National
Comprehensive
Cancer
Network®

NCCN

Breast Cancer, Version 4.2017

Clinical Practice Guidelines in Oncology

William J. Gradishar, MD; Benjamin O. Anderson, MD;
Ron Balassanian, MD; Sarah L. Blair, MD;
Harold J. Burstein, MD, PhD; Amy Cyr, MD;
Anthony D. Elias, MD; William B. Farrar, MD;
Andres Forero, MD; Sharon H. Giordano, MD, MPH;
Matthew P. Goetz, MD; Lori J. Goldstein, MD;
Steven J. Isakoff, MD, PhD; Janice Lyons, MD;
P. Kelly Marcom, MD; Ingrid A. Mayer, MD;
Beryl McCormick, MD; Meena S. Moran, MD;
Ruth M. O'Regan, MD; Sameer A. Patel, MD;

Lori J. Pierce, MD; Elizabeth C. Reed, MD;
Kilian E. Salerno, MD; Lee S. Schwartzberg, MD;
Amy Sitapati, MD; Karen Lisa Smith, MD, MPH;
Mary Lou Smith, JD, MBA; Hatem Soliman, MD;
George Somlo, MD; Melinda L. Telli, MD; John H. Ward, MD;
Rashmi Kumar, PhD; and Dorothy A. Shead, MS

Introduction

The American Cancer Society estimates that >60,000 cases of carcinoma in situ of the breast will be diagnosed in the United States in 2018. Carcinoma in situ of the breast represents a heterogenous group of noninvasive lesions confined to the breast ducts (ductal carcinoma in situ [DCIS]) or breast lobules (lobular carcinoma in situ).

Abstract

Ductal carcinoma in situ (DCIS) of the breast represents a heterogeneous group of neoplastic lesions in the breast ducts. The goal for management of DCIS is to prevent the development of invasive breast cancer. This manuscript focuses on the NCCN Guidelines Panel recommendations for the workup, primary treatment, risk reduction strategies, and surveillance specific to DCIS.

NCCN Categories of Evidence and Consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Please Note

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network® (NCCN®) makes no representation or warranties of any kind regarding their content, use, or application and disclaims any responsibility for their applications or use in any way. **The full NCCN Guidelines for Breast Cancer are not printed in this issue of JNCCN but can be accessed online at NCCN.org.**

Disclosures for the NCCN Breast Cancer Panel

At the beginning of each NCCN Guidelines panel meeting, panel members review all potential conflicts of interest. NCCN, in keeping with its commitment to public transparency, publishes these disclosures for panel members, staff, and NCCN itself.

Individual disclosures for the NCCN Breast Cancer Panel members can be found on page 320. (The most recent version of these guidelines and accompanying disclosures are available on the NCCN Web site at NCCN.org.)

These guidelines are also available on the Internet. For the latest update, visit NCCN.org.

Journal of the National Comprehensive Cancer Network

The management of patients with noninvasive or invasive breast cancer is complex and varied. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer include up-to-date recommendations for the clinical management of patients with carcinoma in situ, invasive breast cancer, Paget disease, phyllodes tumor, inflammatory breast cancer, and breast cancer during pregnancy. These guidelines are developed by a multidisciplinary panel of representatives from NCCN Member Institutions with breast cancer–focused expertise in the fields of medical, surgical, and radiation oncology and pathology, reconstructive surgery, and patient advocacy.

This manuscript discusses the workup, primary treatment, risk reduction strategies, and surveillance for DCIS.

Workup

The recommended workup and staging of DCIS includes a history and physical examination; bilateral diagnostic mammography, pathology review, determination of tumor estrogen receptor (ER) status, and MRI as indicated. For pathology reporting, the NCCN panel endorses the College of American Pathologists' protocol for both invasive and noninvasive carcinomas of the breast.[1]

The NCCN Guidelines Panel recommends testing for ER status to determine the benefit of adjuvant endocrine therapy or risk reduction. Although the tumor HER2 status is of prognostic significance in invasive cancer, its importance in DCIS has not been elucidated. To date, studies have either found unclear or weak evidence

NCCN Breast Cancer Panel Members

*William J. Gradishar, MD/Chair‡†
    Robert H. Lurie Comprehensive Cancer Center of
    Northwestern University
*Benjamin O. Anderson, MD/Vice-Chair¶
    Fred Hutchinson Cancer Research Center/
    Seattle Cancer Care Alliance
Ron Balassanian, MD≠
    UCSF Helen Diller Family Comprehensive Cancer Center
Sarah L. Blair, MD¶
    UC San Diego Moores Cancer Center
Harold J. Burstein, MD, PhD†
    Dana-Farber/Brigham and Women's Cancer Center
Amy Cyr, MD¶
    Siteman Cancer Center at Barnes-Jewish Hospital and
    Washington University School of Medicine
Anthony D. Elias, MD†
    University of Colorado Cancer Center
William B. Farrar, MD¶
    The Ohio State University Comprehensive Cancer Center –
    James Cancer Hospital and Solove Research Institute
Andres Forero, MDÞ‡†
    University of Alabama at Birmingham
    Comprehensive Cancer Center
Sharon H. Giordano, MD, MPH†
    The University of Texas MD Anderson Cancer Center
Matthew P. Goetz, MD‡†
    Mayo Clinic Cancer Center
Lori J. Goldstein, MD†
    Fox Chase Cancer Center
Steven J. Isakoff, MD, PhD†
    Massachusetts General Hospital Cancer Center
Janice Lyons, MD§
    Case Comprehensive Cancer Center/
    University Hospitals Seidman Cancer Center
    and Cleveland Clinic Taussig Cancer Institute
P. Kelly Marcom, MD†
    Duke Cancer Institute
Ingrid A. Mayer, MD†
    Vanderbilt-Ingram Cancer Center

Beryl McCormick, MD§
    Memorial Sloan Kettering Cancer Center
Meena S. Moran, MD§
    Yale Cancer Center/Smilow Cancer Hospital
Ruth M. O'Regan, MD†
    University of Wisconsin Carbone Cancer Center
Sameer A. Patel, MDŸ
    Fox Chase Cancer Center
Lori J. Pierce, MD§
    University of Michigan Comprehensive Cancer Center
Elizabeth C. Reed, MD†ξ
    Fred & Pamela Buffett Cancer Center
Kilian E. Salerno, MD§
    Roswell Park Comprehensive Cancer Center
Lee S. Schwartzberg, MD‡†
    St. Jude Children's Research Hospital/
    The University of Tennessee Health Science Center
Amy Sitapati, MDÞ
    UC San Diego Moores Cancer Center
Karen Lisa Smith, MD, MPH†
    The Sidney Kimmel Comprehensive Cancer Center
    at Johns Hopkins
Mary Lou Smith, JD, MBA¥
    Research Advocacy Network
Hatem Soliman, MD†
    Moffitt Cancer Center
George Somlo, MD‡ξ†
    City of Hope Comprehensive Cancer Center
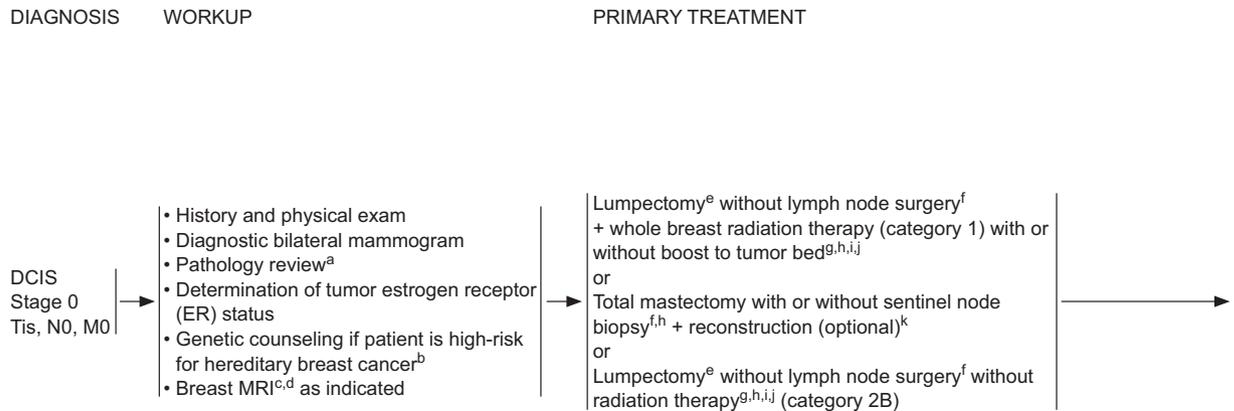Melinda L. Telli, MD†
    Stanford Cancer Institute
John H. Ward, MD‡†
    Huntsman Cancer Institute at the University of Utah

NCCN Staff: Rashmi Kumar, PhD, and Dorothy A. Shead, MS

KEY:
*Discussion Section Writing Committee
†Medical oncology; ‡Hematology/Oncology; ÞInternal Medicine;
¶Surgical Oncology; ≠Pathology; ŸReconstructive Surgery;
§Radiation Oncology; ξBone Marrow Transplantation; ¥Patient
Advocacy

312

National
Comprehensive
Cancer
Network®

DUCTAL CARCINOMA IN SITU

Breast Cancer, Version 4.2017

DIAGNOSIS   WORKUP   PRIMARY TREATMENT

**DCIS
Stage 0
Tis, N0, M0**

• History and physical exam
• Diagnostic bilateral mammogram
• Pathology review[a]
• Determination of tumor estrogen receptor (ER) status
• Genetic counseling if patient is high-risk for hereditary breast cancer[b]
• Breast MRI[c,d] as indicated

Lumpectomy[e] without lymph node surgery[f] + whole breast radiation therapy (category 1) with or without boost to tumor bed[g,h,i,j]
or
Total mastectomy with or without sentinel node biopsy[f,h] + reconstruction (optional)[k]
or
Lumpectomy[e] without lymph node surgery[f] without radiation therapy[g,h,i,j] (category 2B)

*Available online, in these guidelines, at NCCN.org.

[a]The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and noninvasive carcinomas of the breast. http://www.cap.org.

[b]See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian at NCCN.org.

[c]See Principles of Dedicated Breast MRI Testing (BINV-B)*.

[d]The use of MRI has not been shown to increase likelihood of negative margins or decrease conversion to mastectomy. Data to support improved long-term outcomes are lacking.

[e]Re-resection(s) may be performed in an effort to obtain negative margins in patients desiring breast-conserving therapy. Patients in whom adequate surgical margins cannot be achieved with lumpectomy should undergo a total mastectomy. For definition of adequate surgical margins, see Margin Status Recommendations for DCIS and Invasive Breast Cancer (BINV-F)*.

[f]Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven axillary metastatic disease in women with apparent pure DCIS. However, a small proportion of patients with apparent pure DCIS will be found to have invasive cancer at the time of their definitive surgical procedure. Therefore, the

performance of a sentinel lymph node procedure should be strongly considered if the patient with apparent pure DCIS is to be treated with mastectomy or with excision in an anatomic location compromising the performance of a future sentinel lymph node procedure.

[g]See Principles of Radiation Therapy (BINV-I)*.

[h]Patients found to have invasive disease at total mastectomy or re-excision should be managed as having stage I or stage II disease, including lymph node staging.

[i]See Special Considerations to Breast-Conserving Therapy Requiring Radiation Therapy (BINV-G)*.

[j]Whole-breast radiation therapy following lumpectomy reduces recurrence rates in DCIS by about 50%. Approximately half of the recurrences are invasive and half are DCIS. A number of factors determine local recurrence risk: palpable mass, larger size, higher grade, close or involved margins, and age <50 years. If the patient and physician view the individual risk as "low," some patients may be treated by excision alone. Data evaluating the three local treatments show no differences in patient survival.

[k]See Principles of Breast Reconstruction Following Surgery (BINV-H)*.

DCIS-1

Clinical trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

© JNCCN—Journal of the National Comprehensive Cancer Network | Volume 16 Number 3 | March 2018

DCIS POSTSURGICAL TREATMENT

SURVEILLANCE/FOLLOW-UP

Risk reduction therapy for ipsilateral breast following breast-conserving surgery:
- Consider endocrine therapy for 5 years for:
  ‣ Patients treated with breast-conserving therapy (lumpectomy) and radiation therapy[m] (category 1), especially for those with ER-positive DCIS.
  ‣ The benefit of endocrine therapy for ER-negative DCIS is uncertain
  ‣ Patients treated with excision alone[l]
- Endocrine therapy:
  ‣ Tamoxifen[m] for premenopausal patients
  ‣ Tamoxifen[m] or aromatase inhibitor for postmenopausal patients with some advantage for aromatase inhibitor therapy in patients <60 years old or with concerns for thromboembolism

Risk reduction therapy for contralateral breast:
- Counseling regarding risk reduction
  See NCCN Guidelines for Breast Cancer Risk Reduction at NCCN.org

→

- Interval history and physical exam every 6–12 mo for 5 y, then annually
- Mammogram every 12 mo (first mammogram 6–12 mo, after breast conservation therapy, category 2B)
- If treated with endocrine therapy, monitor per NCCN Guidelines for Breast Cancer Risk Reduction at NCCN.org

[l]Available data suggest endocrine therapy provides risk reduction in the ipsilateral breast treated with breast conservation and in the contralateral breast in patients with mastectomy or breast conservation with ER-positive primary tumors. Since a survival advantage has not been demonstrated, individual consideration of risks and benefits is important (See also NCCN Guidelines for Breast Cancer Risk Reduction at NCCN.org).
[m]CYP2D6 genotype testing is not recommended in women who are considering tamoxifen.

DCIS-2

Breast Cancer, Version 4.2017

of HER2 status as a prognostic indicator in DCIS.[2–5] The panel has concluded that knowing the HER2 status in DCIS does not alter the management strategy and is not required.

Genetic counseling is recommended if the patient is considered to be at high risk for hereditary breast cancer as defined by the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian (available at NCCN.org).

The role of MRI in DCIS management remains unclear. MRI has been prospectively shown to have a sensitivity of up to 98% for high-grade DCIS.[6] In a prospective observational study of 193 women with pure DCIS who underwent both mammography and MRI imaging preoperatively, 93 (56%) were diagnosed by mammography and 153 (92%) by MRI (P<.0001). Of the 89 women with high-grade DCIS, 43 (48%) were missed by mammography but diagnosed by MRI alone.[6] However, other studies suggest that MRI can overestimate the extent of disease.[7] Therefore, surgical decisions should not be solely based on MRI results, especially when mastectomy is being contemplated. If MRI findings suggest more extensive disease than seen on mammography, such that a markedly larger resection is required for complete excision, findings should be histologically verified through MRI-guided biopsy of the more extensive enhancement.

Studies have also been performed to determine whether the use of MRI reduces re-excision rates and decreases local recurrence in DCIS. No reduction in re-excision rates was seen in women undergoing lumpectomy following MRI compared with those who did not undergo preoperative MRI.[8,9]

The panel recommends only performing breast MRI for DCIS in select circumstances in which additional information is warranted during the initial workup, noting that the use of MRI has not been shown to increase the likelihood of negative margins or decrease conversion to mastectomy for DCIS.

Primary Treatment

The goal of primary therapy for DCIS is to prevent progression to invasive breast carcinoma. Management strategies for DCIS treatment include surgery (mastectomy or lumpectomy), radiation therapy (RT), and adjuvant endocrine therapy to reduce risk of recurrence.

Surgery

Excision of DCIS using a breast-conserving approach (lumpectomy) with or without whole-breast RT (WBRT) or alternatively, mastectomy, are the primary treatment options for individuals with DCIS.

The choice of local treatment does not impact overall disease-related survival; therefore, the individual patient's acceptance of the potential for an increased risk of local recurrence must be considered. Postexcision mammography is valuable in confirming that an adequate excision of DCIS has been performed, particularly for patients with DCIS who initially present with microcalcifications.[10]

Mastectomy

Patients with DCIS and evidence of widespread disease (ie, disease involving 2 or more quadrants) on diagnostic mammography or other imaging, physical examination, or biopsy may require mastectomy.

Mastectomy permanently alters the lymphatic drainage pattern to the axilla, so that future performance of a sentinel lymph node biopsy (SLNB) is not technically feasible.[11,12] Therefore, for patients with DCIS who intend treatment with mastectomy, or alternatively, for local excision in an anatomic location that could compromise the lymphatic drainage pattern to the axilla (eg, tail of the breast), a SLNB procedure should *strongly* be considered at the time of definitive surgery to avoid necessitating a full axillary lymph node dissection for evaluation of the axilla.[11–14]

Complete axillary lymph node dissection (ALND) is *not* recommended unless there is pathologically documented invasive cancer or axillary lymph node metastatic disease in patients (by either biopsy or SNLB). However, a small proportion of women (about 25%) with seemingly pure DCIS on initial biopsy will have invasive breast cancer at the time of the definitive surgical procedure[15] and thus will ultimately require ALND staging.

Lumpectomy Plus WBRT

Breast-conserving therapy (BCT) includes lumpectomy to remove the tumor with negative surgical margins followed by WBRT to eradicate any residual microscopic disease.

Several prospective randomized trials of pure DCIS have shown that the addition of WBRT after lumpectomy decreases the rate of in-breast disease

Breast Cancer, Version 4.2017

recurrence,[16–23] or distant metastasis-free survival.[24] In the long-term follow-up of the RTOG 9804 trial, at 7 years, the local recurrence rate was 0.9% (95% CI, 0.0%–2.2%) in the RT arm versus 6.7% (95% CI, 3.2%–9.6%) in the observation arm (hazard ratio [HR], 0.11; 95% CI, 0.03–0.47; P<.001). In the subset of patients with good-risk disease features, the local recurrence rate was low with observation but was decreased significantly with the addition of RT.[23] A meta-analysis of 4 large multicenter randomized trials confirms the results of the individual trials, demonstrating that the addition of WBRT after lumpectomy for DCIS provides a statistically and clinically significant reduction in ipsilateral breast events (HR, 0.49; 95% CI; 0.41–0.58, P<.00001).[25] However, these trials did not show that the addition of RT has an overall survival benefit. The long-term follow-up of the NSABP B-17 showed that at 15 years, RT resulted in a 52% reduction of ipsilateral invasive recurrence compared with excision alone (HR, 0.48; 95% CI, 0.33–0.69, P<.001).[22] However, overall survival (OS) and cumulative all-cause mortality rates through 15 years were similar between the 2 groups (HR for death, 1.08; 95% CI, 0.79–1.48).[22] Similar findings were reported by a large observational study of the SEER database that included 108,196 patients with DCIS.[26] In a subgroup analysis at 10 years, of 60,000 women treated with BCT with or without RT, RT was associated with a 50% reduction in the risk of ipsilateral recurrence (adjusted HR, 0.47; 95% CI, 0.42–0.53; P<.001), however, breast cancer–specific mortality was found to be similar (HR, 0.86; 95% CI, 0.67–1.10; P=.22).[26]

More recently, in a population-based study, the use of WBRT in patients with higher-risk DCIS (eg, higher nuclear grade, younger age, and larger tumor size) was demonstrated to be associated with a modest, but statistically significant improvement in survival.[27]

RT Boost
The use of RT boost has been demonstrated to provide a small but statistically significant reduction in ipsilateral breast tumor recurrence (IBTR) risk (4% at 20 years) in all age groups for invasive breast cancers.[28–31]

Recently, a pooled analysis of patient-level data from 10 academic institutions evaluated outcomes of pure DCIS patients, all treated with lumpectomy and WBRT (n=4,131) who either received RT boost with a median dose of 14 Gy (n=2,661) or received no boost (n=1,470). The median follow-up of patients was 9 years. A decrease in IBTR was seen in patients who received boost compared with those who did not at 5 years (97.1% vs 96.3%), 10 years (94.1% vs 92.5%), and 15 years (91.6% vs 88.0%) (P=.0389 for all). The use of RT boost was associated with significantly decreased IBTR across the entire cohort of patients (HR, 0.73; 95% CI, 0.57–0.94; P=.01).[32] In a multivariate analysis that took into account factors associated with lower IBTR, including grade, ER-positive status, use of adjuvant tamoxifen, margin status, and age, the benefit of RT boost still remained statistically significant (HR, 0.69; 95% CI, 0.53–0.91;P<.010).[32] Even in patients considered very low risk based on negative margins status (defined as ink on tumor as per National Surgical Adjuvant Breast and Bowel Project definition, or margins <2 mm as per SSO/ASTRO/ASCO definition), the RT boost remained statistically significant for decreasing the rate of local relapse. Similar to with invasive cancers, although RT boost was beneficial in all age groups studied, the magnitude of the absolute benefit of the boost was greatest in younger patients. Two ongoing randomized, phase 3 trials are studying whether an RT boost reduces recurrence in patients with DCIS (ClinicalTrials.gov Identifiers: NCT00470236 and NCT00907868).

While considering RT boost for DCIS, the NCCN Panel recommends an individualized approach based on patient preference and other factors such as longevity.

Lumpectomy Alone Without WBRT
Several trials have examined omission of RT after lumpectomy in carefully selected, low-risk patients. There are retrospective series suggesting that selected patients have a low risk of in-breast recurrence when treated with excision alone (without WBRT).[33–36] For example, in one retrospective review, 10-year disease-free survival (DFS) rates of 186 patients with DCIS treated with lumpectomy alone was 94% for patients with low-risk DCIS and 83% for patients with both intermediate- and high-risk DCIS.[33]

In another retrospective study of 215 patients with DCIS treated with lumpectomy without RT, endocrine therapy, or chemotherapy, the recurrence rate over 8 years was 0%, 21.5%, and 32.1% in pa-

tients with low-, intermediate- or high-risk DCIS, respectively.[34]

A multi-institutional, nonrandomized, prospective study of selected patients with low-risk DCIS treated without radiation has also provided some support for the use of excision without radiation in the treatment of DCIS.[37] Patients were enrolled onto 1 of 2 low-risk cohorts: a) low- or intermediate-grade DCIS, tumor size 2.5 cm or smaller (n=561); or b) high-grade DCIS, tumor size 1 cm or smaller (n=104). Protocol specifications included excision of the DCIS tumor with a minimum negative margin width of at least 3 mm. Only 30% of the patients received tamoxifen. Of note, margins were substantially wider than the 3 mm protocol requirement in many patients (ie, the low/intermediate-risk patient group margins were ≥ 5 mm in 62% of patients and >10 mm or no tumor on re-excision in 48% of patients).[37] Although the rate of IBTR was acceptably low for the low-/intermediate grade group at 5 years, at a median follow-up time of 12.3 years, the rates of developing an IBTR were 14.4% for low/intermediate-grade and 24.6% for high-grade DCIS (P=.003). This suggests that IBTR events may be delayed but not prevented in the seemingly low-risk population.

Therefore, the NCCN Panel concluded that for patients with DCIS treated with lumpectomy alone (without radiation), irrespective of margin width, the risk of IBTR is substantially higher than with treatment with excision followed by WBRT (even for predefined low-risk subsets of patients with DCIS).

Margin Status After BCT
Prospective randomized trials have not been performed to analyze whether wider margins can replace the need for RT for DCIS. Results from a retrospective study of 445 patients with pure DCIS treated by excision alone indicated that margin width was the most important independent predictor of local recurrence, although the trend for decreasing local recurrence risk with increasing margin width was most apparent with margins less than 1 mm and greater than or equal to 10 mm.[38] In a meta-analysis of 4,660 patients with DCIS treated with breast-conserving surgery and radiation, a surgical margin of less than 2 mm was associated with increased rates of IBTR compared with margins of 2 mm, although no significant differences were observed when margins of greater than 2 mm to 5 mm or greater than 5 mm were compared with 2-mm margins.[39]

A fairly recent study retrospectively reviewed a database of 2,996 patients with DCIS who underwent breast-conserving surgery to investigate the association between margin width and recurrence, controlling all other characteristics.[40] Wider margins were significantly associated with a lower rate of recurrence only in women who did not receive RT (P<.0001), but not in those treated with radiation (P=.95).[40]

According to the 2016 guidelines by SSO/ASTRO/ASCO, the use of at least 2-mm margins in DCIS treated with WBRT is associated with low rates of IBTR.[41] Additional factors to consider in assessing adequacy of excision for DCIS include presence of residual calcifications, which margin is close (anterior against skin or posterior against muscle versus medial, superior, inferior, or lateral), and life expectancy of the patient. Notably, in situations where DCIS is admixed with invasive carcinoma, SSO/ASTRO/ASCO guidelines support "no tumor on ink" as an adequate margin applying to both the invasive and noninvasive components in this mixed tumor scenario.

NCCN Recommendations for Primary Treatment of DCIS
Trials are ongoing to determine if there might be a selected favorable biology DCIS subgroup where surgical excision is not required. Until such time that definitive evidence regarding the safety of this non-surgical approach is demonstrated, the NCCN Panel continues to recommend surgical excision for DCIS. According to the panel, primary treatment options for women with DCIS, along with their respective categories of consensus, are lumpectomy plus WBRT with or without boost (category 1); total mastectomy, with or without SLNB with optional reconstruction (category 2A); or lumpectomy alone (category 2B). The option of lumpectomy alone should be considered only in cases in which the patient and the physician view the individual as having a low risk of disease recurrence.

Contraindications to BCT with RT are listed in the algorithm (see "Special Considerations to Breast-Conserving Therapy Requiring Radiation Therapy" in the NCCN Guidelines for Breast Cancer, available at NCCN.org). Women treated with

Breast Cancer, Version 4.2017

mastectomy are appropriate candidates for breast reconstruction (see "Principles of Breast Reconstruction Following Surgery" in the NCCN Guidelines for Breast Cancer).

According to the panel, complete resection should be documented by analysis of margins and specimen radiography. Postexcision mammography should also be performed whenever uncertainty about adequacy of excision remains. Clips are used to demarcate the biopsy area because DCIS may be clinically occult and further surgery may be required pending the margin status review by pathology.

The NCCN Panel accepts the definitions of negative margins after BCS from the 2016 SSO/ASTRO/ASCO Guidelines for DCIS.[41] For pure DCIS treated by BCS and WBRT, margins of at least 2 mm are associated with a reduced risk of IBTR relative to narrower negative margin widths in patients receiving WBRT. The routine practice of obtaining negative margin widths wider than 2 mm is not supported by the evidence. An analysis of specimen margins and specimen radiographs should be performed to ensure that all mammographically detectable DCIS has been excised. In addition, a postexcision mammogram should be considered where appropriate (eg, the mass and/or microcalcifications are not clearly within the specimen).

Management of DCIS After Primary Treatment

DCIS falls between atypical ductal hyperplasia and invasive ductal carcinoma within the spectrum of breast proliferative abnormalities. The Breast Cancer Prevention Trial performed by the National Surgical Adjuvant Breast and Bowel Project (NSABP) showed a 75% reduction in the occurrence of invasive breast cancer in patients with atypical ductal hyperplasia treated with tamoxifen.[42,43] These data also showed that tamoxifen led to a substantial reduction in the risk of developing benign breast disease.[44] The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) overview analysis showed that, with 5 years of tamoxifen therapy, women with ER-positive or receptor-unknown invasive tumors had a 39% reduction in the annual odds of recurrence of invasive breast cancer.[45]

Similarly, the NSABP B-24 trial found a benefit from tamoxifen for women with DCIS after treatment with breast conservation surgery and RT. In that study, women with DCIS who were treated with BCT were randomized to receive placebo or tamoxifen. At a median follow-up of 13.6 years, patients who received tamoxifen had a 3.4% absolute reduction in ipsilateral in-breast tumor recurrence risk (HR, 0.30; 95% CI, 0.21–0.42; P<.001) and a 3.2% absolute reduction in contralateral breast cancers (HR, 0.68; 95% CI, 0.48–0.95; P=.023).[22] The women receiving tamoxifen had a 10-year cumulative rate of 4.6% for invasive and 5.6% for noninvasive breast cancers in the ipsilateral breast compared with 7.3% for invasive and 7.2% for noninvasive breast cancers in placebo-treated women. The cumulative 10-year frequency of invasive and noninvasive breast cancer in the contralateral breast was 6.9% and 4.7% in the placebo and tamoxifen groups, respectively. No differences in OS were noted. A retrospective analysis of ER expression in NSABP B-24 suggests that increased levels of ER expression predict for tamoxifen benefit in terms of risk reduction for ipsilateral and contralateral breast cancer development following BCT.[46]

A phase III trial for women with excised DCIS randomized subjects in a 2 X 2 fashion to tamoxifen or not and WBRT or not.[21] With 12.7 years of median follow-up, the use of tamoxifen decreased all new breast events (HR, 0.71; 95% CI, 0.58–0.88; P=.002). The use of tamoxifen decreased ipsilateral and contralateral breast events in the subjects not given WBRT (ipsilateral HR, 0.77; 95% CI, 0.59–0.98; contralateral HR, 0.27; 95% CI, 0.12–0.59), but not in those receiving WBRT (ipsilateral HR, 0.93; 95% CI, 0.50–1.75; P=.80; contralateral HR, 0.99; 95% CI, 0.39–2.49; P=1.0).

In women with ER-positive and/or progesterone receptor-positive DCIS treated by wide local excision with or without breast radiotherapy, a large, randomized, double-blind, placebo-controlled trial (IBIS-II) compared anastrozole (n=1471) with tamoxifen (n=1509). The results demonstrated noninferiority of anastrozole to tamoxifen.[47] After a median follow-up of 7.2 years, 67 recurrences were reported with anastrozole versus 77 with tamoxifen (HR, 0.89; 95% CI, 0.64–1.23). A total of 33 deaths were recorded for anastrozole and 36 for tamoxifen (HR, 0.9393; 95% CI, 0.58–1.50; P=.78).[47] Although the number of women reporting any adverse event was similar between anastrozole (1,323 women, 91%) and tamoxifen (1,379

Breast Cancer, Version 4.2017

women, 93%); the side-effect profiles of the 2 drugs were different. There were more fractures, musculoskeletal events, hypercholesterolemia, and strokes reported with anastrozole and more muscle spasms, gynecologic cancers and symptoms, vasomotor symptoms, and deep vein thromboses reported with tamoxifen.

The NSABP B-35 study randomly assigned 3,104 postmenopausal patients to tamoxifen or anastrozole for 5 years. All patients received breast RT. Before being randomly assigned, patients were stratified by age—younger or older than 60 years. The primary endpoint was breast cancer–free interval.[48] Anastrozole treatment resulted in an overall statistically significant decrease in breast cancer-free interval events compared with tamoxifen (HR, 0.73; 95% CI, 0.56–0.96; P=.0234). The significant difference in breast cancer-free interval between the 2 treatments was apparent in the study only after 5 years of follow-up. The estimated percentage of patients with a 10-year breast cancer-free interval was 89.1% in the tamoxifen group and 93.1% in the anastrozole group.[48] In addition, anastrozole resulted in further improvement in breast cancer-free interval, in younger postmenopausal patients (younger than 60 years). With respect to adverse effects, the overall incidence of thrombosis or embolism was higher in the tamoxifen group while the anastrozole group had slightly more cases of arthralgia and myalgia.[48]

The results of the IBIS-II and the NSAP-B-35 studies indicate that anastrozole provides at least a comparable benefit as adjuvant treatment for postmenopausal women with hormone-receptor-positive DCIS, with a different toxicity profile.

NCCN Recommendations for Management of DCIS After Primary Treatment

According to the NCCN Panel, endocrine therapy, with tamoxifen (for premenopausal and postmenopausal women) or an aromatase inhibitor (for post-menopausal women, especially those under 60 years of age or those with concerns of embolism), may be considered as a strategy to reduce the risk of ipsilateral breast cancer recurrence in women with ER-positive DCIS treated with BCT (category 1 for those undergoing breast-conserving surgery followed by RT; category 2A for those undergoing excision alone). The benefit of endocrine therapy for ER-negative DCIS is not known.

Strategies for reducing the risk of recurrence to the contralateral breast are described in the NCCN Guidelines for Breast Cancer Risk Reduction, available at NCCN.org.

Surveillance

Surveillance after treatment for DCIS helps early recognition of disease recurrences (either DCIS or invasive disease) and evaluation and management of therapy-related complications. Most recurrences of DCIS are in-breast recurrences after BCT, and recurrences mostly occur in close proximity to the location of the prior disease. Overall, approximately one half of the local recurrences after initial treatment for a pure DCIS are invasive in nature, whereas the remainder recur as pure DCIS.

NCCN Recommendations for Surveillance

According to the NCCN Panel, follow-up of women with DCIS includes interval history and physical examination every 6 to 12 months for 5 years and then annually, as well as yearly diagnostic mammography. In patients treated with BCT, the first follow-up mammogram should be performed 6 to 12 months after the completion of breast-conserving RT (category 2B). Patients receiving risk reduction agents should be monitored as described in the NCCN Guidelines for Breast Cancer Risk Reduction (available at NCCN.org).

References

1. College of American Pathologists. Protocols and guidelines. Available at: http://www.cap.org. Accessed February 26, 2018.
2. Kerlikowske K, Molinaro AM, Gauthier ML, et al. Biomarker expression and risk of subsequent tumors after initial ductal carcinoma in situ diagnosis. J Natl Cancer Inst 2010;102:627–637.
3. Stackievicz R, Paran H, Bernheim J, et al. Prognostic significance of HER-2/neu expression in patients with ductal carcinoma in situ. Isr Med Assoc J 2010;12:290–295.
4. Zhou W, Jirstrom K, Johansson C, et al. Long-term survival of women with basal-like ductal carcinoma in situ of the breast: a population-based cohort study. BMC Cancer 2010;10:653.
5. Lari SA, Kuerer HM. Biological markers in DCIS and risk of breast recurrence: a systematic review. J Cancer 2011;2:232–261.
6. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. Lancet 2007;370:485–492.
7. Allen LR, Lago-Toro CE, Hughes JH, et al. Is there a role for MRI in the preoperative assessment of patients with DCIS? Ann Surg Oncol 2010;17:2395–2400.
8. Davis KL, Barth RJ, Jr., Gui J, et al. Use of MRI in preoperative planning for women with newly diagnosed DCIS: risk or benefit? Ann Surg Oncol 2012;19:3270–3274.

Breast Cancer, Version 4.2017

9. Pilewskie M, Olcese C, Eaton A, et al. Perioperative breast MRI is not associated with lower locoregional recurrence rates in DCIS patients treated with or without radiation. Ann Surg Oncol 2014;21:1552–1560.

10. Waddell BE, Stomper PC, DeFazio JL, et al. Postexcision mammography is indicated after resection of ductal carcinoma-in-situ of the breast. Ann Surg Oncol 2000;7:665–668.

11. Cody HS, Van Zee KJ. Point: sentinel lymph node biopsy is indicated for patients with DCIS. J Natl Compr Canc Netw 2003;1:199–206.

12. Virnig BA, Tuttle TM, Shamliyan T, Kane RL. Ductal carcinoma in situ of the breast: a systematic review of incidence, treatment, and outcomes. J Natl Cancer Inst 2010;102:170–178.

13. Edge SB, Sheldon DG. Counterpoint: sentinel lymph node biopsy is not indicated for ductal carcinoma in situ. J Natl Compr Canc Netw 2003;1:207–212.

14. 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 2005;23:7703–7720.

15. Brennan ME, Turner RM, Ciatto S, et al. Ductal carcinoma in situ at core-needle biopsy: meta-analysis of underestimation and predictors of invasive breast cancer. Radiology 2011;260:119–128.

16. Bijker N, Meijnen P, Peterse JL, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma-in-situ: ten-year results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853—a study by the EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. J Clin Oncol 2006;24:3381–3387.

17. Emdin SO, Granstrand B, Ringberg A, et al. SweDCIS: radiotherapy after sector resection for ductal carcinoma in situ of the breast. Results of a randomised trial in a population offered mammography screening. Acta Oncol 2006;45:536–543.

18. Fisher B, Dignam J, Wolmark N, et al. Lumpectomy and radiation therapy for the treatment of intraductal breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-17. J Clin Oncol 1998;16:441–452.

19. Houghton J, George WD, Cuzick J, et al. Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breast in the UK, Australia, and New Zealand: randomised controlled trial. Lancet 2003;362:95–102.

20. Julien JP, Bijker N, Fentiman IS, et al. Radiotherapy in breast-conserving treatment for ductal carcinoma in situ: first results of the EORTC randomised phase III trial 10853. EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. Lancet 2000;355:528–533.

21. Cuzick J, Sestak I, Pinder SE, et al. Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. Lancet Oncol 2011;12:21–29.

22. Wapnir IL, Dignam JJ, Fisher B, et al. Long-term outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS. J Natl Cancer Inst 2011;103:478–488.

23. McCormick B, Winter K, Hudis C, et al. RTOG 9804: a prospective randomized trial for good-risk ductal carcinoma in situ comparing radiotherapy with observation. J Clin Oncol 2015;33:709–715.

24. Holmberg L, Garmo H, Granstrand B, et al. Absolute risk reductions for local recurrence after postoperative radiotherapy after sector resection for ductal carcinoma in situ of the breast. J Clin Oncol 2008;26:1247–1252.

25. Goodwin A, Parker S, Ghersi D, Wilcken N. Post-operative radiotherapy for ductal carcinoma in situ of the breast--a systematic review of the randomised trials. Breast 2009;18:143–149.

26. Narod SA, Iqbal J, Giannakeas V, et al. Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol 2015;1:888–896.

27. Sagara Y, Freedman RA, Vaz-Luis I, et al. Patient prognostic score and associations with survival improvement offered by radiotherapy after breast-conserving surgery for ductal carcinoma in situ: a population-based longitudinal cohort study. J Clin Oncol 2016;34:1190–1196.

28. Bartelink H, Horiot JC, Poortmans PM, et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. J Clin Oncol 2007;25:3259–3265.

29. Bartelink H, Maingon P, Poortmans P, et al. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. Lancet Oncol 2015;16:47–56.

30. Romestaing P, Lehingue Y, Carrie C, et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997;15:963–968.

31. Polgar C, Fodor J, Orosz Z, et al. Electron and high-dose-rate brachytherapy boost in the conservative treatment of stage I-II breast cancer first results of the randomized Budapest boost trial. Strahlenther Onkol 2002;178:615–623.

32. Moran MS, Zhao Y, Ma S, et al. Association of radiotherapy boost for ductal carcinoma in situ with local control after whole-breast radiotherapy. JAMA Oncol 2017;3:1060–1068.

33. Di Saverio S, Catena F, Santini D, et al. 259 Patients with DCIS of the breast applying USC/Van Nuys prognostic index: a retrospective review with long term follow up. Breast Cancer Res Treat 2008;109:405–416.

34. Gilleard O, Goodman A, Cooper M, et al. The significance of the Van Nuys prognostic index in the management of ductal carcinoma in situ. World J Surg Oncol 2008;6:61–61.

35. Silverstein MJ, Lagios MD, Craig PH, et al. A prognostic index for ductal carcinoma in situ of the breast. Cancer 1996;77:2267–2274.

36. Silverstein MJ, Lagios MD, Groshen S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. N Engl J Med 1999;340:1455–1461.

37. Hughes LL, Wang M, Page DL, et al. Local excision alone without irradiation for ductal carcinoma in situ of the breast: a trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2009;27:5319–5324.

38. MacDonald HR, Silverstein MJ, Mabry H, et al. Local control in ductal carcinoma in situ treated by excision alone: incremental benefit of larger margins. Am J Surg 2005;190:521–525.

39. Dunne C, Burke JP, Morrow M, Kell MR. Effect of margin status on local recurrence after breast conservation and radiation therapy for ductal carcinoma in situ. J Clin Oncol 2009;27:1615–1620.

40. Van Zee KJ, Subhedar P, Olcese C, et al. Relationship between margin width and recurrence of ductal carcinoma in situ: analysis of 2996 women treated with breast-conserving surgery for 30 years. Ann Surg 2015;262:623–631.

41. Morrow M, Van Zee KJ, Solin LJ, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma In situ. J Clin Oncol 2016;34:4040–4046.

42. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. J Natl Cancer Inst 2005;97:1652–1662.

43. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst 1998;90:1371–1388.

44. Tan-Chiu E, Wang J, Costantino JP, et al. Effects of tamoxifen on benign breast disease in women at high risk for breast cancer. J Natl Cancer Inst 2003;95:302–307.

45. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687–1717.

46. Allred DC, Bryant J, Land S, et al. Estrogen receptor expression as a predictive marker of the effectiveness of tamoxifen in the treatment of DCIS: findings from the NSABP Protocol B-24 [abstract]. Breast Cancer Res Treat 2002;76(Suppl 1):Abstract A30.

47. Forbes JF, Sestak I, Howell A, et al. Anastrozole versus tamoxifen for the prevention of locoregional and contralateral breast cancer in postmenopausal women with locally excised ductal carcinoma in situ (IBIS-II DCIS): a double-blind, randomised controlled trial. Lancet 2016;886–873.

48. Margolese RG, Cecchini RS, Julian TB, et al. Anastrozole versus tamoxifen in postmenopausal women with ductal carcinoma in situ undergoing lumpectomy plus radiotherapy (NSABP B-35): a randomised, double-blind, phase 3 clinical trial. Lancet 2016;849–856.

Breast Cancer, Version 4.2017

Individual Disclosures for Breast Cancer Panel

Panel Member	Clinical Research Support/ Data Safety Monitoring Board	Scientific Advisory Boards, Consultant, or Expert Witness	Promotional Advisory Boards, Consultant, or Speakers Bureau	Date Completed
Benjamin O. Anderson, MD	None	Pfizer Inc.	None	8/3/17
Ron Balassanian, MD	None	None	None	9/27/17
Sarah L. Blair, MD	None	None	None	2/1/18
Harold J. Burstein, MD, PhD	None	None	None	10/5/17
Amy Cyr, MD	None	None	Genomic Health, Inc.	1/30/18
Anthony D. Elias, MD	Astellas Pharma US, Inc.; CytRx Corporation; Eli Lilly and Company; Genentech, Inc.; Immune Design; Incyte Corporation; and Innocrin Pharmaceuticals, Inc.	Genentech, Inc.; Innocrin Pharmaceuticals, Inc.; and SIX1 Therapeutics	None	7/16/17
William B. Farrar, MD	None	None	None	2/6/18
Andres Forero, MD	Abbott Laboratories; Celgene Corporation; Daiichi-Sankyo, Co.; Genentech, Inc.; GlaxoSmithKline; Incyte Corporation; Novartis Pharmaceuticals Corporation; Oncothyreon, Inc.; Pfizer Inc.; Pharmacyclics, Inc.; Seattle Genetics, Inc.; Synta Pharmaceuticals Corp.; TRACON Pharmaceuticals; and YM BioSciences Inc.	Incyte Corporation; and Seattle Genetics, Inc.	None	11/24/17
Sharon H. Giordano, MD, MPH	None	None	None	8/3/17
Matthew P. Goetz, MD	Biotheranostics, Inc.; Eisai Inc.; Eli Lilly and Company; Myriad Genetic Laboratories, Inc.; and Pfizer Inc.	Biotheranostics, Inc.; and Eli Lilly and Company	None	5/8/17
Lori J. Goldstein, MD	Dompe; Novartis Pharmaceuticals Corporation; and Roche Laboratories, Inc.	None	Novartis Pharmaceuticals Corporation	2/2/18
William J. Gradishar, MD	Genentech, Inc.; and Pfizer Inc.	Eisai Inc.; and Genentech, Inc.	None	6/30/17
Steven J. Isakoff, MD, PhD	Abbott Laboratories; AstraZeneca Pharmaceuticals LP; Exelixis Inc.; Genentech, Inc.; Merck & Co., Inc.; OncoPep, Inc.; Pharmamar.; and Rogers Sciences, Inc.	None	None	1/23/18
Janice Lyons, MD	None	None	None	8/18/17
P. Kelly Marcom, MD	Abbott Laboratories; Genentech, Inc.; Novartis Pharmaceuticals Corporation; and Veridex, LLC	None	None	7/27/17
Ingrid A. Mayer, MD, MSCI	Novartis Pharmaceuticals Corporation; and Pfizer Inc.	AstraZeneca Pharmaceuticals LP; Eli Lilly and Company; Genentech, Inc.; and Novartis Pharmaceuticals Corporation	None	8/10/17
Beryl McCormick, MD[a]	None	None	None	7/26/17
Meena S. Moran, MD	None	None	None	11/1/17
Ruth M. O'Regan, MD	AbbVie Inc.; Eisai Inc.; Novartis Pharmaceuticals Corporation; and Pfizer Inc.	BioTheranostics, Inc.; Eli Lilly and Company; and Genomic Health, Inc.	None	10/24/17
Sameer A. Patel, MD, FACS	None	None	None	7/26/17
Lori J. Pierce, MD[a]	None	None	None	11/27/17
Elizabeth C. Reed, MD	Novartis Pharmaceuticals Corporation; and Pfizer Inc.	UnitedHealthcare	None	6/13/17
Kilian E. Salerno, MD	None	None	None	10/25/17
Lee S. Schwartzberg, MD, FACP[a]	Bayer HealthCare; and Spectrum Pharmaceuticals, Inc.	Bristol-Myers Squibb Company; and Caris Life Sciences	Biocept, Inc.; Helsinn Therapeutics (US) Inc.; Merck & Co., Inc.; and NanoString Technologies, Inc.	9/21/17
Amy Sitapati, MD	None	None	None	8/12/17
Karen Lisa Smith, MD, MPH[b]	Johns Hopkins; and neuroCare Group	None	None	8/29/17
Mary Lou Smith, JD, MBA[a]	Novartis Pharmaceuticals Corporation	Novartis Pharmaceuticals Corporation	None	10/24/17
Hatem Soliman, MD	Altor Bioscience; Amgen Inc.; and Genentech, Inc.	AstraZeneca Pharmaceuticals LP; Eli Lilly and Company; and Etubics Corporation	Celgene Corporation	5/8/17
George Somlo, MD	Abbott Laboratories; Agendia BV; AstraZeneca Pharmaceuticals LP; Celgene Corporation; Genentech, Inc.; Merck & Co., Inc.; Millennium Pharmaceuticals, Inc.; National Cancer Institute; and Pfizer Inc.	AstraZeneca Pharmaceuticals LP; Celgene Corporation; Pfizer Inc.; and PUMA	Celgene Corporation; Millennium Pharmaceuticals, Inc.; and Pfizer Inc.	9/27/17
Melinda L. Telli, MD	AbbVie Inc.; Calithera Biosciences; G1 Therapeutics; Genentech, Inc.; Medivation, Inc.; Merck KGaA; Novartis Pharmaceuticals Corporation; OncoSec Medical Incorporated; Pfizer Inc.; PharmaMar; sanofi-aventis U.S. LLC; Tesaro Bio, Inc.; and Vertex Pharmaceuticals Incorporated	AstraZeneca Pharmaceuticals LP; PharmaMar; and Tesaro Bio, Inc.	None	11/15/17
John H. Ward, MD	None	None	None	10/23/17

The NCCN Guidelines Staff have no conflict of interest to disclose.

[a]The following individuals have disclosed that they have an Employment/ Governing Board, Patent, Equity, or Royalty conflict:
    Beryl McCormick, MD: Varian Medical Systems, Inc.
    Lori Pierce, MD: PFS Genomics, Inc., and UpToDate
    Lee Schwartzberg, MD, FACP: Caris Life Sciences, and GTx, Inc.
    Mary Lou Smith, MBA, JD: Gateway for Cancer Research Foundation National Accreditation Program for Breast Centers
[b]The following individuals have disclosed that they have a spouse/domestic partner/dependent with a potential conflict:
    Karen Lisa Smith, MD, MPH: Abbott Laboratories, and AbbVie, Inc.