PhD[12]; Deepti Pradhan, PhD[13]; Samantha Shams, MD[14]; Raymond Mailhot Vega, MD, MPH[15]; Alastair M. Thompson, MD, MBChB[16]; and Mylin A. Torres, MD[17]

DOI https://doi.org/10.1200/JCO-25-00099

ABSTRACT

ASCO Guidelines provide recommendations with comprehensive review and analyses of the relevant literature for each recommendation, following the guideline development process as outlined in the ASCO Guidelines Methodology Manual. ASCO Guidelines follow the ASCO Conflict of Interest Policy for Clinical Practice Guidelines.

Clinical Practice Guidelines and other guidance ("Guidance") provided by ASCO is not a comprehensive or definitive guide to treatment options. It is intended for voluntary use by clinicians and should be used in conjunction with independent professional judgment. Guidance may not be applicable to all patients, interventions, diseases or stages of diseases. Guidance is based on review and analysis of relevant literature, and is not intended as a statement of the standard of care. ASCO does not endorse third-party drugs, devices, services, or therapies and assumes no responsibility for any harm arising from or related to the use of this information. See complete disclaimer in Appendix 1 and 2 (online only) for more.

PURPOSE To update the ASCO evidence-based recommendations on the use of sentinel lymph node biopsy (SLNB) in patients with early-stage breast cancer treated with initial surgery.

METHODS ASCO convened an Expert Panel to develop updated recommendations based on a systematic literature review (January 2016-May 2024).

RESULTS Eleven randomized clinical trials (14 publications), eight meta-analyses and/or systematic reviews, and one prospective cohort study met the inclusion criteria for this systematic review. Expert Panel members used available evidence and informal consensus to develop practice recommendations.

RECOMMENDATIONS Clinicians should not recommend routine SLNB in select patients who are postmenopausal and ≥50 years of age and with negative findings on preoperative axillary ultrasound for grade 1-2, small (≤2 cm), hormone receptor–positive, human epidermal growth factor receptor 2–negative breast cancer and who undergo breast-conserving therapy. Clinicians may offer postmastectomy radiation (RT) with regional nodal irradiation (RNI) and omit axillary lymph node dissection (ALND) in patients with clinically node-negative invasive breast cancer ≤5 cm who receive mastectomy and have one to two positive sentinel nodes. Clinicians may offer SLNB in patients who have cT3-T4c or multicentric tumors (clinically node-negative) or ductal carcinoma in situ treated with mastectomy, and in patients who are obese, male, or pregnant, or who have had prior breast or axillary surgery. Clinicians should not recommend ALND for patients with early-stage breast cancer who do not have nodal metastases, and clinicians should not recommend ALND for patients with early-stage breast cancer who have one or two sentinel lymph node metastases and will receive breast-conserving surgery and whole-breast RT with or without RNI.

Additional information is available at www.asco.org/breast-cancer-guidelines.

This guideline has been endorsed by the American Society for Radiation Oncology (ASTRO).

ACCOMPANYING CONTENT

Appendix

Data Supplement

Accepted January 22, 2025
Published April 10, 2025

Evidence Based Medicine Committee approval: January 8, 2025

J Clin Oncol 00:1-22

View Online Article

TARGET POPULATION AND AUDIENCE

Target Population
Patients with early-stage breast cancer (stages I and II) treated with upfront surgery.

Target Audience
Medical oncologists, surgical oncologists, radiation oncologists, hospitalists, oncology nurses, patients, radiologists, and other relevant oncologic professionals.

INTRODUCTION

The purpose of this guideline is to update the ASCO evidence-based recommendations on the use of sentinel lymph node biopsy (SLNB) in early-stage breast cancer. ASCO first published a practice guideline on SLNB in 2005,[1] with updated guidelines published in 2014[2] and 2017.[3] This update addresses new evidence published since the latest guidance on this topic (Figs 1 and 2). This guideline has been endorsed by the American Society for Radiation Oncology (ASTRO).

GUIDELINE QUESTIONS

This clinical practice guideline update addresses six overarching clinical questions: (1) Can SLNB be omitted in select patients? (2) How are radiation (RT) and systemic treatment decisions impacted by omission of a SLNB? (3) Is axillary lymph node dissection (ALND) necessary for patients with clinically node-negative early-stage breast cancer who have one or two sentinel lymph node (SLN) metastases and will receive breast-conserving surgery with whole-breast RT? (4) Is ALND necessary for patients with nodal metastases who are planning to undergo mastectomy? (5) Can completion ALND be omitted in patients with early-stage breast cancer who do not have nodal metastases? (6) What is the role of SLNB in special circumstances in clinical practice, including large or locally advanced invasive tumors, multicentric tumors, inflammatory breast cancer, ductal carcinoma in situ (DCIS), obesity, male breast cancer, pregnancy, patients who are breastfeeding or lactating, evaluation of the internal mammary (IM) nodes, presence of suspicious palpable axillary nodes, presence of multiple suspicious axillary nodes on imaging with biopsy confirmation, and prior breast or axillary surgery?

METHODS

Guideline Development Process

This systematic review–based guideline product was developed by a multidisciplinary Expert Panel, which included a patient representative and an ASCO guidelines staff member with health research methodology expertise (Appendix Table A1, online only).

The recommendations were developed based on a systematic review of evidence published after the previous guideline, identified through online searches of PubMed (January 1, 2016-May 6, 2024), and based on clinical experience. The electronic search that informed most of the clinical questions was limited to randomized phase III clinical trials and meta-analyses. For the special circumstances and populations clinical question, prospective comparative cohort trials were also included. Finally, for the question concerning which patients with early-stage breast cancer require SLNB, the practice recommendations were adapted from the Ontario Health-ASCO Management of the Axilla in Early-Stage Breast Cancer guideline and revised based on evidence published after this guideline.[4] Articles were selected for inclusion in the systematic review based on the following criteria:

- Population: Patients with early-stage breast cancer (stages I and II) treated with upfront surgery
- Interventions: SLNB
- Comparisons: ALND, no axillary surgery (including no SLNB)
- Outcomes: disease-free survival (DFS), overall survival (OS), health-related quality of life (QoL), harms (eg, lymphedema and nerve injury)

Articles were excluded from the systematic review if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, letters, news articles, case reports, and narrative reviews; and (3) published in a non-English language.

Two full-panel meetings were held, and members were asked to provide ongoing input on the updated guideline development protocol, quality and assessment of the evidence, generation of recommendations, draft content, as well as review and approve drafts during the entire development of the guideline. ASCO staff met routinely with the Expert Panel co-chairs and corresponded with the Expert Panel via e-mail to coordinate the process to completion. Ratings for the strength of the recommendation and evidence quality are provided with each recommendation, defined in Appendix Table A2. The quality of the evidence for each outcome was assessed using the Cochrane Risk of Bias tool and elements of the GRADE quality assessment and recommendations development process.[5,6] GRADE quality assessment labels (ie, high, moderate, low, and very low) were assigned for each outcome by the project methodologist in collaboration with the Expert Panel co-chairs and reviewed by the full Expert Panel. All funding for the administration of the project was provided by ASCO.

Guideline Review and Approval

The draft recommendations were released to the public for open comment from September 3, 2024, through

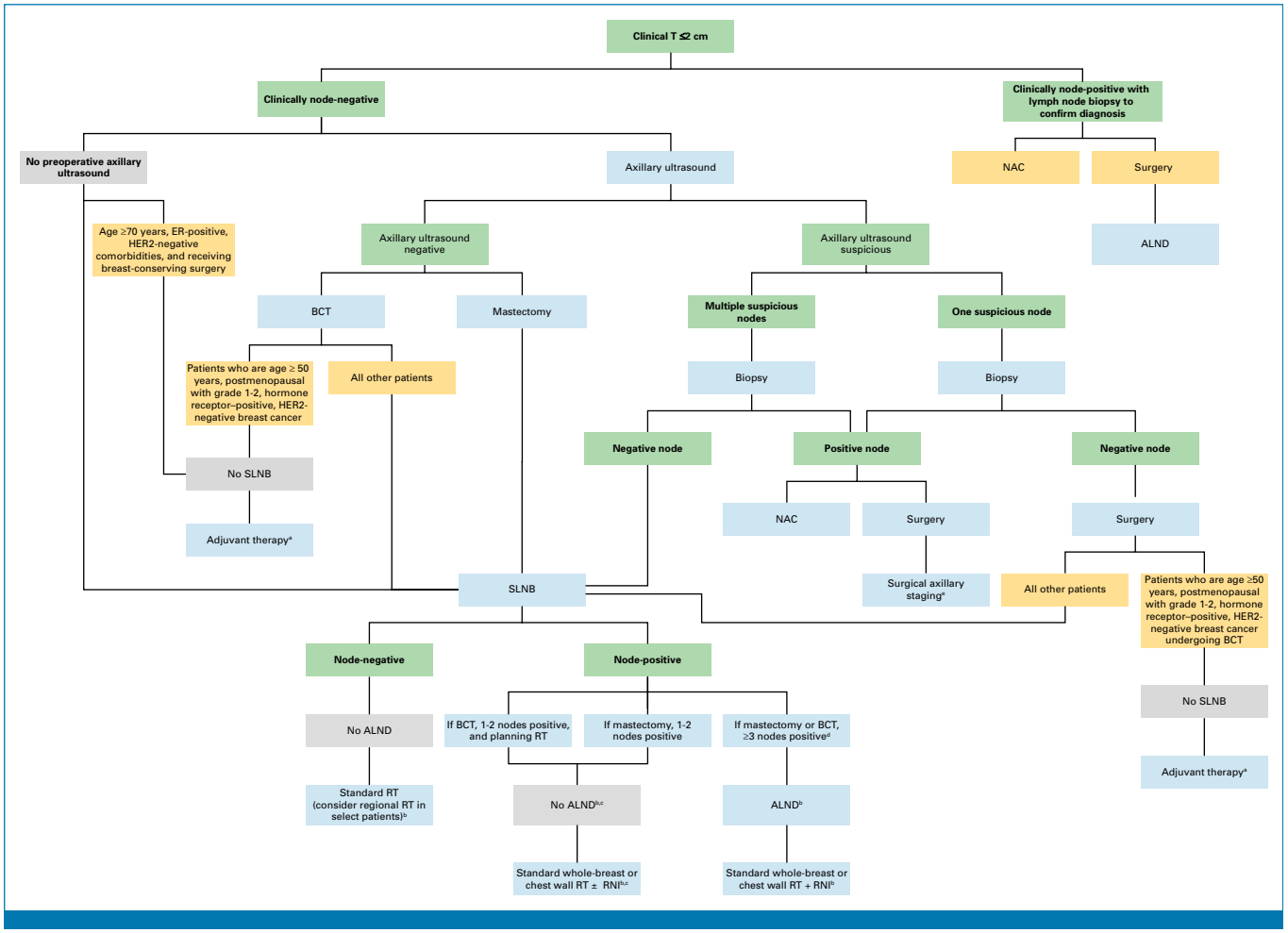

FIG 1. Management of the axilla for patients with clinical T ≤2 cm breast cancer. [a]Multidisciplinary discussion of adjuvant therapy options should occur prior to surgery when omitting sentinel lymph node biopsy. Please see full guideline (section on Systemic and RT Treatment Decisions with Omission of SLNB) for expanded discussion. [b]Decision making should be made on a case-by-case basis, and include a patient-centered approach; that is, consider and discuss pros and cons of various options in light of patient's specific circumstances, values, and preferences. [c]Full lymph node dissection may mitigate the need for RT in select patients. [d]Patients with three positive nodes were underrepresented in trials evaluating the omission of completion ALND. [e]There are no clinical trial data comparing SLNB/targeted axillary dissection (localized removal of clipped biopsy-proven positive node) to complete axillary lymph node dissection at this time, and either may be options for patients. ALND, axillary lymph node dissection; BCT, breast-conserving therapy; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; NAC, neoadjuvant chemotherapy; PMRT, postmastectomy RT; RNI, regional nodal irradiation; RT, radiation; SLNB, sentinel lymph node biopsy; T, tumor; US, ultrasound. Adapted from Brackstone et al.[4]

September 17, 2024. Response categories of "Agree as written," "Agree with suggested modifications," and "Disagree. See comments" were captured for every proposed recommendation with a total of 99 written comments received from 66 respondents across the nine draft recommendations submitted for comment. An average of 93% of the respondents (range, 87%-100%) either agreed or agreed with slight modifications with the draft recommendations and an average of 7.8% of respondents disagreed (range, 0%-14%). The Expert Panel Co-Chairs reviewed comments from all sources and determined whether to maintain original draft recommendations, to revise with minor language changes, or to consider major recommendation revisions.

The draft was submitted to six external reviewers with content expertise. Review comments such as, "details regarding RT are underrepresented in the narrative and the supporting tables and should be specified and included," were reviewed by the Expert Panel and integrated into the manuscript. All changes were incorporated into the final manuscript prior to ASCO Evidence Based Medicine Committee (EBMC) review and approval. Additionally, a guideline implementability review was conducted. No edits to the guideline were recommended through the implementability review. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO EBMC before submission to the *Journal of Clinical Oncology* for editorial review and consideration for publication.

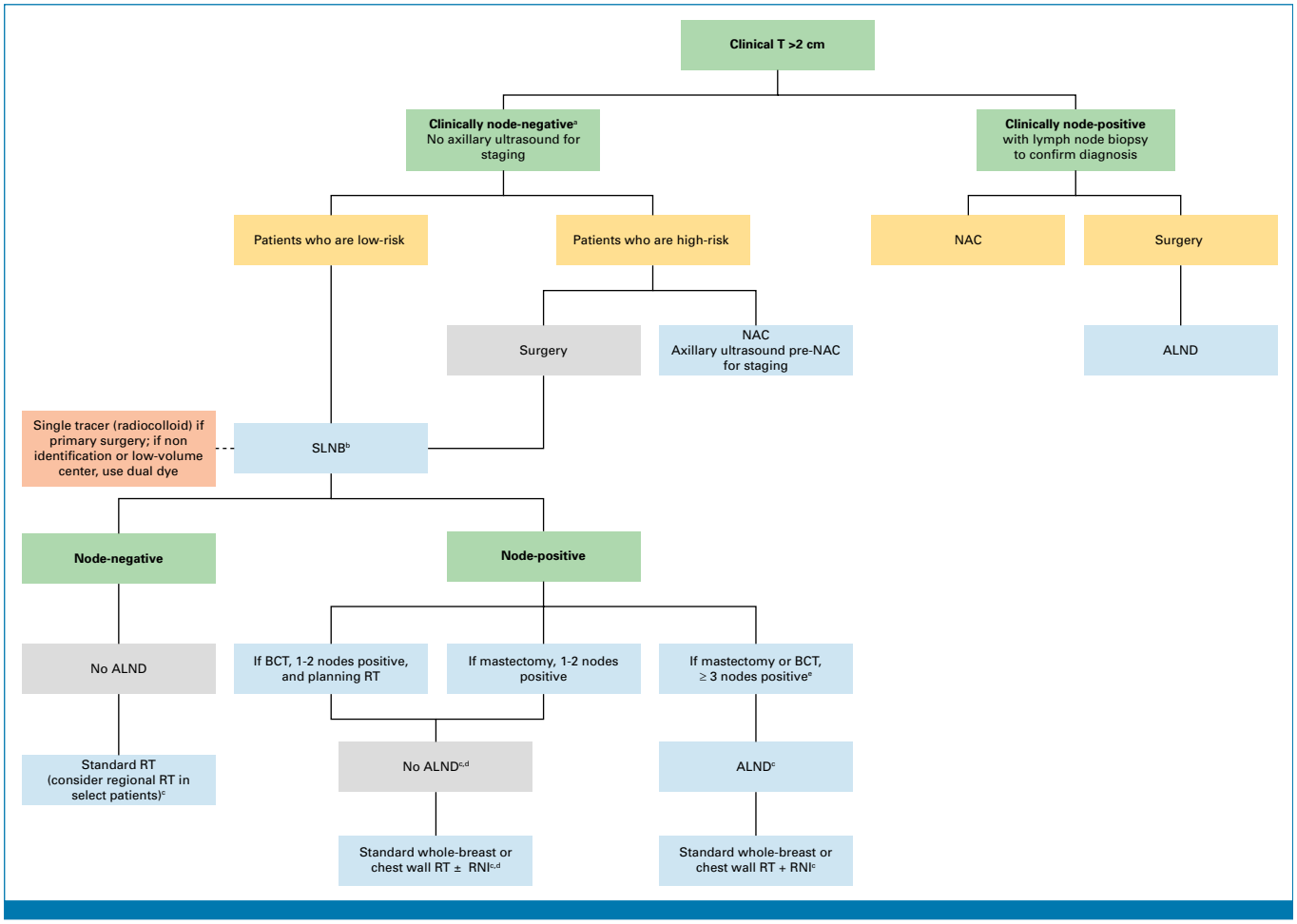

FIG 2. Management of the axilla for patients with clinical T >2 cm breast cancer. [a]Refers to all patients with no palpable axillary nodes on physical examination, including those who may have had an ultrasound that was equivocal, abnormal, or even biopsy-proven positive. [b]Do not recommend SLNB before chemotherapy except in special circumstances after multidisciplinary discussion. [c]Decision making should be made on a case-by-case basis, and include a patient-centered approach; that is, consider and discuss pros and cons of various options in light of patient's specific circumstances, values, and preferences. [d]Full lymph node dissection may mitigate the need for RT in select patients. [e]Patients with three positive nodes were underrepresented in trials evaluating the omission of completion ALND. ALND, axillary lymph node dissection; BCT, breast-conserving therapy; NAC, neoadjuvant chemotherapy; RT, radiation; SLNB, sentinel lymph node biopsy; T, tumor; US, ultrasound. Adapted from Brackstone et al.[4]

Guideline Updating

The ASCO Expert Panel and guidelines staff will work with co-chairs to keep abreast of any substantive updates to the guideline. Based on formal review of the emerging literature, ASCO will determine the need to update. The ASCO Guidelines Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the guideline update process. This is the most recent information as of the publication date.

RESULTS

Characteristics of Studies Identified in the Updated Literature Search

A total of 632 abstracts were found by the broad literature search conducted to address Clinical Questions 1 through 5 (see Data Supplement S1 and S2 for more details of the searches, online only). After applying the eligibility criteria, 11 randomized clinical trials (RCTs; 14 publications) and four systematic reviews and/or meta-analyses[7-10] remained, forming the evidentiary basis for the new and updated guideline recommendations.

The identified trials were published between 2016 and 2024. Two broad sets of randomized trials are represented[11]: (1) nine RCTs compared SLNB alone versus SLNB plus complete ALND (ACOSOG Z0011 [Alliance],[12,13] Canavese et al,[14] OTOASOR,[15] IBCSG 23-01,[16] GF-GS01,[17] SINODAR-ONE,[18] RACS SNAC1,[19] After Mapping of the Axilla: Radiotherapy or Surgery? [AMAROS],[20] and SENOMAC[21,22]); and (2) two RCTs compared SLNB versus no axillary surgery, SOUND[23] and Intergroup Sentinel Mamma (INSEMA).[24] Characteristics of the trials identified by the systematic review conducted for the guideline are reported in Data Supplement S3,

and a summary of the key outcomes of interest and adverse events are reported in Data Supplement S4. The search identified four systematic reviews and/or meta-analyses of SLNB RCTs that provided confirmatory, supplementary evidence[7-10]; the main findings from these publications are presented in Data Supplement S5.

A series of targeted literature searches was conducted to inform recommendations on the range of SLNB special circumstances and populations addressed in Clinical Question 6. A total of 820 abstracts were found by these searches and, after applying the inclusion criteria, one prospective cohort study of SLNB and DCIS,[25] three meta-analyses of DCIS and SLNB,[26-28] and one systematic review of pregnancy and SLNB[29] remained. These constitute the limited evidentiary basis for the new and updated recommendations for the use of SLNB in the special circumstances and populations included in the guideline.

Evidence Quality Assessment

The quality of evidence was assessed for each outcome of interest. This rating includes factors such as study design, consistency of results, directness of evidence, precision, publication bias, and magnitude of effect, assessed by one reviewer. Evidence quality ratings for the RCTs are provided in the Data Supplement (Table S6, Study Quality Assessment). All 11 trials were deemed to have a moderate certainty level. Refer to Appendix Table A2 for definitions for the quality of the evidence, and the Methodology Manual for more information.

RECOMMENDATIONS

All recommendations are available in Table 1.

SLN BIOPSY

Clinical Question 1

Can SLNB be omitted in select patients?

Literature Review

The systematic literature review identified two studies that inform the question of whether SLNB can be omitted in select patients with a small breast cancer and a negative finding on preoperative axillary lymph node (ALN) ultrasound (US). The prospective, phase III RCT, Sentinel Node versus Observation After Axillary Ultra-Sound (SOUND) evaluated whether omission of axillary surgery was noninferior to SLNB in patients with small (up to 2 cm) breast cancer with a negative finding on preoperative US of the ALNs.[23] The primary end point of the SOUND trial was distant disease-free survival (DDFS). In this trial, 1,405 women undergoing surgery upfront were randomly assigned to SLNB versus no SLNB after a negative preoperative axillary US (or if one suspicious node was visualized, this was negative by fine-needle aspiration [FNA]). The 5-year DDFS was not different between the two groups with low rates of local-regional relapse (1.7% in the SLNB group *v* 1.6% in the no axillary surgery). The majority of patients were postmenopausal with hormone receptor–positive and human epidermal growth factor receptor 2 (HER2)–negative, invasive ductal carcinoma. The median tumor size was 1.1 cm (IQR, 0.8-1.5). In the group that underwent axillary surgery, the rate of upstaging of the axilla after a negative axillary US was low (13.1% had one to three positive lymph nodes on surgery, 0.6% had four or more positive nodes).

The prospective, randomized, noninferiority phase III trial INSEMA[24] evaluated whether SLNB was noninferior to omission of axillary surgery in patients with clinically node-negative (cN0), T1 or T2 (tumor size, ≤5 cm), invasive breast cancer scheduled to undergo breast-conserving surgery (BCS). Ninety percent of patients had clinical T1 cancer and 79% of patients had pathological T1 cancer. Patients were randomly assigned to treatment without axillary staging (n = 962) or to SLNB (n = 3,896). The primary efficacy end point of the trial was invasive disease-free survival (IDFS). Trial results for the per-protocol population indicated that, after a median follow-up of 73.6 months (about 6 years), omission of axillary surgery was noninferior to SLNB. Among patients in the axillary surgery omission group, the 5-year IDFS rate was 91.9%; the IDFS rate was 91.7% among patients in the SLNB group (hazard ratio [HR], 0.91 [95% CI, 0.73 to 1.14]). These results were confirmed in the intention-to-treat population analysis of IDFS: omission of axillary surgery was noninferior to SLNB. Analyses of short-term surgical complication rates in the two study arms confirmed findings reported previously.[30] With respect to long-term safety outcomes, patients in the axillary surgery omission group had a lower incidence of restriction of arm or shoulder mobility (2.0% *v* 3.5%), lymphedema (1.8% *v* 5.7%), and pain associated with arm or shoulder movement (2.0% *v* 4.2%) than patients in the SLNB group.

Clinical Interpretation

Characteristics of the study population in the SOUND and INSEMA trials. When assessing the appropriate candidates for omission of SLNB, the recommendations in Table 1 are based on the populations that were well represented in the SOUND and INSEMA trials. However, it is important to consider patients who were not well represented in the trials, such as patients age <50 years (18.6% in SOUND, 10.8% in INSEMA), premenopausal patients (21.3% in SOUND), and those with grade 3 invasive carcinoma (18% in SOUND, 3.6% in INSEMA), Ki-67 ≥20 (36% in SOUND), Ki-67 >20 (12.9% in INSEMA), invasive lobular carcinoma (8.5% in SOUND), lobular or mixed lobular carcinoma (12.7% in INSEMA), tubular carcinoma (4.3% in SOUND), HER2-positive (6.8% in SOUND, 3.6% in INSEMA), and triple-negative breast cancer (5.4% in SOUND, 1.2% in INSEMA). Although tubular carcinoma was

TABLE 1. Summary of All Recommendations

CQ	Recommendation
General Note. The following recommendations (strong or conditional) and terminology (Data Supplement) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible.	
1. Can SLNB be omitted in select patients?	1.1. SLNB can be omitted for select patients with a small (≤2 cm) breast cancer and a negative finding on preoperative ALN ultrasound and who fulfill all of the following criteria and for whom the detection of metastatic sentinel lymph node(s) would not change treatment recommendations. (Evidence quality: Moderate; Strength of recommendation: Strong) Postmenopausal and ≥50 years Unifocal invasive ductal carcinoma smaller than or equal to 2 cm Nottingham grades 1-2 Hormone receptor–positive, HER2-negative in patients intending to receive adjuvant endocrine therapy No suspicious lymph nodes on axillary US or only one suspicious node and biopsy is benign and concordant with axillary US findings. Undergoing upfront breast-conservation surgery followed by whole-breast RT in patients <65 years of age (see Good Practice Statement 1.2 and Qualifying statements for patients ≥65 years of age).
	Qualifying statements for Recommendation 1.1 In the INSEMA trial, ultrasound was primarily used to assess breast tumor size, and, when unavailable, mammogram followed by MRI were used in that order. Similarly, in the SOUND trial, preoperative tumor size was assessed by ultrasound but also physical examination and mammogram. MRI was performed in a minority of patients. For patients over age 70, the Choosing Wisely Statement does not require axillary US for determining omission of SLNB The SOUND clinical trial excluded patients with multiple suspicious lymph nodes, multifocality or multicentricity, bilateral breast cancer, synchronous distant metastases, previous cancer, ongoing pregnancy, or lactation. In the INSEMA trial, multifocal tumors were allowed; multicentricity was not allowed.
	1.2 For patients ≥65 years of age and who qualify by the following criteria for omission of SLNB, RT post breast-conserving surgery is not mandatory (extrapolating from the PRIME II trial and CALGB 9343), as the risk of lymph node involvement is very low: postmenopausal, invasive carcinoma smaller than or equal to 2 cm, Nottingham grades 1-2, hormone receptor–positive, HER2-negative in patients intending to receive adjuvant endocrine therapy, no suspicious lymph nodes on axillary US or only one suspicious node on axillary US and biopsy is benign and concordant. (Good Practice Statement; Refer to the Clinical Interpretation section corresponding to this recommendation for further discussion.)
2. How are RT and systemic treatment decisions impacted by omission of a SLNB?	2.1. RT treatment decisions should not be altered by omission of SLNB in the appropriate candidates (those who fulfill criteria outlined in CQ1). (Good Practice Statement)
	2.2. Genomic assay testing and subsequent systemic therapy decisions should not be altered by omission of SLNB in the appropriate candidates (those who fulfill criteria outlined in CQ1). (Good Practice Statement)
	Notes for Recommendation 2.2 The use of genomic assay testing (including the 21-gene recurrence score) for adjuvant chemotherapy decision making is outlined in the 2022 ASCO guideline, Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update Genomic assay testing, specifically the 21-gene recurrence score, can be performed in the setting of SLNB omission
3. Is ALND necessary for patients with clinically node-negative early-stage breast cancer who have one or two sentinel lymph node metastases and will receive breast-conserving surgery with whole-breast RT?	3.1. Clinicians should not recommend ALND for patients with early-stage, clinically node-negative breast cancer who have one or two positive sentinel lymph node metastases and will receive breast-conserving surgery with whole-breast RT. (Evidence quality: High; Strength of recommendation: Strong)
	Qualifying statements for Recommendation 3.1 Completion ALND after demonstration of node positivity with SLNB is not necessary if the patient already meets candidacy for CDK4/6 inhibitor or olaparib based on genetic and primary tumor characteristics. If a patient with 1-2 positive nodes on SLNB is not otherwise eligible for CDK4/6 inhibitor or olaparib based on other tumor features, completion ALND can be considered. However, the rate of four or more nodal metastases with completion ALND (after one to two positive SLNB) is low (13%), and given the significantly higher morbidity of completion ALND compared with SLNB, physician-patient shared decision making is warranted.
4. Is ALND necessary for patients with nodal metastases who are planning to undergo mastectomy?	4.1. ALND is not necessary and can be omitted in patients with clinically node-negative invasive breast cancer ≤5 cm who receive mastectomy and have one to two positive sentinel nodes, and postmastectomy RT (PMRT) with regional nodal irradiation (RNI) can be offered. (Evidence quality: High; Strength of recommendation: Strong)
	4.2. In patients with pT1-T2, pN1 disease undergoing mastectomy but not receiving PMRT or RNI, completion ALND is recommended. (Evidence quality: High; Strength of recommendation: Strong)
	Notes for Recommendations 4.1 and 4.2 In the SENOMAC trial, only 6% of patients had T3 disease and 34% of patients had extranodal extension. Thirty-six percent of patients in the SENOMAC trial had mastectomy. In the AMAROS trial, axillary lymph node dissection did not improve cancer outcomes in patients who are clinically node-negative with positive sentinel nodes.
	4.3. ALND should be performed and followed by PMRT for patients who receive mastectomy and have ≥3 positive nodes. (Evidence quality: High; Strength of recommendation: Strong)
5. Can completion ALND be omitted in patients with early-stage breast cancer who do not have nodal metastases?	5.1. Clinicians should not recommend ALND for axillary staging in patients with early-stage breast cancer who do not have nodal metastases. (Evidence quality: High; Strength of recommendation: Strong)

(continued on following page)

TABLE 1. Summary of All Recommendations (continued)

CQ	Recommendation
6. What is the role of SLNB in special circumstances in clinical practice including large or locally advanced invasive tumors, multicentric tumors, inflammatory breast cancer, DCIS, obesity, male breast cancer, pregnancy, patients who are breastfeeding or lactating, evaluation of the internal mammary nodes, presence of suspicious palpable axillary nodes, presence of multiple suspicious axillary nodes on imaging with biopsy confirmation, and prior breast or axillary surgery?	6.1. Clinicians may offer SLNB for patients who have operable breast cancer who have one or more of the following circumstances. (Evidence quality: Low; Strength of recommendation: Conditional) 6.1.1. Multicentric tumors (clinically node-negative) 6.1.2. Male breast cancer 6.1.3. Pregnancy 6.1.4. Obesity 6.1.5. cT3-cT4c N0 6.1.6. DCIS and will undergo mastectomy 6.1.7. Prior breast or axillary surgery
	Qualifying statements for Recommendation 6.1.3 There are limited safety data regarding SLNB with radioactive colloids in patients who are pregnant under 30 weeks' gestation. Limited data estimate technetium-99m sulfur colloid is safe to use while isosulfan blue dye and methylene blue dye are not safe. Use of SLNB in pregnancy warrants shared patient-clinician decision making. Use of breast milk from lactation within 24 hours should be avoided after SLNB as radioactive colloid can be excreted in breast milk.
	6.2. Clinicians should not offer routine SLNB for patients in one or more of the following circumstances. (Evidence quality: Low; Strength of recommendation: Conditional) 6.2.1. DCIS after breast-conserving surgery 6.2.2. For sole purpose of evaluating the internal mammary nodes
	6.3. ALND (not SLNB) should be performed for patients who have operable breast cancer who have one or more of the following circumstances. (Evidence quality: Low; Strength of recommendation: Conditional) 6.3.1. Inflammatory breast cancer 6.3.2. Presence of biopsy-proven palpable axillary nodes 6.3.3. Presence of matted axillary lymph nodes, multiple suspicious level 3 axillary or supraclavicular lymph nodes

NOTE. The strength of the recommendation is defined as follows. Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional/weak: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not.
Abbreviations: ALN, axillary lymph node; ALND, axillary lymph node dissection; CDK, cyclin-dependent kinase; cm, centimeter; CQ, clinical question; DCIS, ductal carcinoma in situ; HER2, human epidermal growth factor receptor 2; MRI, magnetic resonance imaging; PMRT, postmastectomy RT; RNI, regional nodal irradiation; RT, radiation; SLNB, sentinel lymph node biopsy; US, ultrasound.

not well represented in the SOUND trial, it is likely safe to omit SLNB, given the extremely low rate of lymph node involvement in this histologic subtype.[31] Menopausal status (eg, perimenopausal *v* postmenopausal) was assessed clinically and laboratory confirmation was not required by the SOUND study protocol. However, since the median age was 60 years in the SOUND study, 74% of patients were postmenopausal while only 5% were perimenopausal (personal communication with authors). Of note, while menopausal status was not reported in the INSEMA trial, the median age was 62 years; only 10.8% were age <50 years. The SOUND trial also excluded patients with multiple "doubtful or suspicious" lymph nodes, extensive multifocality or multicentricity, bilateral breast cancer, diagnosis of synchronous distant metastases, previous cancer, and ongoing pregnancy or lactation. In the INSEMA trial, multicentricity was not allowed but multifocal tumors were allowed and comprised approximately 3% in each group (n = 128 [3.3%] SLNB; n = 37 [3.8%] no SLNB). Furthermore, the SOUND and INSEMA studies did not explicitly exclude but also did not collect data on presence or absence of lymphovascular invasion in the breast. Presence of lymphovascular invasion is a known risk factor for axillary nodal metastasis.[32-34]

If estimates on probability of SLN involvement are important for shared decision making on omission of SLNB, existing nomograms that estimate probability of SLN involvement may be beneficial.[32,35,36] The use of nomograms to estimate probability of SLN involvement can be especially helpful for those who are considering adjuvant systemic therapy but without access to genomic testing (see section from clinical question 2 on genomic assay testing) or for those who are also candidates for partial breast irradiation (PBI; see section on RT considerations). Lastly, while the SOUND or INSEMA trials did not specifically exclude pathogenic germline genetic mutation carriers, the number of carriers enrolled on theses studies was not tracked but is assumed to be low, given the overall low prevalence of pathogenic germline mutations in patients with breast cancer generally and that many pathogenic mutation carriers undergo risk-reduction surgeries with mastectomy rather than BCS, which was the required surgery in both trials.[24,37] Therefore, the oncologic safety of omitting SLNB following BCS in patients with pathogenic germline genetic mutations cannot be determined from the SOUND and INSEMA studies.

RT considerations. In the INSEMA trial, whole-breast irradiation (WBI) was mandated per protocol and the

axilla was not intentionally targeted. Use of regional nodal RT, with treatment to the supraclavicular, high axillary, and IM nodes, or high tangents was not allowed unless patients in the surgical arm were found to have four or more involved lymph nodes. While eligible candidates for the SOUND trial were those recommended BCS and RT, the protocol did not mandate specific RT targets, treatment dose, or modality. Although both WBI and PBI were permitted in the SOUND trial, it is important to acknowledge that >80% of patients were treated with WBI in this trial of predominantly early-stage hormone receptor–positive breast cancer and no patients received PBI on the INSEMA study. Multiple other randomized trials, however, indicate no differences in breast cancer recurrence rates in patients with early-stage hormone receptor–positive breast cancer treated with PBI versus WBI with several indicating superior overall cosmesis with partial breast treatment. Of note, none of these trials of WBI *v* PBI for the treatment of invasive breast cancer were performed in the context of omission of SLNB. However, given the overall low number of patients with nodal metastases among patients randomly assigned to the SLNB arm (13.1% with pN1 disease and 0.6% with pN2 disease in the SOUND trial; 14.9% with pN1 disease and 0.2% with pN2 disease in the INSEMA trial), the majority of patients on the SOUND and INSEMA trials would have been candidates for PBI due to a high rate of pN0 disease. Regional nodal irradiation (RNI) was also not clinically indicated in the majority of patients enrolled on the SOUND trial, although data regarding RNI were not provided. Thus, patients who would generally be candidates for omission of SLNB are also unlikely to have indications for or benefit from RNI. Additional RT-related considerations are discussed in detail in clinical question 2 section.

Role of magnetic resonance imaging. In the SOUND trial, preoperative tumor size was assessed by physical examination, mammogram, and US. In both the INSEMA and SOUND trials, breast magnetic resonance imaging (MRI) was not routinely used. Axillary US is widely used for axillary nodal assessment globally. However, breast MRI is considered the most accurate imaging modality to assess preoperative breast tumor size.[38-41] Although the lower axilla can be visualized on a breast MRI, this imaging modality is often not used as the initial test for imaging the axilla in early-stage breast cancer. If performed, MRI may help confirm tumor size ≤2 cm and the applicability of the SOUND or INSEMA trial results.

If the oncologist or surgeon desires to include the full axilla in an MRI done for extent of disease, they should communicate that to the radiology team, since only the low axilla is required for standard breast MRI.[42] Modifications to the standard field of view, stack size, and scan time should be expected. If the field of view is opened, resolution will change and for some patients, this may cause an issue with homogeneous fat saturation in the breast tissue and axilla along with positioning challenges. Given the similar sensitivity and specificity of US and MRI in evaluating ALNs, it is reasonable that the same standards may apply.[43] As in the SOUND trial, if there are no suspicious lymph nodes on preoperative MRI or only one suspicious node with a subsequent benign and concordant biopsy, then the results of the SOUND and INSEMA trials with preoperative US may be extrapolated and used in the setting of a negative breast MRI inclusive of the full axilla. In these cases, SLNB may be omitted.

Role of axillary US. CALGB 9343[44] and other similar studies[45-47] did not require preoperative axillary US, calling into question the role of axillary US in applying the SOUND and INSEMA trials. The Choosing Wisely statement recommending omission of SLNB in patients over age 70 years with qualifying early-stage breast cancer does not require preoperative axillary US.[48] Thus, in patients age 70 years or older with hormone receptor–positive, HER2-negative invasive breast carcinoma, surgical axillary staging with SLNB is not recommended if clinically node-negative (without explicit use of axillary US). In the SOUND trial, 84.6% had a negative SLNB and 13.1% upgraded to pN1 (of which 5.1% pN1mi), and 0.6% to pN2 after a negative preoperative axillary US. Similarly, the INSEMA trial[24,30] was a noninferiority study assessing no SLNB versus SLNB after negative axillary US in patients with tumor ≤5 cm. Patients with positive SLNB were further randomly assigned to SLNB alone *v* completion ALND. Among the 3,896 patients who were randomly assigned to SLNB, 3.5% (n = 133) had pN1mi disease, 11.4% (n = 438) had pN1 disease, and 0.2% (n = 8) had pN2 disease. These studies were not designed to assess the sensitivity or specificity of axillary US, nor did they evaluate the timing of axillary US relative to timing of the breast biopsy. However, the low number of patients with extensive axillary nodal involvement (ie, pN2 disease) and very low axillary recurrence rate (ARR) of 1% or less at 5 years support the use of US to screen patients for clinically meaningful axillary nodal involvement when omission of SLNB is being considered.

FNA versus core needle biopsy of lymph node. When one suspicious node was visualized, FNA was performed in both the SOUND and INSEMA trials, with the INSEMA trial also allowing core needle biopsy to rule out nodal metastases. Thus, if appropriate resources allow FNA for cytologic evaluation, it is recommended instead of core needle biopsy of the suspicious ALN. While core biopsy has questionable increased sensitivity,[49-51] it is also associated with increased patient complications including pain and cost compared to FNA[49,52,53]; if appropriate resources and experience are available to perform FNA, then based on the SOUND trial, assessment of a suspicious node with FNA is recommended. If core needle biopsy is performed instead of FNA, then vacuum-assisted biopsy should be avoided due to risk of complications without improved sensitivity.[54] A biopsy needs to be both benign and considered concordant on US by the treating radiologist in order to omit SLNB.

SYSTEMIC AND RT TREATMENT DECISIONS WITH OMISSION OF SLNB

Clinical Question 2

How are RT and systemic treatment decisions impacted by omission of a SLNB?

Literature Review

There is no direct evidence from randomized clinical trials regarding the question of how RT treatment decisions are impacted by omission of a SLNB. The recommendation offered is based on the best clinical opinion of the Expert Panel; on the ASTRO clinical practice guideline, Partial Breast Irradiation for Patients with Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ[55]; and on indirect evidence from the CALGB 9343[44] and PRIME II[56] RCTs, as detailed in the subsequent section.

Clinical Interpretation

Although many RT details are not available in the SOUND trial, 10% of all patients enrolled received 21 Gy of intraoperative RT (IORT) with electrons (ELIOT), and another 4%-5% in both arms received an IORT boost of 12 Gy with electrons followed by hypofractionated whole-breast RT (37.05 Gy in 13 fractions). At the majority of enrolling sites, patients received WBI according to the standard of care of the participating center, with most receiving 5 weeks of conventionally fractionated RT, but in the latter years of enrollment, more patients were treated with 3 weeks of WBI. In the INSEMA trial, WBI was required for all patients. When the study was first designed, the breast was treated to a dose of 50 to 50.4 Gy in 25-28 fractions with a boost to the lumpectomy cavity of 10-16 Gy in 5-8 fractions. However, the protocol was later amended to permit moderate whole-breast hypofractionation irradiation to 40 Gy in 15 fractions, to allow simultaneous integrated boost but only in patients treated with conventionally fractionated RT, and to allow omission of a boost dose of RT in patients older than 60 years and with small, favorably prognostic tumors who are at low risk of local recurrence.[24] Unlike PBI, WBI incidentally treats a portion of the lower axilla due to RT fields that are tangential to the chest wall, and indeed, upon central review of the RT records of 276 patients participating in the central quality-assurance process of the INSEMA trial, 50% received at least 80% of the prescribed RT breast dose to the level I axilla, which is assumed to be curative for low-volume nodal disease. However, incidental axillary RT treatment is unlikely to have played a therapeutic role in the majority of patients enrolled on the SOUND and INSEMA trials, as 85% of patients did not have pathologically involved nodes warranting treatment. Nevertheless, subsequent analysis is planned to examine the incidental axillary irradiation doses collected from all patients enrolled on the INSEMA trial.

Although the majority of patients enrolled on the SOUND and INSEMA studies were treated with WBI, the low likelihood of nodal involvement in the majority of patients who are appropriately selected for omission of SLNB also suggests that these same patients are candidates for PBI per the ASTRO guideline on PBI for patients with early-stage invasive breast cancer.[55] Several randomized trials comparing PBI and WBI indicate equivalent local control and survival rates and similar if not better cosmetic outcomes and treatment convenience with the typically shorter course treatment involved with PBI (eg, 1 week) versus whole-breast treatment with moderate hypofractionation regimens of 3-4 weeks[57-60] or conventionally fractionated regimens of 5 weeks. However, none of these trials were conducted in patients where the SLNB was omitted. Patients who are postmenopausal and have pT1, grade 1 or 2, ductal carcinomas that are strongly hormone receptor–positive and HER2-negative are candidates for SLNB omission because they are unlikely to have cancer involvement of the lymph nodes, a factor which also makes these patients suitable for PBI.[32,35,36] Given that SLNB is associated with as much as a 10% rate of lymphedema and chronic arm morbidity,[61] some patients may prefer to omit SLNB after a negative axillary US, even when planning to receive PBI. Therefore, careful and thorough shared decision making in the context of a preoperative multidisciplinary discussion is advised when considering the administration of PBI following omission of SLNB, as PBI is not recommended in patients with node-positive breast cancer.[55] Nomograms that estimate the probability of SLN involvement may be helpful for shared decision making in these clinical contexts when pathologic confirmation of the lymph nodes is likely to affect postoperative recommendations for adjuvant treatments like PBI.[32,35,36] When WBI is administered, RT dosing should be administered in alignment with ASTRO RT for the whole-breast guideline recommendations[62] advocating for moderate hypofractionation, or other regimens supported by published phase III trials including ultrashort RT regimens delivered over 1 week,[63] and should not be altered by omission of SLNB.

Importantly, the SOUND and INSEMA trials[23,24] did not specifically evaluate whether omission of both RT and SLNB after BCS is a viable option in appropriate candidates. However, data from the CALGB study 9343 indicate that, in women age 70 years or older, omission of both RT and SLNB following BCS does not increase risk of distant metastasis and does not impair survival outcomes in patients taking adjuvant tamoxifen for cT1N0M0, estrogen receptor (ER)–positive breast cancer.[44] Notably, 63% of patients randomly assigned to WBI or no RT arms on CALGB 9343 did not receive any axillary surgery, and, among these women, no axillary recurrences occurred in those who received RT and tamoxifen, while only six axillary recurrences (3%) occurred in those who received tamoxifen alone without RT. Like the CALGB 9343 trial, the PRIME II study[56] randomly assigned women with early-stage hormone receptor–positive, node-negative breast cancer to endocrine therapy alone or endocrine therapy and WBI. However, in this phase III trial, slightly younger women were enrolled (ie, 65 years or older) with tumors up to 3 cm in largest dimension, and the protocol mandated axillary surgical staging with BCS. While omission of RT did not negatively impact rates of distant metastasis and OS in both CALGB 9343 and PRIME II, the design of PRIME II precluded formal evaluation of omission of both RT and SLNB in this slightly younger patient population. The current data most strongly support the

recommendation that the decision to omit RT should not be altered by omission of a SLNB in women age 70 years or older with cT1N0M0, ER-positive breast cancer who will take endocrine therapy. In the future, there may be an opportunity for shared decision making regarding single-modality endocrine therapy or RT, given the results of the EUROPA trial showing greater reduction in health-related QoL with endocrine therapy in patients age 70 years or older with luminal-A, early-stage breast cancer.[64] The long-term oncologic outcomes are still under investigation. Overall, given the low incidence of nodal positivity coupled with the low locoregional recurrence risk among women age 65 years or older with T1, ER-positive, HER2-negative tumors, omission of SLNB and RT may be considered when patients are committed to the prescribed course of endocrine therapy.

Literature Review and Analysis (genomic assay testing and subsequent systemic therapy)

No studies that satisfied the systematic review inclusion criteria were identified by the electronic search conducted to inform the question of how systemic treatment decisions should be impacted by omission of a SLNB. The recommendation offered is based on (1) findings from large-scale studies evaluating the clinical utility of genomic assay testing to guide adjuvant therapy decision making,[65-67] (2) updates of ASCO guidelines on biomarkers for adjuvant therapy in early-stage breast cancer,[68] and (3) phase III trials evaluating optimal adjuvant chemotherapy and targeted therapy for early-stage breast cancer.[69]

Clinical Interpretation

Genomic assay testing (eg, 21-gene recurrence score) to guide adjuvant systemic therapy decisions was not used in either the SOUND or INSEMA clinical trials. Adjuvant chemotherapy was used in 18.8% of patients in the SOUND study and in 12.4% of patients in the INSEMA study. While prior guidelines such as the 2022 ASCO guideline includes decision making based on nodal status, genomic assays testing is recommended to guide systemic therapy decisions of hormone receptor–positive, HER2-negative breast cancers, even in patients with one to three positive nodes who are postmenopausal or over 50 years of age.[68] Genomic assay testing results, however, do not influence adjuvant systemic therapy decisions in patients with four or more positive nodes and hormone receptor–negative breast cancer regardless of menopausal status. For example, the addition of cytotoxic chemotherapy and/or CDK4/6 inhibitor is recommended in all patients with hormonal receptor–positive pN2 disease irrespective of genomic assay score. Nevertheless, the likelihood of having pN2 disease in the appropriate postmenopausal candidates who qualify for omission of SLNB is extremely low (<1%). Given surgical axillary staging information does not impact systemic therapy decision making in the appropriate patients (eg, postmenopausal patients with invasive breast cancer that have pN0 or pN1 disease and a recurrence score of 25 or lower per RxPONDER and TAILORx criteria),[65-67] access to genomic assay testing and subsequent results influencing systemic therapy decisions should not be predicated on surgical nodal status and should not be altered by omission of SLNB. Genomic assay testing, specifically the 21-gene recurrence score, can be performed in the setting of SLNB omission. SLNB can be considered if the pathologic nodal status may impact the type of chemotherapy (ie, use of anthracycline) recommended.

The ASCO 2024 update on adjuvant targeted therapy highlights the use of abemaciclib in combination with endocrine therapy for patients with resected, hormone receptor–positive, HER2-negative, node-positive early breast cancer at high risk of recurrence.[69] Specifically, abemaciclib for 2 years plus endocrine therapy for at least 5 years may be offered to patients meeting the criteria of the intention-to-treat monarchE population, defined as having ≥4 positive ALNs or one to three positive ALNs with additional high-risk features such as grade 3 disease, tumor size ≥5 cm, or a Ki-67 index ≥20%. Although the US Food and Drug Administration's language is broad, the Panel recommends abemaciclib primarily for those eligible under monarchE trial criteria. Given that the patients from Recommendation 1.1 do not have primary tumor characteristics warranting abemaciclib treatment, and only 0.6% had pN2 disease, it is unlikely that the omission of SLNB will impact abemaciclib use recommendations in these select patients.

Additionally, the efficacy of ribociclib with a nonsteroidal aromatase inhibitor was evaluated in the NATALEE trial, which included patients with hormone receptor–positive, HER2-negative breast cancers and any ALN macroinvolvement. This study also included patients with node-negative breast cancer, specifically, patients with >5 cm tumors or with 2 to 5 cm tumors that were grade 2 and had either a Ki67 ≥ 20% or high genomic risk score. Patients with grade 3 node negative breast cancers measuring 2 to 5 cm were also eligible.[70] As the majority of patients who are appropriate candidates for omission of SLNB have a low likelihood of nodal involvement, recommendations regarding the use of ribociclib should not be altered by omission of SLNB as the decision to use this medication stems primarily from assessment of the primary breast tumor. However, in those with pT1 disease, grade 3, hormone receptor–positive cancers, SLNB may be prudent in these patients with higher likelihood of positive ALN in which case ribociclib would be considered if a patient is found to have a positive SLN. Use of nomograms to predict likelihood of positive SLN may help guide shared decision making regarding the value of a SLNB in these cases.[32,35,36]

COMPLETION ALND

Clinical Question 3

Is ALND necessary for patients with clinically node-negative early-stage breast cancer who have one or two SLN metastases and will receive BCS with whole-breast RT?

Literature Review

The systematic review completed for the update identified four articles that bear on this clinical question.[12,13,16,21] The ACOSOG Z0011 noninferiority trial enrolled patients with cT1-T2 tumors and clinically uninvolved nodes by physical examination. Eligible patients were those found to one to three positive sentinel nodes and were randomly assigned to a full ALND (n = 446) or no further surgery after SLNB (n = 445). Giuliano et al[13] reported the 10-year locoregional recurrence rates in 2016. All patients had BCS and planned whole-breast irradiation. The analyses completed on the intention-to-treat sample—436 patients in the SLNB-only arm and 420 in the SLNB + ALND arm—showed no statistically significant difference in locoregional recurrence-free survival ($P = .13$) after a median follow-up of 9.25 years. For the ALND and SLNB-only arms, the 10-year cumulative locoregional recurrence was 6.2% and 5.3%, respectively, $P = .36$. The 10-year OS results reported for this same sample in 2017[12] revealed that OS for patients treated with SLNB alone (86.3%) was noninferior to OS in patients treated with ALND (83.6%; HR, 0.85 [one-sided 95% CI, 0 to 1.16]; noninferiority $P = .02$) at a median follow-up of 9.3 years. DFS was also not statistically significant between the two arms: 78.2% in the ALND group and 80.2% in the SLNB-alone group (HR, 0.85 [95% CI, 0.62 to 1.17]; $P = .32$).

Galimberti et al[16] reported the 10-year DFS results of the phase III IBCSG 23-01 noninferiority trial that randomly assigned patients with breast cancer (maximum diameter of 5 cm) and sentinel node micrometastases to no axillary dissection (n = 469) or axillary dissection (n = 465). The primary end point of the trial was DFS; OS was a secondary end point. No difference in DFS was observed between the two study arms after a median follow-up of 9.7 years. DFS in the no completion axillary dissection group was 76.8% (95% CI, 72.5 to 81.0) and was 74.9% (95% CI, 70.5 to 79.3) in the axillary dissection group (HR, 0.85 [95% CI, 0.65 to 1.11]; log-rank $P = .24$; $P = .0024$ for noninferiority). There was also no difference in OS between the two arms.

The SENOMAC prospective, randomized, phase III trial enrolled 2540 patients with clinically node-negative, primary T1 to T3 breast cancer with one or two sentinel node macrometastases.[21] Patients were randomly assigned to undergo SLNB only (n = 1,335) or completion ALND (n = 1,205). OS was the primary end point of the trial; de Boniface et al[21] reported on recurrence-free survival (RFS; includes invasive recurrence and death), a prespecified secondary end point at a median follow-up of 46.8 months. Analyses revealed that SLNB was noninferior to completion ALND. The estimated 5-year RFS was 89.7% (95% CI, 87.5 to 91.9) among patients in the SLNB-only group and 88.7% (95% CI, 86.3 to 91.1) among patients in the ALND group.

In a post hoc analysis, de Boniface et al[22] investigated the possible benefits (avoidance of IDFS events with adjuvant abemaciclib) and harms (severe arm morbidity) of completion ALND in a subset of patients from the per-protocol population of the SENOMAC trial in whom the indication for adjuvant abemaciclib was pN2-3 status (four or more nodal metastases). Sixty-seven percent (1,705 of 2,540) of patients from the per-protocol SENOMAC population met eligibility criteria for this post hoc analysis. Of this group, 47% had completion ALND and 53% had SLNB alone. The analysis showed that completion ALND would need to be performed in 104 patients to avoid one IDFS event at 5 years with 2 years of adjuvant abemaciclib; this same completion ALND would lead to nine patients experiencing severe or very severe arm morbidity 1 year after completion ALND.

Clinical Interpretation

The ACOSOG Z0011 trial established that ALND does not improve oncologic outcomes in patients with one to three positive sentinel nodes but does increase lymphedema rates.[71] In this study, WBI without RNI was specified in the protocol but RT records revealed that 19% of patients received RT to the supraclavicular fossa contrary to protocol-specified treatment.[72] The delivery of RNI to the supraclavicular fossa was associated with greater nodal involvement (ie, three positive nodes *v* one positive node) in patients enrolled on ACOSOG Z0011[72] reflecting RT treatment decisions made in response to data demonstrating that, when more sentinel nodes are involved, the higher the likelihood of additional nonsentinel node involvement. In these cases, more comprehensive locoregional treatment was administered to address this increased risk of nodal burden.[21] Recent studies indicate that the addition of RNI increases acute adverse effects while not improving OS.[73] However, the use of RNI does improve DFS and lowers both breast cancer recurrence and breast cancer mortality rates with the benefits of RNI most strongly observed in patients with ER-negative, progesterone receptor (PR)–negative tumors.[73,74] Therefore, it is reasonable to consider regional nodal treatment in patients with node-positive disease. Importantly, in ACOSOG Z0011, nodal burden was relatively low among all patients enrolled, as 40% of patients had only micrometastasis within the sentinel node, and in cases like these, RNI does not appear warranted.

The SENOMAC trial[21] further confirmed the results of ACOSOG Z0011 in a broader group of patients with cT1-T3 N0 tumors and one to three positive sentinel node macrometastases with or without extranodal extension. Unlike Z0011, preoperative axillary US was mandatory. Patients were randomly assigned to a full lymph node dissection or no further surgery after sentinel node biopsy. At 5 years, RFS was not improved by a full lymph node dissection. Per protocol, RT included the breast and/or chest wall as well as the regional nodes, which was administered in 89% of patients, supporting the use of regional nodal treatment in these patients with macrometastatic node-positive disease.

Clinical Question 4

Is ALND necessary for patients with nodal metastases who are planning to undergo mastectomy?

Literature Review and Analysis

Five studies from the updated systematic review inform the clinical question of whether ALND is necessary for patients with clinically node-negative invasive breast cancer ≤5 cm who receive mastectomy and have one to two positive sentinel nodes.[15,16,20,21,75] OTOSAR (Optimal Treatment Of the Axilla—Surgery Or Radiotherapy) was a prospective, single-center, phase III, noninferiority trial that randomly assigned 474 patients with early-stage invasive breast cancer who are SLN-positive to either completion ALND (n = 244) or RNI without completion ALND (n = 230). The primary end point of the trial was axillary recurrence; secondary end points included OS, breast cancer–specific survival, DFS, and distant DFS. Sávolt et al[15] reported long-term outcomes after a mean follow-up of 97 months. Results showed that RNI was noninferior to completion ALND: The axillary recurrence in the completion ALND arm was 2.0% compared to 1.7% in the RNI arm (P = 1.00). In the RNI arm, 30 patients (16%) underwent mastectomy; in the completion ALND arm, 44 patients (18%) underwent mastectomy. The results of this study support the use of RNI in place of completion ALND in these patients.

The phase III IBCSG 23-01 noninferiority trial reviewed earlier that randomly assigned patients to no axillary dissection or axillary dissection included a small proportion of patients—86 of 931 total patients (9%)—who underwent mastectomy. The authors noted that comparable findings from post hoc exploratory analyses for a range of outcomes in the BCS and the mastectomy groups suggest that omitting completion ALND could be an acceptable option for patients scheduled to receive mastectomy.

The EORTC 10981-22023 AMAROS multicenter, phase III noninferiority trial[20] compared ALND and axillary RT (ART) in patients with node-negative breast cancer and a positive SLNB. Patients who had a positive sentinel node were randomly assigned to either ALND (n = 744) or ART (n = 681). Five-year ARR was the primary end point; secondary end points included OS, DFS, axillary recurrence-free survival, as well as lymphedema, shoulder mobility, and QoL. About 17% of patients in each arm were treated with mastectomy. Bartels et al[20] reported on the 10-year ARR which after ALND was 0.93% (95% CI, 0.18 to 1.68) and after ART was 1.82% (95% CI, 0.74 to 2.94; HR, 1.71 [95% CI, 0.67 to 4.39]). There were no between-group differences in either OS (HR, 1.17 [95% CI, 0.89 to 1.52]) or DFS (HR, 1.19 [95% CI, 0.97 to 1.46]). There was a higher lymphedema rate in the ALND group in updated analyses compared to the ART group (24.5% *v* 11.9%, respectively; P < .001). QoL scales did not differ by treatment arm.

The SENOMAC trial compared SLNB only and completion ALND, and included 920 patients who underwent mastectomy, or 36% of all patients; the SINODAR-ONE trial[18] included 218 patients who underwent mastectomy, or 24.8% of all patients. SINODAR-ONE, a prospective, noninferiority phase III trial, randomly assigned patients to SLNB only (n = 440) or ALND (n = 439). The primary end point was OS; secondary end points were regional (lymph node recurrence) or distant recurrence (RFS). Analyses performed on the intention-to-treat population at a median follow-up of 34.0 months showed that 3-year survival, regional, and distant relapse rates of patients in the SLNB-only group were noninferior to those in the ALND group. In a subanalysis of patients in the SINODAR-ONE trial who were treated with mastectomy (n = 218), Tinterri et al[75] compared the OS and RFS rates of patients who had been randomly assigned to the ALND group (n = 111) or to the SLNB-alone group (n = 107). Consistent with analyses from the larger study, survival and recurrence rates in the SLNB-only group were noninferior to those in the ALND group: The 5-year OS rate in the SLNB-only group was 98.7% and in the ALND group was 97.8% (P = .597); the 5-year RFS rate in the SLNB-only group was 94.1% and in the ALND group was 95.7% (P = .821).

Clinical Interpretation

As noted previously, the SENOMAC trial[21] further confirmed that a completion ALND is not necessary in a broader group of patients with clinically node-negative, sentinel node–positive disease, including those treated with mastectomy (36% of patients). Five-year survival, a secondary end point of the trial, was not improved by ALND in patients who were found to have one or two sentinel node macrometastases. The majority of patients received RNI in this trial in addition to chest wall treatment with good oncologic outcomes, and thus the findings support RNI in patients with positive sentinel macrometastatic nodes who do not undergo completion ALND.

Additionally, in the AMAROS trial, oncologic outcomes were equivalent in cT1-T2N0 patients with sentinel node–positive disease who were randomly assigned to SLNB with regional nodal and whole-breast or chest wall irradiation or to full ALND without RNI. Significantly higher rates of lymphedema were observed in patients treated with a full lymph node dissection.[76] Notably, 17% of patients on this study were treated with mastectomy.[76] Finally, the OTOASOR trial[15] confirmed the findings of AMAROS and found no differences in oncologic outcomes between ALND and RNI without ALND after BCS or mastectomy (16% of patients), with RNI associated with less morbidity. Collectively, these trials provide strong evidence that postmastectomy

RT with RNI is recommended in place of completion ALND in patients with clinically node-negative invasive breast cancer that is ≤5 cm, who receive mastectomy and have one to two positive sentinel nodes. Decisions regarding the addition of RNI may be based on increasing number of involved sentinel nodes as well as the size of the metastasis with RNI reserved for macrometastasis versus micrometastasis. In patients who receive mastectomy and have ≥3 positive nodes, ALND followed by RNI RT should be recommended.

Clinical Question 5

Can completion ALND be omitted in patients with early-stage breast cancer who do not have nodal metastases?

Literature Review and Analysis

This recommendation is unchanged from the 2017 ASCO Sentinel Lymph Node Biopsy for Patients with Early-Stage Breast Cancer[3] and the 2021 joint Ontario Health (OH; Cancer Care Ontario)-ASCO Management of the Axilla in Early-Stage Breast Cancer guideline.[4] The literature search conducted for the present update did not yield any new evidence that would change the OH-ASCO recommendation. In a 15-year follow-up analysis of patients who were clinically node-negative, Canavese et al[14] observed no statistically significant differences between the SLNB (n = 110) and the ALND (n = 115) arms in either event-free survival (72.8% *v* 72.9%, *P* = .953) or OS (82.0% *v* 78.8%, *P* = .502). Roy et al[17] similarly found no between-group OS differences in the randomized, phase III noninferiority GF-GS01 trial that compared SLNB followed by systemic ALND (sALND; n = 770) to ALND restricted to cases with positive SLNB (n = 774) in patients with invasive breast cancer who were clinically node-negative. This GS01 trial reported an 11.5% (95% CI, 7.5 to 15.6) reduction in the risk of postsurgical complications associated with limiting ALND to patients with a positive SLNB.

Clinical Interpretation

Since the introduction of SLNB in melanoma in the 1990s,[77] the use of SLNB has been validated in breast cancer in numerous studies.[78-80] In particular, NSABP B-32 trial evaluated the oncologic outcomes of SLNB compared to ALND in patients with clinically node-negative breast cancer.[81] There were no significant differences seen in disease-free survival (82.4% *v* 81.5%) or OS (91.8% *v* 90.3%) rates. Given the increased risk of lymphedema after ALND, routine ALND is not recommended in patients with early-stage breast cancer who do not have nodal metastases.

Special Commentary on Isolated Tumor Cells

Isolated tumor cells (ITCs) are defined as metastasis in the lymph node with size ≤0.2 mm, often detected by immunohistochemistry (IHC). Clinical significance of ITCs and its utility in clinical decision making for patients treated with surgery upfront has been evaluated previously. The ACOSOG Z0010 was designed as a prospective observation trial that enrolled women who had negative SLNs by hematoxylin and eosin (H&E) staining. SLN blocks were then sent for central laboratory IHC staining to look for ITCs. Treating physicians were blinded to the IHC results (thus they treated everyone based on the negative H&E staining). Among the 3326 H&E-negative nodes, 349 (10.5%) had IHC-positive SLNs. There was no difference in 5-year OS rates between patients who were IHC-negative and IHC-positive (95.7% *v* 95.1%; *P* = .64).[82] In the NSABP B-32 subanalysis, 15.9% of patients with H&E-negative SLNs had positive metastasis by IHC (11.1% ITCs, 4.4% micrometastases, and 0.4% macrometastases). Unlike the Z0010 study, 5-year OS rate was statistically but not clinically significant in this study, as the difference was very small (94.6% in patients who were IHC-positive [which includes 4.4% with micrometastases and 0.4% with macrometastases] *v* 95.8% in patients who were IHC-negative; *P* = .03).[83] Thus, routine use of ITC in SLN for clinical decision making is not warranted as ITCs do not have clinically significant impact on breast cancer recurrence or survival of patients treated with initial surgery.

SLNB IN SPECIAL CIRCUMSTANCES

Clinical Question 6

What is the role of SLNB in special circumstances in clinical practice including large or locally advanced invasive tumors, multicentric tumors, inflammatory breast cancer, DCIS, obesity, male breast cancer, pregnancy, patients who are breastfeeding or lactating, evaluation of the IM nodes, presence of suspicious palpable axillary nodes, presence of multiple suspicious axillary nodes on imaging with biopsy confirmation, and prior breast or axillary surgery?

Literature Review and Analysis

As with previous versions of this ASCO guideline,[1-3] there is very little high-quality evidence on which to base recommendations concerning these various special circumstances and conditions. The literature search conducted for this update identified three meta-analyses[26-28] and one prospective cohort study[25] relevant to the question of the role of SLNB in DCIS, and one systematic review of the use of SLNB in pregnant patients with breast cancer.[29]

Davey et al[27] performed a systematic review and meta-analysis of prospective studies to assess the necessity of routine SLNB in patients receiving surgery for DCIS. The 16 studies included 4,388 patients, of whom 3,156 (72.5%) underwent SLNB; of these 3,156 patients, 4.9% (153/3,153) had a positive SLNB, which represents a <1% likelihood of the likelihood of having a positive SLNB. Two clinicopathological factors—presence of tumor necrosis (*P* = .001) and undergoing mastectomy (*P* = .016)—were both associated

with having a positive SLNB for DCIS surgery. The authors suggest that this estimated <1% relative risk of having metastatic disease after SLNB performed for DCIS challenges the case for routinely performing upfront SLNB as for patients with DCIS, although certain clinicopathological features may influence this practice.

The risk of having metastatic disease after SLNB for DCIS was investigated by El Hage Chehade et al[28] in a systematic review and meta-analysis of 29 retrospective and 19 prospective studies (including 9,803 patients). El Hage Chehade et al[28] evaluated whether SLNB use in patients with DCIS is appropriate and examined factors that might increase the risk of invasive disease in this patient population. The percentage of patients with DCIS undergoing SLNB who had a positive SLNB was the primary end point. Meta-analysis results indicated that the mean percentage of positive SLNBs was higher in patients with a preoperative DCIS diagnosis (5.95%) than in patients a with postoperative DCIS diagnosis (3.02%; P = .0201). Meta-regression analysis revealed that two factors were significantly associated with SLNB positivity, larger tumor size (P = .0333) and higher grade (P = .00839).

Chiu et al[26] conducted a systematic review and meta-analysis of real-world data from 69 retrospective studies and 43 prospective studies (including a combined 44,001 patients) to evaluate SLNB-positivity rates, and the rates and predictors of upstaging to invasive disease among patients initially diagnosed as having DCIS. Analyses indicated that the pooled estimate of the upstaging rate, based on 70 studies, was 25.8% (95% CI, 0.230 to 0.286); the pooled estimate of the SLN-positivity rate was 4.9% (95% CI, 0.042 to 0.055) based on 89 studies. Meta-regression analysis results showed that the upstaging rate was higher among patients with high, nuclear-grade tumors, a palpable mass, ER-negative status, tumor size >2 cm on imaging, and in patients diagnosed with DCIS on core needle biopsy.

In a prospective, observational study of 530 patients with a preoperative diagnosis of clinically and radiologically node-negative DCIS, Bellver et al[25] investigated whether axillary assessment could be omitted in a group of patients. Selective SLNB was performed in 397 patients (75%); axillary node involvement was seen in 2.15% in the group with a postoperative diagnosis of DCIS (six patients). Bellver et al[25] observed a 24.5% rate of underdiagnosis of invasive breast cancer (130 of 530 patients); type of biopsy was the strongest factor with the rate of underdiagnosis, 1.34 times higher seen with core needle biopsy compared to vacuum-assisted biopsy. Risk of ALN involvement was significantly higher with lymphovascular invasion.

Bothou et al[29] published a systematic review of 63 articles (guidelines, narrative reviews, and reports of cohort studies, case-control studies, and case series studies) to provide a summary of available evidence and perspectives regarding the safety and effectiveness of SLNB in pregnant patients (382 women overall) who had been diagnosed with breast cancer. Forty-seven of the 63 (65) articles were "Strongly in favor of SLNB" in this population, four (6%) were "Partially in favor of SLNB"; two were "Partially against SLNB"; and 10 were "Strongly against SLNB."

Clinical Interpretation

SLNB in multicentric or multifocal breast cancer. The ACOSOG Z11102 study is a prospective single-arm study that evaluated the local recurrence rate of 204 patients with multiple ipsilateral breast cancer who underwent BCS followed by whole-breast RT with RT boost.[84] In this study, axillary surgery was required to be performed—84.3% underwent SLNB. Thus, while the feasibility and accuracy of SLNB was not explicitly tested in multicentric or multifocal tumors, it is generally accepted as a viable way to assess the axilla, as demonstrated in the Z11102 study.

SLNB for DCIS. In the context of patients with DCIS undergoing mastectomy, SLNB is often considered due to the potential for an upgrade in diagnosis to invasive cancer. This upgrade rate justifies the use of SLNB, particularly in mastectomy procedures, where the opportunity for successful lymphatic mapping diminishes post-mastectomy.[85] Consequently, SLNB is frequently performed concurrently with mastectomy. In contrast, for patients undergoing lumpectomy, there is flexibility to perform SLNB later if necessary.[86] Newer lymphatic tracers such as superparamagnetic iron oxide that can stay in the SLNs for 30 days offer opportunity for delayed SLNB, even in the setting of mastectomy.[87-89]

Repeat SLNB in recurrent breast cancer. The prognostic significance of repeat SLNB is still under investigation. The Sentinel Node and Recurrent Breast Cancer (SNARB) study group from Netherlands is the largest study regarding recurrent breast cancer: 36 Dutch hospitals compiled prospective data from 150 patients followed by an additional 386 retrospectively collected.[90] Of the 515 patients with recurrence, 230 had successful negative repeat SLNB. After median follow-up of 4.7 (range, 0.9-12.7) years, regional recurrence occurred in 4.5% of patients after negative repeat SLNB. Of the nine patients with regional recurrence as first event after negative repeat SLNB, 55.4% had a triple-negative recurrent tumor compared with 10.4% of the patients without regional recurrence as first event (P = .002). In this cohort of patients, 48.3% of the repeat SLNBs were located in an aberrant lymph node station (outside the ipsilateral axilla). Thus, for these patients, ALND would not have been a more accurate staging tool than SLNB. These findings are supported by two systematic reviews that concluded the overall repeat SLNB success rate of 64.3%-66.4% and aberrant drainage rate of 32.6%-39%.[91,92]

Evaluation of internal mammary lymph nodes. Historically, removal of the internal mammary (IM) nodal chain was completed through an open approach during Halsted mastectomy and radical mastectomy. Numerous

TABLE 2. Ongoing Trials Evaluating Omission of SLNB in Early-Stage Breast Cancer

Trial	Dates; Accrued	Schema	Primary End Point
BOOG 2013-08 (Dutch)	2014—Goal; N = 1,644	T1-T2, cN0/iN0 → randomly assigned to SLNB *v* no axillary surgery	5-year regional recurrence
SOAPET (China)	2019—Goal; N = 1,734	T1-T2, cN0/iN0 → prospective observational study of omission of axilla surgery in PET-negative	5-year DDFS, LRFS
NAUTILUS (Korea)	2020—Goal; N = 1,734	T1-T2, cN0/iN0 → randomly assigned to SLNB *v* no axillary surgery	5-year IDFS
VENUS (Brazil)	2020—Goal; N = 800	T1-T2, cN0/iN0 → randomly assigned to SLNB *v* no axillary surgery	5-year IDFS

Abbreviations: DDFS, distant disease-free survival; IDFS, invasive disease-free survival; LRFS, local recurrence-free survival; PET, positron emission tomography; SLNB, sentinel lymph node biopsy.

studies starting in the 1950s have demonstrated worse prognosis in patients with IM metastases than those without, independent of their axillary node status.[93] While prognostic, these legacy trials have demonstrated that dissection of the IM node did not improve survival.[94] With the use of lymphoscintigraphy, the rate of IM node drainage identification ranges from 13% to 37%.[93] The rate of isolated IM metastases is not common; systemic reviews found that the rate of finding a metastatic IM node among those with negative axillary node ranged from 4% to 17%.[93,95] Given the morbidity of IM node sampling, including pneumothorax and IM vessel bleeding, abnormal IM nodes detected by imaging (MRI or positron emission tomography/CT scan) are often used as surrogates for metastatic involvement.[95,96] Without clear evidence that retrieval of IM nodes will impact oncologic outcomes, given the morbidities associated with IM node retrieval, SLNB is not recommended for routine evaluation of IM nodes.

LIMITATIONS OF THE RESEARCH AND DIRECTIONS FOR FUTURE RESEARCH

The existing clinical trials studying different therapies evaluated the oncologic safety of de-escalating or omitting one aspect of the local-regional therapy, either surgical evaluation of the axilla or RT. RT studies evaluated WBI de-escalation to PBI or no RT where most in the trial received standard surgical approaches including SLNB, and medical oncology studies evaluated chemotherapy omission where everyone in the trial received standard surgery, surgical nodal evaluation with at least an SLNB, and RT when indicated.[55,67]

The current treatment recommendations and guidelines are based on available data and in the absence of a trial that tested all the different combinations of the local-regional therapy in early-stage breast cancer (eg, SLNB+ WBI+, SLNB+ PBI+, SLNB+ RT-, SLNB− WBI+, SLNB− PBI+, and SLNB− RT−). Such a comprehensive trial is likely not feasible due to the low cancer recurrence rate, requiring decades and tens of thousands of patients to accrue. Thus, the concern is valid that in certain instances, SLNB information is necessary, as it may influence RT decision and adjuvant systemic therapy decision. In those circumstances where SLN status is likely to influence adjuvant systemic therapy and RT decisions, then SLNB should be performed. However, the sweeping statement that SLNB is required for all patients with early-stage breast cancer undergoing surgery is no longer valid. Given the morbidity of SLNB and RT, multidisciplinary discussions prior to surgical decision making are strongly encouraged. Details of ongoing trials that are evaluating the omission of SLNB in early-stage breast cancer are provided in Table 2.

PATIENT AND CLINICIAN COMMUNICATION

Despite the Society of Surgical Oncology Choosing Wisely Campaign recommending against routine use of SLNB in women 70 years and older with early-stage hormone receptor-positive, HER2-negative breast cancer and data showing no survival benefit of RT after breast conserving surgery in these patients, both SLNB and RT continue to be used at a high rate in this patient population in the United States.[97-102]

In a recent sequential explanatory mixed-method study of patients at least age 70 years with hormone receptor–positive breast cancer, qualitative analysis of semistructured interviews conducted among high and low utilizers of both SLNB and postlumpectomy RT revealed that patient trust in the clinician and patient desire for peace of mind were the most important factors influencing decisions around SLNB and postlumpectomy RT.[103] These data suggest that patient-clinician communication may promote high-quality decision making and improve rates of omission of SLNB and RT in the appropriate patients.

In another qualitative study of semistructured interviews with surgical, medical, and RT oncologists, there was wide variation on physician perspectives regarding the recommendation and data to support omitting SLNB in patients age 70 years and older with cT1N0, hormone receptor–positive, HER2-negative disease.[104] The decision to omit SLNB was based on several nuanced patient- and disease-level factors. The study concluded that interventions aimed at educating physicians, facilitating preoperative multidisciplinary conversation, and improving patient-clinician communication may also help to deimplement SLNB per the Choosing Wisely recommendations.

Finally, perspectives on breast cancer treatments were assessed in a qualitative study of 30 participants, age 70 years or older and without a previous diagnosis of breast cancer.[105] While half of the participants agreed that age-based guidelines were appropriate based on low breast cancer recurrence risk, the majority believed that a person's overall health and expected life expectancy rather than chronological age should drive treatment decisions. Others had difficulty understanding treatment de-escalation with omission of SLNB and RT in older patients as favorable and not indicative of a poor prognosis. Among participants, 40% perceived SLNB as providing peace of mind and relatively low risk, while 73% preferred to omit RT due to lack of benefit, inconvenience, and perceived risks. The results suggested that emphasizing a high likelihood of a positive breast cancer–specific prognosis while maintaining a high QoL and functional status could assuage patient concerns related to age discrimination and could persuade patients to avoid overtreatment and overestimating the benefits of SLNB and RT while underestimating the risks.

These studies indicate that while guidelines may recommend omission of SLNB and RT in appropriate patients following lumpectomy, high-quality patient-clinician communication and education are necessary to disseminate and implement these recommendations. For recommendations and strategies to optimize patient-clinician communication, see Patient-Clinician Communication: ASCO Consensus Guideline.[106]

HEALTH EQUITY CONSIDERATIONS

Social determinants of health, defined by the World Health Organization as the conditions in which an individual is born, grows, lives, works, and ages, can undermine ASCO's expert recommendations on best practices for prevention, screening, palliative and supportive care, and disease management for many patients with cancer.[107] It is important to acknowledge that many people in the United States and elsewhere do not receive the highest level of cancer care due to the long-term impact of structural racism and the consequential unequal distribution of wealth and health care access among racial groups.[108] For example, racial disparities in the adoption of SLNB in patients with pathologically node-negative breast cancer persisted long after SLNB was recognized as standard of care.[109] In an analysis of SEER-Medicare data from 2002 to 2007, SLNB was performed in significantly more White than Black patients (74% *v* 62%, respectively, $P < .001$) with pathologically node-negative breast cancer. The higher rate of ALND use in Black patients contributed to higher rates of lymphedema in Black than White patients (12% *v* 8%, respectively, $P < .001$). Given these data, it will be important to study if there are racial differences in the adoption of omission of axillary surgical staging in the appropriate patients and whether lymphedema rates may differ based on race due to continued surgical staging in marginalized populations.

With respect to the SOUND and INSEMA trials, eligible participants required a plan to undergo RT. Patterns-of-care analyses using the SEER and National Cancer Database have demonstrated that Black and Hispanic women receive recommended breast RT postlumpectomy less often than their White counterparts.[110,111] In fact, such disparity in access has extended to appropriate RT receipt for Hispanic women even enrolled on clinical trial.[112] As the management of breast cancer is a multidisciplinary undertaking, appropriate de-escalation requires appropriate and timely referrals and initiation of treatments including surgery, RT, and systemic therapies. It is also important that these multidisciplinary discussions involve representatives from all treating clinician team members: surgical, medical, and RT oncologists. Inappropriate de-escalation and delays in care may yield worse outcomes for marginalized groups for whom appropriate adjuvant therapies are not recommended.

Health inequity plays a significant role in BCS, impacting access, outcomes, and decision making for patients across different demographic groups. These disparities can be influenced by socioeconomic factors, race, geographic location, and health care access, ultimately leading to differences in treatment and survival outcomes. Patients with lower socioeconomic status may have limited access to specialized breast cancer care, including multidisciplinary teams and facilities that offer breast conservation.[113] Financial barriers such as inadequate insurance coverage or high out-of-pocket costs can deter patients from seeking appropriate treatments, leading them to opt for mastectomy or forego treatment altogether. Women from lower socioeconomic backgrounds are more likely to be diagnosed at later stages due to delayed or inadequate screening, reducing the eligibility for BCS. Studies show that Black and Hispanic women are less likely to undergo BCS than White women. Black women, in particular, are more likely to present with larger, more aggressive tumors that preclude the option of breast conservation.[113-115]

In most low- to middle-income countries, advanced stages at diagnosis and low diagnostic and treatment capacities contribute to poorer breast cancer survival rates.[116,117] Five-year breast cancer survival rates exceed 90% in high-income countries, compared with 66% in India and 40% in South Africa.[118] The oncologic outcomes disparities are observed also based on insurance status. In Brazil, for example, the breast cancer incidence as well the mortality rate of stages III-IV differ substantially between private and public health systems.[119] To address this inequity, applying approaches that have worked well in high-income countries to settings with fewer resources is required, but these approaches must be tailored to local contexts.[120,121]

Rural patients often have less access to high-quality breast cancer care and advanced technologies such as RT, which is integral to BCS. Delays in RT treatment adversely impact outcomes.[122-124] This lack of access can lead to higher mastectomy rates in rural populations. Inequities in

communication between health care clinicians and patients can influence treatment decisions. For instance, patients with lower health literacy or those from underserved communities may not fully understand the benefits of BCS or may not receive adequate information about their treatment options. Cultural and language barriers also play a role, particularly for non–English-speaking patients who may not receive proper counseling regarding breast conservation.[113-115]

In the United States, many patients remain unable to reap the benefits of innovative prevention and early detection programs, biomarker testing, and new cancer therapies due to structural barriers including lack of transportation, stable housing, and adequate insurance coverage as well as food insecurity, health literacy, proximity to a dedicated cancer center, and cost of treatment and other services.[125] Additionally, sexual and gender minority people experience stigma along with barriers to cancer screening, prevention, and treatment that contribute to these cancer disparities.[126]

Furthermore, geographic disparities can also impact the quality of care patients receive. Rural patients are more likely to have worse survivorship outcomes and experience higher mortality rates compared to nonrural patients. This can be attributed, in part, to a lower density of specialists and dedicated cancer centers, as only 21% of nonmetropolitan counties in the United States have one or more practicing oncologists.[127]

MULTIPLE CHRONIC CONDITIONS

Patients with multiple chronic conditions (MCC), two or more chronic conditions, may have additional complexities and needs when clinicians are developing treatment and follow-up plans. The complexity and uncertainty created by MCC highlights the importance of shared decision making regarding implementation of guideline-recommended care.

COST IMPLICATIONS

Cost-effectiveness analysis of SLNB versus omission of SLNB after a negative axillary US for patients with early-stage breast cancer, for postmenopausal women with cT1-T2 N0, hormone receptor–positive, HER2-negative breast cancer demonstrated that omission of SLNB was associated with lower costs and higher QoL.[128] Increasingly, individuals with cancer are required to pay a larger proportion of their treatment costs through deductibles and coinsurance.[129] Higher patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended cancer treatments.[130,131] Discussion of cost can be an important part of shared decision making,[132] and has the potential to decrease out-of-pocket expenses for the patient.[133] These discussions may be limited by the lack of accessible, easily interpretable, and detailed health care cost data in the United States.[128] Clinicians should, however, discuss with patients the use of less expensive alternatives when it is practical and feasible for treatment of the patient's disease and when there are two or more treatment options that are comparable in terms of benefits and harms.[132] Patient out-of-pocket costs may vary depending on insurance coverage. Coverage may originate in the medical or pharmacy benefit, which may have different cost-sharing arrangements. Patients should be aware that different products may be preferred or covered by their particular insurance plan. Even with the same insurance plan, the price may vary between different pharmacies. When discussing financial issues and concerns, patients should be made aware of any financial counseling services available to address this complex and heterogeneous landscape.[132]

Breast cancer–related lymphedema is an unpredictable occurrence that can happen years after axillary surgery.[134] Lymphedema is associated with risk of infection, restricted mobility, significant financial toxicity, and decreased QoL and psychosocial well-being.[135,136] Breast RT is related to acute and late toxicities including RT dermatitis, fatigue, cardiotoxicity, and lymphedema.[137-139] In the SOUND[23] and INSEMA[24,30] trials, patients in the SLNB group, compared to the no axillary surgery group, showed significantly and clinically relevant breast and arm symptoms including pain, arm swelling, and impaired mobility and disability.

In a study evaluating the cost-effectiveness of SLNB versus omission of SLNB after a negative axillary US for patients with early-stage breast cancer, for postmenopausal women with cT1-T2 N0, hormone receptor–positive, HER2-negative breast cancer, omission of SLNB was associated with lower costs and higher QoL.[128] The choice of RT protocols are another important factor in cost of overall care. However, RT cost-effectiveness studies demonstrating cost-effectiveness of PBI did not evaluate cost in the context of SLNB use or omission.[140-143] Furthermore, studies demonstrating decreased cost with omission of SLNB did not compare the cost-effectiveness stratified by different RT type or use (WBI *v* PBI *v* no RT). Therefore, there are no current data evaluating overall cost-effectiveness of omission of SLNB and different standard RT approaches.

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The guideline recommendations table and accompanying tools (available at www.asco.org/breast-cancer-guidelines) were designed to facilitate implementation of recommendations. ASCO guidelines are

posted on the ASCO website and most often published in the *Journal of Clinical Oncology*.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

For current information, including selected updates, supplements, slide sets, and clinical tools and resources, visit www.asco.org/breast-cancer-guidelines. The Data Supplement for this guideline includes a table summarizing study characteristics, and evidence summary table, and a quality-of-evidence table. Guideline recommendations and algorithms are also available in the free ASCO Guidelines app (available for download in the Apple App Store and Google Play Store). Listen to key recommendations and insights from panel members on the ASCO Guidelines podcast. The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.org.

ASCO welcomes your comments on this guideline, including implementation challenges, new evidence, and how this guideline impacts you. To provide feedback, contact us at guidelines@asco.org. Comments may be incorporated into a future guideline update. To submit new evidence or suggest a topic for guideline development, complete the form available at www.asco.org/guidelines.

RELATED ASCO GUIDELINES

- Patient-Clinician Communication[106] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)
- Management of the Axilla in Early-Stage Breast Cancer[4] (https://ascopubs.org/doi/10.1200/JCO.21.00934)

GENDER-INCLUSIVE LANGUAGE

ASCO is committed to promoting the health and well-being of individuals regardless of sexual orientation or gender identity.[144] Transgender and nonbinary people, in particular, may face multiple barriers to oncology care including stigmatization, invisibility, and exclusiveness. One way exclusiveness or lack of accessibility may be communicated is through gendered language that makes presumptive links between gender and anatomy.[145] With the acknowledgment that ASCO guidelines may impact the language used in clinical and research settings, ASCO is committed to creating gender-inclusive guidelines. For this reason, guideline authors use gender-inclusive language whenever possible throughout the guidelines. In instances in which the guideline draws upon data based on gendered research (eg, studies regarding women with breast cancer), the guideline authors describe the characteristics and results of the research as reported.

AFFILIATIONS

[1]Brigham and Women's Hospital, Dana-Farber Cancer Institute, Boston, MA
[2]American Society of Clinical Oncology, Alexandria, VA
[3]Penn State Health Milton S. Hershey Medical Center, Hershey, PA
[4]Department of Surgery, University of Western Ontario, London, ON, Canada
[5]Providence Cancer Institute, Portland, OR
[6]Brazilian Society of Mastology, Belo Horizonte, Brazil
[7]Emily Couric Clinical Cancer Center, Charlottesville, VA
[8]Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada
[9]Stephanie Spielman Comprehensive Breast Center, The Ohio State University Medical Center, Columbus, OH
[10]University of Washington School of Medicine, Seattle, WA
[11]University of Nigeria Teaching Hospital, Enugu, Nigeria
[12]University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA
[13]Yale University, New Haven, CT
[14]Piedmont Cancer Institute, Atlanta, GA
[15]University of Florida, Jacksonville, FL
[16]Dan L. Duncan Comprehensive Cancer Center, Houston, TX
[17]Glenn Family Breast Center at Winship Cancer Institute, Atlanta, GA

CORRESPONDING AUTHOR

American Society of Clinical Oncology; e-mail: guidelines@asco.org.

EQUAL CONTRIBUTION

K.U.P. and M.A.T. were Expert Panel Co-Chairs.

EDITOR'S NOTE

This ASCO Clinical Practice Guideline Update provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at www.cancer.org, is available at www.asco.org/breast-cancer-guidelines.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO-25-00099.

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Administrative support: Mark R. Somerfield
Collection and assembly of data: All authors
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

The Expert Panel wishes to thank the members of the ASCO Breast Cancer Guideline Advisory Group members Nagi S. El Saghir, MD, Shipra Gandhi, MD, Shilpi Gupta, MD, and Allison W. Kurian, MD; ASTRO external reviewers Alvin Cabrera, MD, Janice Lyons, MD, and Kilian Salerno, MD; SSO external reviewers Eduard-Alexandru Bonci, MD, PhD, Frederick M Dirbas, MD, and Nicholas Tranakas, MD; EBMC reviewers Yanin Chávarri-Guerra, MD, and Richard C. Zellars, MD; and the Evidence Based Medicine Committee for their thoughtful reviews and insightful comments on this guideline

REFERENCES

1. Lyman GH, Giuliano AE, Somerfield MR, et al: American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 23: 7703-7720, 2005
2. Lyman GH, Temin S, Edge SB, et al: Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 32:1365-1383, 2014
3. Lyman GH, Somerfield MR, Bosserman LD, et al: Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 35:561-564, 2017
4. Brackstone M, Baldassarre FG, Perera FE, et al: Management of the axilla in early-stage breast cancer: Ontario Health (Cancer Care Ontario) and ASCO guideline. J Clin Oncol 39: 3056-3082, 2021
5. Higgins JPT: Cochrane Collaboration: Cochrane Handbook for Systematic Reviews of Interventions (ed 2). Hoboken, NJ, Wiley-Blackwell, 2019
6. Balshem H, Helfand M, Schunemann HJ, et al: GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 64:401-406, 2011
7. Fan YJ, Li JC, Zhu DM, et al: Efficacy and safety comparison between axillary lymph node dissection with no axillary surgery in patients with sentinel node-positive breast cancer: A systematic review and meta-analysis. BMC Surg 23:209, 2023
8. Bromham N, Schmidt-Hansen M, Astin M, et al: Axillary treatment for operable primary breast cancer. Cochrane Database Syst Rev 1:CD004561, 2017
9. Heiranizadeh N, Rafiei Shahamabadi M, Dehghan HR, et al: Comparing early-stage breast cancer patients with sentinel lymph node metastasis with and without completion axillary lymph node dissection: A systematic review and meta-analysis. Asian Pac J Cancer Prev 23:2561-2571, 2022
10. Castelo M, Hu SY, Dossa F, et al: Comparing observation, axillary radiotherapy, and completion axillary lymph node dissection for management of axilla in breast cancer in patients with positive sentinel nodes: A systematic review. Ann Surg Oncol 27:2664-2676, 2020
11. Hersh EH, King TA: De-escalating axillary surgery in early-stage breast cancer. Breast 62:S43-S49, 2022 (suppl 1)
12. Giuliano AE, Ballman KV, McCall L, et al: Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: The ACOSOG Z0011 (Alliance) randomized clinical trial. JAMA 318:918-926, 2017
13. Giuliano AE, Ballman K, McCall L, et al: Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: Long-term follow-up from the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 randomized trial. Ann Surg 264:413-420, 2016
14. Canavese G, Bruzzi P, Catturich A, et al: Sentinel lymph node biopsy versus axillary dissection in node-negative early-stage breast cancer: 15-year follow-up update of a randomized clinical trial. Ann Surg Oncol 23:2494-2500, 2016
15. Savolt A, Peley G, Polgar C, et al: Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla - Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer: A randomized, single centre, phase III, non-inferiority trial. Eur J Surg Oncol 43:672-679, 2017
16. Galimberti V, Cole BF, Viale G, et al: Axillary dissection versus no axillary dissection in patients with breast cancer and sentinel-node micrometastases (IBCSG 23-01): 10-year follow-up of a randomised, controlled phase 3 trial. Lancet Oncol 19:1385-1393, 2018
17. Roy P, Leizorovicz A, Villet R, et al: Systematic versus sentinel-lymph-node-driven axillary-lymph-node dissection in clinically node-negative patients with operable breast cancer. Results of the GF-GS01 randomized trial. Breast Cancer Res Treat 170:303-312, 2018
18. Tinterri C, Gentile D, Gatzemeier W, et al: Preservation of axillary lymph nodes compared with complete dissection in T1-2 breast cancer patients presenting one or two metastatic sentinel lymph nodes: The SINODAR-ONE multicenter randomized clinical trial. Ann Surg Oncol 29:5732-5744, 2022
19. Campbell I, Wetzig N, Ung O, et al: 10-year axillary recurrence in the RACS SNAC1 randomised trial of sentinel lymph node-based management versus routine axillary lymph node dissection. Breast 70:70-75, 2023
20. Bartels SAL, Donker M, Poncet C, et al: Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer: 10-year results of the randomized controlled EORTC 10981-22023 AMAROS trial. J Clin Oncol 41:2159-2165, 2023
21. de Boniface J, Filtenborg Tvedskov T, Ryden L, et al: Omitting axillary dissection in breast cancer with sentinel-node metastases. N Engl J Med 390:1163-1175, 2024
22. de Boniface J, Appelgren M, Szulkin R, et al: Completion axillary lymph node dissection for the identification of pN2-3 status as an indication for adjuvant CDK4/6 inhibitor treatment: A post-hoc analysis of the randomised, phase 3 SENOMAC trial. Lancet Oncol 25:1222-1230, 2024
23. Gentilini OD, Botteri E, Sangalli C, et al: Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: The SOUND randomized clinical trial. JAMA Oncol 9:1557-1564, 2023
24. Reimer T, Stachs A, Veselinovic K, et al: Axillary surgery in breast cancer—primary results of the INSEMA trial. N Engl J Med 10.1056/NEJMoa2412063 [epub ahead of print on December 12, 2024]
25. Bellver G, Buch E, Ripoll F, et al: Is axillary assessment of ductal carcinoma in situ of the breast necessary in all cases? J Surg Res 271:145-153, 2022
26. Chiu CW, Chang LC, Su CM, et al: Precise application of sentinel lymph node biopsy in patients with ductal carcinoma in situ: A systematic review and meta-analysis of real-world data. Surg Oncol 45:101880, 2022
27. Davey MG, O'Flaherty C, Cleere EF, et al: Sentinel lymph node biopsy in patients with ductal carcinoma in situ: Systematic review and meta-analysis. BJS Open 6, 2022
28. El Hage Chehade H, Headon H, Wazir U, et al: Is sentinel lymph node biopsy indicated in patients with a diagnosis of ductal carcinoma in situ? A systematic literature review and meta-analysis. Am J Surg 213:171-180, 2017
29. Bothou A, Margioula-Siarkou C, Petousis S, et al: Sentinel lymph node biopsy for breast cancer during pregnancy: A comprehensive update. Eur J Clin Invest 54:e14134, 2024
30. Reimer T, Stachs A, Veselinovic K, et al: Patient-reported outcomes for the Intergroup Sentinel Mamma study (INSEMA): A randomised trial with persistent impact of axillary surgery on arm and breast symptoms in patients with early breast cancer. EClinicalMedicine 55:101756, 2023
31. Metovic J, Bragoni A, Osella-Abate S, et al: Clinical relevance of tubular breast carcinoma: Large retrospective study and meta-analysis. Front Oncol 11:653388, 2021
32. Bevilacqua JL, Kattan MW, Fey JV, et al: Doctor, what are my chances of having a positive sentinel node? A validated nomogram for risk estimation. J Clin Oncol 25:3670-3679, 2007
33. Wong JS, O'Neill A, Recht A, et al: The relationship between lymphatic vessell invasion, tumor size, and pathologic nodal status: Can we predict who can avoid a third field in the absence of axillary dissection? Int J Radiat Oncol Biol Phys 48:133-137, 2000
34. Olivotto IA, Jackson JS, Mates D, et al: Prediction of axillary lymph node involvement of women with invasive breast carcinoma: A multivariate analysis. Cancer 83:948-955, 1998
35. MD Anderson Cancer Center: Breast Cancer Nomogram to Predict Positive Sentinel Lymph Nodes, Without Neoadjuvant Chemotherapy. 2024. https://www3.mdanderson.org/app/medcalc/bc_nomogram3/index.cfm?pagename=sln
36. Memorial Sloan Kettering Cancer Center: Breast Cancer Nomogram: Sentinel Lymph Node Metastasis, 2024. https://nomograms.mskcc.org/Breast/BreastSLNodeMetastasisPage.aspx
37. Gentilini O, Veronesi U: Abandoning sentinel lymph node biopsy in early breast cancer? A new trial in progress at the European Institute of Oncology of Milan (SOUND: Sentinel node vs Observation after axillary UltraSouND). Breast 21:678-681, 2012
38. Youn I, Choi S, Choi YJ, et al: Contrast enhanced digital mammography versus magnetic resonance imaging for accurate measurement of the size of breast cancer. Br J Radiol 92:20180929, 2019
39. Choi WJ, Cha JH, Kim HH, et al: The accuracy of breast MR imaging for measuring the size of a breast cancer: Analysis of the histopathologic factors. Clin Breast Cancer 16:e145-e152, 2016
40. Sanderink WBG, Caballo M, Strobbe LJA, et al: Reliability of MRI tumor size measurements for minimal invasive treatment selection in small breast cancers. Eur J Surg Oncol 46:1463-1470, 2020
41. Shin HC, Han W, Moon HG, et al: Limited value and utility of breast MRI in patients undergoing breast-conserving cancer surgery. Ann Surg Oncol 19:2572-2579, 2012

42. American College of Radiology: MRI Exam-Specific Parameters. Breast, 2024. https://accreditationsupport.acr.org/support/solutions/articles/11000114407-mri-exam-specific-parameters-breast-revised-5-2-2024
43. Valente SA, Levine GM, Silverstein MJ, et al: Accuracy of predicting axillary lymph node positivity by physical examination, mammography, ultrasonography, and magnetic resonance imaging. Ann Surg Oncol 19:1825-1830, 2012
44. Hughes KS, Schnaper LA, Bellon JR, et al: Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: Long-term follow-up of CALGB 9343. J Clin Oncol 31:2382-2387, 2013
45. Agresti R, Martelli G, Sandri M, et al: Axillary lymph node dissection versus no dissection in patients with T1N0 breast cancer: A randomized clinical trial (INT09/98). Cancer 120:885-893, 2014
46. Martelli G, Boracchi P, De Palo M, et al: A randomized trial comparing axillary dissection to no axillary dissection in older patients with T1N0 breast cancer: Results after 5 years of follow-up. Ann Surg 242:1-6, 2005; discussion 7-9
47. Martelli G, Boracchi P, Orenti A, et al: Axillary dissection versus no axillary dissection in older T1N0 breast cancer patients: 15-year results of trial and out-trial patients. Eur J Surg Oncol 40: 805-812, 2014
48. Society of Surgical Oncology: Choosing, Wisely: Five Things Physicians and Patients Should Question, 2020. https://www.surgonc.org/wp-content/uploads/2024/04/FINAL_Choosing_Wisely_5.30.23-SSO-5things-List_2021-Updates.pdf
49. Ganott MA, Zuley ML, Abrams GS, et al: Ultrasound guided core biopsy versus fine needle aspiration for evaluation of axillary lymphadenopathy in patients with breast cancer. ISRN Oncol 2014: 703160, 2014
50. Houssami N, Ciatto S, Turner RM, et al: Preoperative ultrasound-guided needle biopsy of axillary nodes in invasive breast cancer: meta-analysis of its accuracy and utility in staging the axilla. Ann Surg 254:243-251, 2011
51. Expert Panel on Breast Imaging; McDonald ES, Scheel JR, et al: ACR Appropriateness Criteria® imaging of invasive breast cancer. J Am Coll Radiol 21:S168-S202, 2024
52. Rao R, Lilley L, Andrews V, et al: Axillary staging by percutaneous biopsy: Sensitivity of fine-needle aspiration versus core needle biopsy. Ann Surg Oncol 16:1170-1175, 2009
53. Balasubramanian I, Fleming CA, Corrigan MA, et al: Meta-analysis of the diagnostic accuracy of ultrasound-guided fine-needle aspiration and core needle biopsy in diagnosing axillary lymph node metastasis. Br J Surg 105:1244-1253, 2018
54. Maxwell AJ, Bundred NJ, Harvey J, et al: A randomised pilot study comparing 13 G vacuum-assisted biopsy and conventional 14 G core needle biopsy of axillary lymph nodes in women with breast cancer. Clin Radiol 71:551-557, 2016
55. Shaitelman SF, Anderson BM, Arthur DW, et al: Partial breast irradiation for patients with early-stage invasive breast cancer or ductal carcinoma in situ: An ASTRO clinical practice guideline. Pract Radiat Oncol 14:112-132, 2024
56. Kunkler IH, Williams LJ, Jack WJL, et al: Breast-conserving surgery with or without irradiation in early breast cancer. N Engl J Med 388:585-594, 2023
57. Coles CE, Griffin CL, Kirby AM, et al: Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. Lancet 390:1048-1060, 2017
58. Bhattacharya IS, Haviland JS, Kirby AM, et al: Patient-reported outcomes over 5 years after whole- or partial-breast radiotherapy: Longitudinal analysis of the IMPORT LOW (CRUK/06/003) phase III randomized controlled trial. J Clin Oncol 37:305-317, 2019
59. Grendarova P, Roumeliotis M, Quirk S, et al: Accelerated partial breast irradiation using 5 daily fractions: A prospective, phase 2, multicenter trial of cosmetic outcomes and toxicity-ACCEL final results. Int J Radiat Oncol Biol Phys 118:1041-1048, 2024
60. Meattini I, Marrazzo L, Saieva C, et al: Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: Long-term results of the randomized phase III APBI-IMRT-florence trial. J Clin Oncol 38:4175-4183, 2020
61. Bucci LK, Brunelle CL, Bernstein MC, et al: Subclinical lymphedema after treatment for breast cancer: Risk of progression and considerations for early intervention. Ann Surg Oncol 28:8624-8633, 2021
62. Smith BD, Bellon JR, Blitzblau R, et al: Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Pract Radiat Oncol 8:145-152, 2018
63. Brunt AM, Haviland JS, Sydenham M, et al: Ten-year results of FAST: A randomized controlled trial of 5-fraction whole-breast radiotherapy for early breast cancer. J Clin Oncol 38: 3261-3272, 2020
64. Meattini I, De Santis MC, Visani L, et al: Single-modality endocrine therapy versus radiotherapy after breast-conserving surgery in women aged 70 years and older with luminal A-like early breast cancer (EUROPA): A preplanned interim analysis of a phase 3, non-inferiority, randomised trial. Lancet Oncol 26:37-50, 2025
65. Kalinsky K, Barlow WE, Gralow JR, et al: 21-gene assay to inform chemotherapy benefit in node-positive breast cancer. N Engl J Med 385:2336-2347, 2021
66. Sparano JA, Gray RJ, Makower DF, et al: Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. N Engl J Med 379:111-121, 2018
67. Sparano JA, Gray RJ, Ravdin PM, et al: Clinical and genomic risk to guide the use of adjuvant therapy for breast cancer. N Engl J Med 380:2395-2405, 2019
68. Andre F, Ismaila N, Allison KH, et al: Biomarkers for adjuvant endocrine and chemotherapy in early-stage breast cancer: ASCO guideline update. J Clin Oncol 40:1816-1837, 2022
69. Freedman RA, Caswell-Jin JL, Hassett M, et al: Optimal adjuvant chemotherapy and targeted therapy for early breast cancer-cyclin-dependent kinase 4 and 6 inhibitors: ASCO guideline rapid recommendation update. J Clin Oncol 42:2233-2235, 2024
70. Slamon D, Lipatov O, Nowecki Z, et al: Ribociclib plus endocrine therapy in early breast cancer. N Engl J Med 390:1080-1091, 2024
71. Giuliano AE, McCall L, Beitsch P, et al: Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: The American College of Surgeons Oncology Group Z0011 randomized trial. Ann Surg 252:426-432, 2010; discussion 432-433
72. Jagsi R, Chadha M, Moni J, et al: Radiation field design in the ACOSOG Z0011 (Alliance) trial. J Clin Oncol 32:3600-3606, 2014
73. Whelan TJ, Olivotto IA, Parulekar WR, et al: Regional nodal irradiation in early-stage breast cancer. N Engl J Med 373:307-316, 2015
74. Poortmans PM, Weltens C, Fortpied C, et al: Internal mammary and medial supraclavicular lymph node chain irradiation in stage I-III breast cancer (EORTC 22922/10925): 15-year results of a randomised, phase 3 trial. Lancet Oncol 21:1602-1610, 2020
75. Tinterri C, Canavese G, Gatzemeier W, et al: Sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer patients undergoing mastectomy with one to two metastatic sentinel lymph nodes: Sub-analysis of the SINODAR-ONE multicentre randomized clinical trial and reopening of enrolment. Br J Surg 110:1143-1152, 2023
76. Donker M, van Tienhoven G, Straver ME, et al: Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): A randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol 15:1303-1310, 2014
77. Morton DL, Wen DR, Wong JH, et al: Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 127:392-399, 1992
78. Krag D, Weaver D, Ashikaga T, et al: The sentinel node in breast cancer--a multicenter validation study. N Engl J Med 339:941-946, 1998
79. Giuliano AE, Kirgan DM, Guenther JM, et al: Lymphatic mapping and sentinel lymphadenectomy for breast cancer. Ann Surg 220:391-398, 1994; discussion 398-401
80. Veronesi U, Paganelli G, Viale G, et al: A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med 349:546-553, 2003
81. Krag DN, Anderson SJ, Julian TB, et al: Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: Overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol 11:927-933, 2010
82. Giuliano AE, Hawes D, Ballman KV, et al: Association of occult metastases in sentinel lymph nodes and bone marrow with survival among women with early-stage invasive breast cancer. JAMA 306:385-393, 2011
83. Weaver DL, Ashikaga T, Krag DN, et al: Effect of occult metastases on survival in node-negative breast cancer. N Engl J Med 364:412-421, 2011
84. Boughey JC, Rosenkranz KM, Ballman KV, et al: Local recurrence after breast-conserving therapy in patients with multiple ipsilateral breast cancer: Results from ACOSOG Z11102 (Alliance). J Clin Oncol 41:3184-3193, 2023
85. Piltin MA, Hoskin TL, Day CN, et al: Overuse of axillary surgery in patients with ductal carcinoma in situ: Opportunity for de-escalation. Ann Surg Oncol 29:7705-7712, 2022
86. Heymans C, van Bastelaar J, Visschers RGJ, et al: Sentinel node procedure obsolete in lumpectomy for ductal carcinoma in situ. Clin Breast Cancer 17:e87-e93, 2017
87. Cui RBJ, Hawes S, Azimi F, et al: Avoiding unnecessary sentinel lymph node biopsy with the use of superparamagnetic iron oxide mapping agents (Magtrace®) in breast surgery. ANZ J Surg 94: 1090-1095, 2024
88. Karakatsanis A, Eriksson S, Pistiolis L, et al: Delayed sentinel lymph node dissection in patients with a preoperative diagnosis of ductal cancer in situ by preoperative injection with superparamagnetic iron oxide (SPIO) nanoparticles: The SentiNot study. Ann Surg Oncol 30:4064-4072, 2023
89. Samaha M, Fellner A, Raque K, et al: Magnetic lymphatic tracing for omission of sentinel lymph node biopsies in mastectomy patients: A community cancer center experience. Breast Cancer Res Treat 10.1007/s10549-024-07482-9 [epub ahead of print on September 24, 2024]
90. Poodt IGM, Vugts G, Maaskant-Braat AJG, et al: Risk of regional recurrence after negative repeat sentinel lymph node biopsy in patients with ipsilateral breast tumor recurrence. Ann Surg Oncol 25:1312-1321, 2018

91. Poodt IGM, Vugts G, Schipper RJ, et al: Repeat sentinel lymph node biopsy for ipsilateral breast tumor recurrence: A systematic review of the results and impact on prognosis. Ann Surg Oncol 25: 1329-1339, 2018
92. Ge I, Erbes T, Juhasz-Boss I: Prognostic value and management of regional lymph nodes in locoregional breast cancer recurrence: A systematic review of the literature. Arch Gynecol Obstet 306: 943-957, 2022
93. Chen RC, Lin NU, Golshan M, et al: Internal mammary nodes in breast cancer: Diagnosis and implications for patient management—a systematic review. J Clin Oncol 26:4981-4989, 2008
94. Veronesi U, Marubini E, Mariani L, et al: The dissection of internal mammary nodes does not improve the survival of breast cancer patients. 30-year results of a randomised trial. Eur J Cancer 35: 1320-1325, 1999
95. Eckert KM, Boughey JC, Piltin MA: Internal mammary lymphadenopathy in breast cancer: A narrative review and update. Transl Breast Cancer Res 5:11, 2024
96. Piltin MA, Norwood P, Ladores V, et al: Internal mammary lymphadenopathy does not impact oncologic outcomes in patients treated with neoadjuvant chemotherapy: Results from the I-SPY2 Clinical Trial. Ann Surg Oncol 31:7420-7428, 2024
97. Wang T, Baskin AS, Dossett LA: Deimplementation of the choosing wisely recommendations for low-value breast cancer surgery: A systematic review. JAMA Surg 155:759-770, 2020
98. Chagpar AB, Horowitz N, Sanft T, et al: Does lymph node status influence adjuvant therapy decision-making in women 70 years of age or older with clinically node negative hormone receptor positive breast cancer? Am J Surg 214:1082-1088, 2017
99. Shumway DA, Griffith KA, Sabel MS, et al: Surgeon and radiation oncologist views on omission of adjuvant radiotherapy for older women with early-stage breast cancer. Ann Surg Oncol 24: 3518-3526, 2017
100. Taylor LJ, Steiman JS, Anderson B, et al: Does persistent use of radiation in women > 70 years of age with early-stage breast cancer reflect tailored patient-centered care? Breast Cancer Res Treat 180:801-807, 2020
101. Rhieu BH, Rajagopalan MS, Sukumvanich P, et al: Patterns of care for omission of radiation therapy for elderly women with early-stage breast cancer receiving hormonal therapy. Pract Radiat Oncol 5:e267-e273, 2015
102. Downs-Canner SM, Gaber CE, Louie RJ, et al: Nodal positivity decreases with age in women with early-stage, hormone receptor-positive breast cancer. Cancer 126:1193-1201, 2020
103. Wang T, Baskin A, Miller J, et al: Trends in breast cancer treatment de-implementation in older patients with hormone receptor-positive breast cancer: A mixed methods study. Ann Surg Oncol 28: 902-913, 2021
104. Minami CA, Bryan AF, Freedman RA, et al: Assessment of oncologists' perspectives on omission of sentinel lymph node biopsy in women 70 years and older with early-stage hormone receptor-positive breast cancer. JAMA Netw Open 5:e2228524, 2022
105. Wang T, Mott N, Miller J, et al: Patient perspectives on treatment options for older women with hormone receptor-positive breast cancer: A qualitative study. JAMA Netw Open 3:e2017129, 2020
106. Gilligan T, Coyle N, Frankel RM, et al: Patient-clinician communication: American Society of Clinical Oncology consensus guideline. J Clin Oncol 35:3618-3632, 2017
107. Tucker-Seeley R, Abu-Khalaf M, Bona K, et al: Social determinants of health and cancer care: An ASCO policy statement. JCO Oncol Pract 20:621-630, 2024
108. Carlos RC, Obeng-Gyasi S, Cole SW, et al: Linking structural racism and discrimination and breast cancer outcomes: A social genomics approach. J Clin Oncol 40:1407-1413, 2022
109. Black DM, Jiang J, Kuerer HM, et al: Racial disparities in adoption of axillary sentinel lymph node biopsy and lymphedema risk in women with breast cancer. JAMA Surg 149:788-796, 2014
110. Parekh A, Fu W, Hu C, et al: Impact of race, ethnicity, and socioeconomic factors on receipt of radiation after breast conservation surgery: Analysis of the national cancer database. Breast Cancer Res Treat 172:201-208, 2018
111. Yeboa DN, Xu X, Jones BA, et al: Trend in age and racial disparities in the receipt of postlumpectomy radiation therapy for stage I breast cancer: 2004-2009. Am J Clin Oncol 39:568-574, 2016
112. Mailhot VegaRB, Wang S, Brooks ED, et al: Evaluating regional nodal irradiation allocation and association with oncologic outcomes in NSABP B-18, B-27, B-40, and B-41. Int J Radiat Oncol Biol Phys 113:542-551, 2022
113. Fwelo P, Nwosu KOS, Adekunle TE, et al: Racial/ethnic and socioeconomic differences in breast cancer surgery performed and delayed treatment: Mediating impact on mortality. Breast Cancer Res Treat 199:511-531, 2023
114. Cheung MR: Assessing the impact of socio-economic variables on breast cancer treatment outcome disparity. Asian Pac J Cancer Prev 14:7133-7136, 2013
115. Roseland ME, Schwartz K, Ruterbusch JJ, et al: Influence of clinical, societal, and treatment variables on racial differences in ER-/PR- breast cancer survival. Breast Cancer Res Treat 165: 163-168, 2017
116. Benitez Fuentes JD, Morgan E, de Luna Aguilar A, et al: Global stage distribution of breast cancer at diagnosis: A systematic review and meta-analysis. JAMA Oncol 10:71-78, 2024
117. Anderson BO, Cazap E, El Saghir NS, et al: Optimisation of breast cancer management in low-resource and middle-resource countries: Executive summary of the Breast Health Global Initiative consensus, 2010. Lancet Oncol 12:387-398, 2011
118. Allemani C, Matsuda T, Di Carlo V, et al: Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): Analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 391:1023-1075, 2018
119. Freitas-Junior R, Rocha A, Couto HL, et al: COVID-19 and breast cancer diagnosis in Brazil: An analogy to the sinking of the titanic. JCO Glob Oncol 10.1200/GO.23.00108
120. Coles CE, Anderson BO, Cameron D, et al: The Lancet Breast Cancer Commission: Tackling a global health, gender, and equity challenge. Lancet 399:1101-1103, 2022
121. Coles CE, Earl H, Anderson BO, et al: The Lancet Breast Cancer Commission. Lancet 403:1895-1950, 2024
122. Flores-Balcazar CH, Flores-Luna L, Villarreal-Garza C, et al: Impact of delayed adjuvant radiotherapy in the survival of women with breast cancer. Cureus 10:e3071, 2018
123. Gupta S, King WD, Korzeniowski M, et al: The effect of waiting times for postoperative radiotherapy on outcomes for women receiving partial mastectomy for breast cancer: A systematic review and meta-analysis. Clin Oncol (R Coll Radiol) 28:739-749, 2016
124. Huang J, Barbera L, Brouwers M, et al: Does delay in starting treatment affect the outcomes of radiotherapy? A systematic review. J Clin Oncol 21:555-563, 2003
125. Hendren S, Chin N, Fisher S, et al: Patients' barriers to receipt of cancer care, and factors associated with needing more assistance from a patient navigator. J Natl Med Assoc 103:701-710, 2011
126. Alpert AB, Scout NFN, Schabath MB, et al: Gender- and sexual orientation- based inequities: Promoting inclusion, visibility, and data accuracy in oncology. Am Soc Clin Oncol Educ Book 42:1-17, 2022
127. Levit LA, Byatt L, Lyss AP, et al: Closing the rural cancer care gap: Three institutional approaches. JCO Oncol Pract 16:422-430, 2020
128. McEvoy AM, Poplack S, Nickel K, et al: Cost-effectiveness analyses demonstrate that observation is superior to sentinel lymph node biopsy for postmenopausal women with HR + breast cancer and negative axillary ultrasound. Breast Cancer Res Treat 183:251-262, 2020
129. Schnipper LE, Davidson NE, Wollins DS, et al: American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. J Clin Oncol 33: 2563-2577, 2015
130. Streeter SB, Schwartzberg L, Husain N, et al: Patient and plan characteristics affecting abandonment of oral oncolytic prescriptions. J Oncol Pract 7:46s-51s, 2011
131. Dusetzina SB, Winn AN, Abel GA, et al: Cost sharing and adherence to tyrosine kinase inhibitors for patients with chronic myeloid leukemia. J Clin Oncol 32:306-311, 2014
132. Meropol NJ, Schrag D, Smith TJ, et al: American Society of Clinical Oncology guidance statement: The cost of cancer care. J Clin Oncol 27:3868-3874, 2009
133. Hong YR, Salloum RG, Yadav S, et al: Patient-provider discussion about cancer treatment costs and out-of-pocket spending: Implications for shared decision making in cancer care. Value Health 23:1592-1598, 2020
134. McLaughlin SA, Wright MJ, Morris KT, et al: Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: Objective measurements. J Clin Oncol 26:5213-5219, 2008
135. DiSipio T, Rye S, Newman B, et al: Incidence of unilateral arm lymphoedema after breast cancer: A systematic review and meta-analysis. Lancet Oncol 14:500-515, 2013
136. Wang T, Dossett LA: Incorporating value-based decisions in breast cancer treatment algorithms. Surg Oncol Clin N Am 32:777-797, 2023
137. Darby SC, Ewertz M, McGale P, et al: Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 368:987-998, 2013
138. Jagsi R, Griffith KA, Vicini F, et al: Toward improving patients' experiences of acute toxicity from breast radiotherapy: Insights from the analysis of patient-reported outcomes in a large multicenter cohort. J Clin Oncol 38:4019-4029, 2020
139. Wang K, Tepper JE: Radiation therapy-associated toxicity: Etiology, management, and prevention. CA Cancer J Clin 71:437-454, 2021
140. Le Bras A, Belkacemi Y, Bourgier C, et al: Economic evaluation and budget-impact of accelerated partial breast irradiation (APBI) versus standard or hypofractionated whole breast irradiation (WBI) in postmenopausal women with early-stage breast cancer. Results from the French SHARE randomized trial. Radiother Oncol 187:109818, 2023
141. Shah C, Ward MC, Tendulkar RD, et al: Cost and cost-effectiveness of image guided partial breast irradiation in comparison to hypofractionated whole breast irradiation. Int J Radiat Oncol Biol Phys 103:397-402, 2019
142. Shah C, Lanni TB, Saini H, et al: Cost-efficacy of acceleration partial-breast irradiation compared with whole-breast irradiation. Breast Cancer Res Treat 138:127-135, 2013
143. Sher DJ, Wittenberg E, Suh WW, et al: Partial-breast irradiation versus whole-breast irradiation for early-stage breast cancer: A cost-effectiveness analysis. Int J Radiat Oncol Biol Phys 74:440-446, 2009
144. Griggs J, Maingi S, Blinder V, et al: American Society of Clinical Oncology position statement: Strategies for reducing cancer health disparities among sexual and gender minority populations. J Clin Oncol 35:2203-2208, 2017

145. Alpert AB, Gampa V, Lytle MC, et al: I'm not putting on that floral gown: Enforcement and resistance of gender expectations for transgender people with cancer. Patient Educ Couns 104: 2552-2558, 2021
146. Schunemann HJ, Wiercioch W, Etxeandia I, et al: Guidelines 2.0: Systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ 186: E123-E142, 2014

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer: ASCO Guideline Update

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Ko Un Park
Consulting or Advisory Role: Bayer

Alison K. Conlin
Consulting or Advisory Role: Seattle Genetics/Astellas, AstraZeneca, Gilead Sciences
Travel, Accommodations, Expenses: Seattle Genetics/Astellas

Henrique Lima Couto
Honoraria: BD Bard, Siemens Healthineers, Roche, AstraZeneca/Daiichi Sankyo
Consulting or Advisory Role: AstraZeneca/Daiichi Sankyo
Research Funding: Guerbet, Siemens Healthineers, BD Bard

Andrea Eisen
Other Relationship: Cancer Care Ontario

Jeffrey Hawley
Research Funding: Leica Biosystems (Inst)

Samantha Shams
Honoraria: Mirati Therapeutics, Daiichi Sankyo/UCB Japan

Alastair M. Thompson
This author is a Consulting Editor for *Journal of Clinical Oncology*. Journal policy recused the author from having any role in the peer review of this manuscript.
Employment: Lilly
Stock and Other Ownership Interests: Lilly

Mylin A. Torres
Employment: Emory Healthcare
Stock and Other Ownership Interests: Oncology Analytics
Honoraria: MJH Life Sciences, MJH Life Sciences, Varian Medical Systems, OncLive/MJH Life Sciences, Varian Medical Systems, EncoreMed Education, Denali Onclogy Group, Atrium Health, Levine Cancer Institute
Consulting or Advisory Role: Oncology Analytics, Oncohealth, University of Texas Healthcenter, ASTRO's Breast Expert Panel for the VA Measures Project
Research Funding: Pfizer, Pfizer, Genentech, Pfizer/NCCN (Inst)
Travel, Accommodations, Expenses: BioAscent, BioAscent, BioAscent, University of Texas Healthcenter, Denali Oncology, Atium Health

No other potential conflicts of interest were reported.

APPENDIX 1. GUIDELINE DISCLAIMER

The Clinical Practice Guidelines and other guidance published herein are provided by ASCO, Inc to assist clinicians in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating clinician, as the information does not account for individual variation among patients. Recommendations specify the level of confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. Use of the information is voluntary. ASCO does not endorse third party drugs, devices, services, or therapies used to diagnose, treat, monitor, manage, or alleviate health conditions. Any use of a brand or trade name is for identification purposes only. ASCO provides this information on an "as is" basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

APPENDIX 2. GUIDELINE AND CONFLICTS OF INTEREST

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/guideline-methodology). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

TABLE A1. Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer Update Expert Panel Membership

Name	Affiliation	Role or Area of Expertise
Ko Un Park, MD, Co-Chair	Brigham and Women's Hospital, Dana-Farber Cancer Institute, Boston, MA	Surgical oncology
Mylin A. Torres, MD, Co-Chair	Glenn Family Breast Center at Winship Cancer Institute, Atlanta, GA	Radiation oncology
Nirupama Anne, MD	Penn State Health Milton S. Hershey Medical Center, Hershey, PA	Surgical oncology (volunteer corp representative)
Muriel Brackstone, MD, PhD	Department of Surgery, University of Western Ontario, London, ON, Canada	Surgical oncology
Alison K. Conlin, MD	Providence Cancer Institute, Portland, OR	Medical oncology
Henrique Lima Couto, MD, PhD	Brazilian Society of Mastology, Belo Horizonte, Brazil	Mastology
Lynn T. Dengel, MD, MSc	Emily Couric Clinical Cancer Center, Charlottesville, VA	Surgical oncology
Andrea Eisen, MD	Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada	Medical oncology
Jeffrey Hawley, MD	Stephanie Spielman Comprehensive Breast Center, The Ohio State University Medical Center, Columbus, OH	Radiology
Janice N. Kim, MD, MS	University of Washington School of Medicine, Seattle, WA	Radiation oncology
Nwamaka Lasebikan, MBBS	University of Nigeria Teaching Hospital, Enugu, Nigeria	Radiation medicine
Elizabeth S. McDonald, MD, PhD	University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA	Radiology
Deepti Pradhan, PhD	Yale University, New Haven, CT	Patient advocacy
Samantha Shams, MD	Piedmont Cancer Institute, Atlanta, GA	Medical oncology
Raymond Mailhot Vega, MD, MPH	University of Florida, Jacksonville, FL	Radiation oncology
Alastair M. Thompson, MD, MBChB	Dan L. Duncan Comprehensive Cancer Center, Houston, TX	Surgical oncology
Brittany E. Harvey, BS	American Society of Clinical Oncology (ASCO), Alexandria, VA	ASCO practice guideline staff (health research methods)
Mark R. Somerfield, PhD	American Society of Clinical Oncology (ASCO), Alexandria, VA	ASCO practice guideline staff (health research methods)

TABLE A2. Recommendation Rating Definitions

Term	Definition
Quality of evidence	
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Strength of recommendation	
Strong	In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects All or almost all informed people would make the recommended choice for or against an intervention
Conditional/weak	In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists Most informed people would choose the recommended course of action, but a substantial number would not

NOTE. GRADE Handbook[146]