Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer

AUTHORS: Alphonse Taghian, MD, PhD, Sofia D Merajver, MD, PhD
SECTION EDITORS: Gary J Whitman, MD, Claudine Isaacs, MD
DEPUTY EDITOR: Sadhna R Vora, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Aug 30, 2023.**

INTRODUCTION

In the United States, breast cancer is the most commonly diagnosed non-skin cancer and the second most common cause of cancer death in women [1].

Breast cancer is treated with a multidisciplinary approach involving surgical oncology, radiation oncology, and medical oncology, which has been associated with a reduction in breast cancer mortality [2].

This topic will provide an overview of the initial treatment of breast cancer and post-treatment surveillance. The epidemiology, clinical manifestations, diagnosis, staging of breast cancer, and specific discussions of the multimodality treatments for early breast cancer and the approach to metastatic disease are discussed elsewhere. (See "Clinical features, diagnosis, and staging of newly diagnosed breast cancer" and "Overview of the approach to metastatic breast cancer" and "The role of local therapies in metastatic breast cancer".)

Because ductal carcinoma in situ (DCIS) and invasive breast cancer are managed differently, we will restrict discussion in this topic to invasive breast cancer. A discussion on DCIS is covered separately. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis" and "Ductal carcinoma in situ: Treatment and prognosis".)

PATIENT STRATIFICATION

The vast majority of patients with newly diagnosed breast cancer in the United States and developed countries have no evidence of metastatic disease. For these patients, the treatment approach depends on the stage at presentation. For treatment purposes, breast cancer is characterized using the Tumor, Node, Metastasis system (TNM). Where clinical guidance is provided in this topic, the anatomic staging system set forth in the eighth edition of the American Joint Committee on Cancer (AJCC) Staging Manual is used (table 1). Moreover, the AJCC recommends use of the prognostic staging system for breast cancer that incorporates biomarkers, if resources are available (table 2 and table 3). This staging system is discussed in detail elsewhere. (See "Tumor, node, metastasis (TNM) staging classification for breast cancer".)

Nonmetastatic breast cancer is broadly considered in two categories:

- **Early stage** – This includes patients with stage I, IIA, or a subset of stage IIB disease (T2N1).
- **Locally advanced** – This includes a subset of patients with stage IIB disease (T3N0) and patients with stage IIIA to IIIC disease.

Approximately 5 percent of patients will have simultaneous metastatic disease identified at the initial presentation (de novo stage IV breast cancer). The treatment approach to these patients is discussed separately. (See "Overview of the approach to metastatic breast cancer" and "The role of local therapies in metastatic breast cancer".)

EARLY-STAGE BREAST CANCER

In general, patients with early-stage breast cancer undergo primary surgery (lumpectomy or mastectomy) to the breast and regional nodes with or without radiation therapy (RT) (table 4 and algorithm 1).

Following definitive local treatment, adjuvant systemic therapy may be offered, based on primary tumor characteristics such as tumor size, grade, number of involved lymph nodes, the status of estrogen (ER) and progesterone (PR) receptors, and expression of the human epidermal growth factor 2 (HER2) receptor.

However, some patients with early-stage invasive breast cancer (particularly those with HER2-positive or triple-negative disease) may be treated with neoadjuvant therapy first, followed by

surgery. Neoadjuvant therapy is discussed below. (See 'Surgical approach after neoadjuvant treatment' below.)

Breast-conserving therapy — Breast-conserving therapy (BCT) is comprised of breast-conserving surgery (BCS; ie, lumpectomy) plus RT. The goals of BCT are to provide the survival equivalent of mastectomy, a cosmetically acceptable breast, and a low rate of recurrence in the treated breast. BCT allows patients with invasive breast cancer to preserve their breast without sacrificing oncologic outcome. Successful BCT requires complete surgical removal of the tumor (with negative surgical margins) followed by moderate-dose RT to eradicate any residual disease. (See "Breast-conserving therapy".)

Among women with operable breast cancer, randomized trials have demonstrated equivalent disease-free and overall survival between mastectomy and breast-conserving therapy [3-6]. However, since the time that these trials were conducted, progress has been made in adjuvant therapy, and more recent observational studies suggest that breast-conserving therapy is associated with at least comparable survival to mastectomy and even with improved survival in some studies [7-10].

Criteria that **preclude** BCT are as follows (see "Breast-conserving therapy", section on 'Patient selection for BCT'):

- Multicentric disease
- Large tumor size in relation to breast
- Presence of diffuse malignant-appearing calcifications on imaging (ie, mammogram or magnetic resonance imaging [MRI])
- Prior history of chest RT (eg, mantle radiation for Hodgkin disease)
- Pregnancy
- Persistently positive margins despite attempts at re-excision

For patients who desire BCT but are not candidates at the time of presentation, an alternative approach is the use of neoadjuvant therapy, which may allow for BCS without compromising survival outcomes. (See 'Neoadjuvant systemic therapy' below.)

Mastectomy — A mastectomy is indicated for patients who are not candidates for BCT and those who prefer mastectomy. (See "Mastectomy", section on 'Indications for mastectomy'.)

Role of RT — Postmastectomy radiation therapy (RT) is indicated for patients at high risk for local recurrence, such as those with cancer involving the deep margins and pathologically involved axillary lymph nodes.

If the likelihood of postmastectomy RT is high preoperatively, this may affect the choice of mastectomy type, the choice of the reconstructive approach, and optimal timing of the breast reconstruction (immediate versus delayed).

Thus, preoperative coordination of care assures the best outcome. In many centers, this is accomplished by multi-disciplinary breast clinics.

Evaluation of the axillary nodes — The risk for metastases to the axillary nodes is related to tumor size and location, histologic grade, and the presence of lymphatic invasion within the primary tumor. Although internal mammary or supraclavicular nodes may be involved at the initial presentation, they rarely occur in the absence of axillary node involvement. (See "Overview of management of the regional lymph nodes in breast cancer", section on 'Internal mammary lymph nodes' and "Overview of management of the regional lymph nodes in breast cancer", section on 'Supraclavicular lymph nodes'.)

The evaluation of the regional nodes depends on whether axillary involvement is suspected prior to surgery:

- For patients presenting with clinically suspicious axillary lymph nodes, a preoperative work-up including ultrasound plus fine needle aspiration or core biopsy can help to determine the best surgical approach and whether neoadjuvant therapy should be considered. (See 'Neoadjuvant systemic therapy' below.)
  - For patients with a positive biopsy who proceed directly to surgery (rather than neoadjuvant therapy), an axillary node dissection should be performed at the time of breast surgery. (See "Technique of axillary lymph node dissection".)
    - The management of the axilla for those treated with neoadjuvant treatment is discussed below. (See 'Surgical approach after neoadjuvant treatment' below.)
  - For patients presenting with a negative biopsy, no further work-up is required prior to surgery. These patients should undergo a sentinel lymph node biopsy (SLNB) at the time of surgery. (See "Overview of sentinel lymph node biopsy in breast cancer" and "Sentinel lymph node biopsy in breast cancer: Techniques".)
- Patients with a clinically negative axillary examination should undergo an SLNB at the time of surgery. Further evaluation of the regional nodes depends on the findings at SLNB. Patients who have one or two pathologically involved sentinel nodes may not require a complete axillary node dissection [11]. Patients with three or more pathologically involved sentinel nodes typically undergo axillary node dissection, although the patient's

performance status and comorbidities are also considered. (See "Overview of sentinel lymph node biopsy in breast cancer".)

Adjuvant systemic therapy

Systemic therapy refers to the medical treatment of breast cancer using endocrine therapy, chemotherapy, and/or biologic therapy. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer" and "Adjuvant systemic therapy for HER2-positive breast cancer" and "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer".)

Tumor characteristics predict which patients are likely to benefit from specific types of therapy (table 4 and algorithm 1). For example, hormone receptor-positive patients benefit from the use of endocrine therapy. In addition, patients with HER2-positive cancers benefit from treatment using HER2-directed treatment. (See "Prognostic and predictive factors in early, non-metastatic breast cancer".)

For patients with early-stage breast cancer, treatment is based on tumor characteristics, patient status, and patient preferences:

- In general, patients with hormone receptor-positive breast cancer should receive endocrine therapy. Whether they also should receive adjuvant chemotherapy depends on patient and tumor characteristics. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer" and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Indications for treatment'.)
  - We offer chemotherapy to patients with early-stage hormone receptor-positive, HER2-negative cancers that have high-risk characteristics. (See "Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer".)
  - In the absence of high-risk features, we do not administer chemotherapy.
  - Select patients with high-risk, node-positive, ER-positive, HER2-negative breast cancer are candidates for adjuvant treatment with the cyclin-dependent kinase 4/6 inhibitor abemaciclib. Patient selection is discussed elsewhere. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer", section on 'Incorporation of targeted therapies for select patients'.)
- For patients with ER/PR and HER2-negative disease (triple-negative breast cancer), we typically administer adjuvant chemotherapy if the tumor size is ≥0.5 cm. Because these

patients are not candidates for endocrine therapy or treatment with HER2-directed agents, chemotherapy is their only option for adjuvant treatment, following or before radiotherapy. Patients with a triple-negative breast cancer <0.5 cm in size may forego adjuvant chemotherapy in most cases, due to minimal, if any, survival advantage. (See "ER/PR negative, HER2-negative (triple-negative) breast cancer" and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer".)

- Patients with HER2-positive breast cancer with a tumor size >1 cm typically receive a combination of chemotherapy plus HER2-directed therapy. The management of small (≤1 cm) HER2-positive breast cancers is controversial. Following chemotherapy, patients with hormone receptor-positive disease should also receive adjuvant endocrine therapy. (See "Adjuvant systemic therapy for HER2-positive breast cancer" and "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer", section on 'Additional considerations for HER2-positive disease'.)

- Special considerations for those with rare-histology tumors are discussed elsewhere. (See "Breast cancers with rare histologies".)

LOCALLY ADVANCED BREAST CANCER

Locally advanced breast cancer is best managed with multimodality therapy employing systemic and locoregional therapy (table 4 and algorithm 1). (See 'Patient stratification' above.)

Neoadjuvant systemic therapy — Most patients with locally advanced breast cancer, and some with earlier-stage disease (particularly if triple negative or human epidermal growth factor receptor 2 [HER2] positive), are treated with neoadjuvant systemic therapy. The goal of treatment is to induce a tumor response before surgery and enable breast conservation. Neoadjuvant chemotherapy also provides information about response to therapy that may be useful at a future time, if the cancer recurs.

Neoadjuvant therapy results in long-term distant disease-free survival (DFS) and overall survival (OS) comparable to that achieved with primary surgery followed by adjuvant systemic therapy. (See "General principles of neoadjuvant management of breast cancer", section on 'Patient selection'.)

Our approach to the selection of treatment in the neoadjuvant setting is outlined below:

- For most patients with hormone receptor-positive disease receiving neoadjuvant therapy, we offer chemotherapy rather than neoadjuvant endocrine therapy. Chemotherapy is associated with higher response rates in a shorter time period. For select patients with hormone-positive disease, neoadjuvant endocrine therapy may be an appropriate option if there are serious comorbidities or other factors (eg, patient preference) that necessitate that strategy. Patient selection for neoadjuvant chemotherapy versus endocrine therapy among those with hormone receptor-positive disease is discussed elsewhere. (See "Neoadjuvant management of newly diagnosed hormone-positive breast cancer", section on 'Selection of treatment'.)

- For patients with HER2-positive breast cancer, a HER2-directed agent (eg, trastuzumab with or without pertuzumab) should be added to the chemotherapy regimen. (See "Neoadjuvant therapy for patients with HER2-positive breast cancer".)

- For patients with hormone receptor-negative, HER2-negative disease, neoadjuvant therapy consists of chemotherapy, with the addition of immunotherapy for some patients with high-risk disease. (See "ER/PR negative, HER2-negative (triple-negative) breast cancer", section on 'Choice of regimen'.)

Surgical approach after neoadjuvant treatment — All patients should undergo surgery following neoadjuvant systemic therapy, even if they have a complete clinical and/or radiological response. In addition, patients who experience locoregional progression (but not distant spread) while on neoadjuvant systemic therapy should proceed with surgery, rather than switching the chemotherapy regimen. (See "General principles of neoadjuvant management of breast cancer", section on 'Post-treatment evaluation and management'.)

Primary tumor — The choice between breast conservation and mastectomy after neoadjuvant treatment is dependent on the treatment response and patient characteristics (eg, breast size in relation to residual tumor size). Similar criteria used in the treatment of early-stage breast cancer are applied. However, patients who present with a large (ie, T4) breast lesion should undergo a mastectomy following neoadjuvant treatment. (See 'Breast-conserving therapy' above and 'Mastectomy' above.)

Regional nodes — Most patients require a surgical evaluation of the regional nodes following neoadjuvant treatment. (See 'Evaluation of the axillary nodes' above and "General principles of neoadjuvant management of breast cancer", section on 'Management of the axilla'.)

Primary surgery — Although some patients may be candidates for primary surgery at presentation, patients with locally advanced disease have an extremely high risk of local

recurrence and distant metastases [12]. As a result, we prefer to treat patients with locally advanced breast cancer with neoadjuvant systemic therapy first.

For patients who proceed with primary surgery, based on pathologic results, postoperative radiation therapy and adjuvant treatment should be administered. (See "Radiation therapy techniques for newly diagnosed, non-metastatic breast cancer" and 'Adjuvant therapy' below.)

Adjuvant therapy — The use of postoperative (adjuvant) systemic therapy is guided by the patient's clinical status and tumor characteristics (table 4 and algorithm 1):

- Patients who did not receive neoadjuvant systemic therapy should receive adjuvant treatment. The use of chemotherapy, biologic therapy, and/or endocrine therapy is guided by the same principles used to determine treatment for early-stage breast cancer. (See 'Adjuvant systemic therapy' above.)

- For patients who received the full course of planned neoadjuvant chemotherapy, we take the following approach:

  - **Hormone receptor-positive breast cancer** – Patients with hormone receptor-positive breast cancer should receive endocrine therapy to reduce the risk of breast cancer recurrence and breast cancer-related mortality. Further chemotherapy in the form of adjuvant treatment is unlikely to improve OS in this subset. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Patients who received neoadjuvant treatment'.)

    The selection of endocrine therapy is made according to menopausal status. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer", section on 'Indications'.)

    Patients treated with neoadjuvant endocrine therapy who undergo surgery should continue endocrine therapy in the adjuvant setting. Whether or not to administer adjuvant chemotherapy should be individualized. (See "General principles of neoadjuvant management of breast cancer".)

  - **Triple-negative breast cancer** – Patients with hormone receptor-negative, HER2-negative (triple-negative) breast cancer who have a complete response to neoadjuvant therapy would typically not receive further chemotherapy in the adjuvant setting as there is no evidence that the addition of adjuvant chemotherapy improves OS. These patients should begin post-treatment surveillance. (See "Approach to the patient

following treatment for breast cancer", section on 'Guidelines for post-treatment follow-up'.)

In cases where a triple-negative tumor has not had a complete response to neoadjuvant therapy, adjuvant capecitabine may be administered. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Patients who received neoadjuvant treatment'.)

For patients who initiated pembrolizumab in the neoadjuvant setting, this is typically continued in the adjuvant setting. (See "Choice of neoadjuvant chemotherapy for HER2-negative breast cancer", section on 'Incorporation of immunotherapy with NACT in TNBC'.)

- **HER2-positive breast cancer** – Patients with HER2-positive breast cancer who have a pathologic complete response at the time of surgical resection should receive trastuzumab, with or without pertuzumab, following completion of surgery to complete a year of treatment, without the addition of further chemotherapy. This recommendation is based on studies of adjuvant chemotherapy with or without trastuzumab that demonstrated that the addition of one year of trastuzumab significantly improves DFS and OS. (See "Adjuvant systemic therapy for HER2-positive breast cancer", section on 'Patients who were treated with neoadjuvant therapy'.)

  In cases where the tumor has not had a complete response to neoadjuvant therapy, adjuvant ado-trastuzumab emtansine for 14 cycles, rather than trastuzumab, is recommended. (See "Adjuvant systemic therapy for HER2-positive breast cancer", section on 'Residual disease'.)

GERMLINE GENETIC TESTING

Whom to test — Although most breast cancers are sporadic, germline pathogenic variants in breast cancer susceptibility genes 1 and 2 (*BRCA1* and *BRCA2* [*BRCA*]) and other genes account for a small percentage of breast cancers. Criteria for hereditary cancer risk evaluation and possible testing are discussed elsewhere. (See "Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes", section on 'Concerning personal or family history'.)

Those found to have BRCA mutations — Breast cancer susceptibility gene 1 and 2 (*BRCA1* and *BRCA2* [*BRCA*]) mutation carriers have increased risks of developing a second breast cancer. Pathogenic variants in other genes, including tumor protein p53 (*TP53*), phosphatase and tensin

homolog (*PTEN*), and others, also increase the risk of a second breast cancer. Therefore, even though breast-conserving therapy is effective in these patients, they may opt to undergo bilateral mastectomy to reduce their risk of a second breast cancer. For *BRCA1/2* carriers with breast cancer who do not undergo bilateral mastectomy, screening should be performed with annual mammography and breast MRI (age 30 to 75) [13]. (See "Overview of hereditary breast and ovarian cancer syndromes" and "Contralateral prophylactic mastectomy".)

Adjuvant PARP inhibition in high-risk, HER2-negative disease — For select patients with *BRCA1/2* mutations and high-risk early, human epidermal growth factor receptor 2 (HER2)-negative breast cancer, adjuvant treatment with olaparib, an inhibitor of poly(ADP-ribose) polymerase (PARP), has been shown to improve disease-free survival outcomes. This is discussed in detail elsewhere. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'BRCA carriers with high-risk disease'.)

Other radiation and systemic therapy considerations for *BRCA1/2* mutation carriers with early breast cancer are the same as for those who are *BRCA* wildtype (ie, without a pathologic *BRCA* variant). (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer" and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer" and "Adjuvant endocrine therapy for premenopausal women with hormone receptor-positive breast cancer" and "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer".)

SPECIAL CONSIDERATIONS

Rare histologies — Certain very rare subtypes of metaplastic carcinoma (eg, low-grade adenosquamous and low-grade fibromatosis-like carcinoma) have a favorable prognosis without adjuvant systemic therapies [14]. Patients with tumors of such histologies may be offered observation rather than adjuvant systemic therapies, provided that the favorable histologic type is pure (>90 percent as classified on the surgical excision, not core biopsy alone). The critical step in evaluation of such tumors, because of their rarity, is pathologic review by a highly experienced pathology service to corroborate the diagnosis. This is particularly true when omission of adjuvant therapy is being contemplated. (See "Breast cancers with rare histologies".)

Fertility preservation — Clinicians should discuss with patients the risk of infertility and possible interventions to preserve fertility prior to initiating potentially gonadotoxic therapy (eg, cryopreservation of embryos or oocytes). This discussion should occur soon after diagnosis, since some interventions to preserve fertility take time and could delay the start of treatment.

This is consistent with guidance from the American Society of Clinical Oncology [15]. The topic of fertility preservation is covered in detail separately. (See "Fertility and reproductive hormone preservation: Overview of care prior to gonadotoxic therapy or surgery".)

Older women — For some patients with estrogen receptor-positive breast cancer, in whom surgery is not an option or life expectancy is limited, primary hormonal treatment with either tamoxifen or an aromatase inhibitor without surgery or radiation therapy can be used [16]. We prefer to individualize treatment based on the presence of medical comorbidities and patient and clinician preference. (See "Overview of the approach to early breast cancer in older women", section on 'Surgery versus endocrine therapy alone for hormone receptor-positive disease'.)

Osteoclast inhibitors — The topic of osteoclast inhibitors as a potential adjuvant anticancer therapy in postmenopausal women is discussed separately. (See "Use of osteoclast inhibitors in early breast cancer", section on 'Adjuvant bone-modifying treatment for higher-risk breast cancers'.)

Male breast cancer — The topic of male breast cancer is discussed separately. (See "Breast cancer in men".)

Breast cancer in pregnancy — The treatment of breast cancer in pregnancy is discussed separately. (See "Gestational breast cancer: Treatment".)

PROGNOSIS

The majority of breast cancer recurrences occur within the first five years of diagnosis [17], particularly with hormone receptor-negative disease [18]. A discussion of the influence of hormone receptor status on short- and long-term outcomes is found elsewhere. (See "Prognostic and predictive factors in early, non-metastatic breast cancer".)

In a study of over 4000 women with operable breast cancer treated on International Breast Cancer Study Group clinical trials I to V, the annual risk of recurrence was highest during the first five years (10.4 percent) with a peak between years 1 and 2 (15.2 percent) [18]. While the highest rate of relapse is within the first few years of treatment, some recurrences occur much later. In one study of patients with stage I, II, or III breast cancer who were without evidence of disease five years out from the original diagnosis, the recurrence risks in the subsequent 5 and 10 years were still 11 and 19 percent, respectively [19]. While these results reflect outcomes among patients with all biologic subtypes of disease, the long-term risk of recurrence differs according to hormone receptor status, with late recurrences occurring more frequently among

hormone receptor-positive cancers rather than hormone receptor-negative ones. A discussion of prognostic factors including hormone receptor status and other factors is found elsewhere. (See "Prognostic and predictive factors in early, non-metastatic breast cancer".)

POST-TREATMENT SURVEILLANCE

Cancer survivors who have completed treatment for breast cancer should undergo regular follow-up. Annual mammography should also be performed in patients who underwent breast-conserving therapy. The routine use of breast magnetic resonance imaging or whole-breast ultrasound is not recommended for breast cancer survivors because of a lack of evidence to inform their role in this population. In addition, laboratory tests and whole-body imaging in asymptomatic cancer survivors is not recommended. (See "Overview of long-term complications of therapy in breast cancer survivors and patterns of relapse", section on 'Long-term adverse effects of primary therapy' and "Approach to the patient following treatment for breast cancer", section on 'Guidelines for post-treatment follow-up'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Breast cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Breast cancer (The Basics)" and "Patient education: Choosing surgical treatment for early-stage breast cancer (The Basics)")

- Beyond the Basics topics (see "Patient education: Breast cancer guide to diagnosis and treatment (Beyond the Basics)" and "Patient education: Factors that affect breast cancer risk in women (Beyond the Basics)" and "Patient education: Treatment of early-stage, hormone-responsive breast cancer in postmenopausal women (Beyond the Basics)" and "Patient education: Treatment of early-stage, hormone-responsive breast cancer in premenopausal women (Beyond the Basics)" and "Patient education: Surgical procedures for breast cancer — Mastectomy and breast-conserving therapy (Beyond the Basics)" and "Patient education: Treatment of early HER2-positive breast cancer (Beyond the Basics)" and "Patient education: Locally advanced and inflammatory breast cancer (Beyond the Basics)")

SUMMARY

- **Patient stratification** – Patients with a new diagnosis of breast cancer can be stratified as having early or locally advanced disease (see 'Patient stratification' above). Treatment depends on multiple factors, as summarized (table 4 and algorithm 1).

- **Early-stage breast cancer: Surgery**

  - The surgical approach to the primary tumor depends on the size of the tumor and the breast, and whether multifocal disease is present. Options include breast-conserving therapy (breast-conserving surgery plus radiation therapy [RT]) or mastectomy. Both approaches result in equivalent cancer-specific outcomes. (See 'Early-stage breast cancer' above and "Breast-conserving therapy" and "Mastectomy".)

  - The surgical approach to the regional nodes depends on whether there is clinical evidence of lymph node involvement. (See 'Evaluation of the axillary nodes' above.)

- **Early-stage breast cancer: Adjuvant systemic treatment**

  - **Hormone receptor-positive breast cancer** – Patients with hormone receptor-positive breast cancer should receive adjuvant endocrine therapy. The role of adjuvant chemotherapy in these patients requires a risk-stratified approach that takes into account patient and tumor characteristics. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer"

and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Indications for treatment'.)

- **Triple-negative breast cancer** – Most patients with estrogen receptor (ER), progesterone receptor, and human epidermal growth factor receptor 2 (HER2)-negative disease (triple-negative breast cancer) receive chemotherapy, with an exception for very small tumors (≤0.5 cm). (See "ER/PR negative, HER2-negative (triple-negative) breast cancer" and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer".)

- **HER2-positive breast cancer** – Patients with HER2-positive breast cancer >1 cm in size should receive a combination of chemotherapy plus HER2-directed therapy. Following chemotherapy, patients with ER-positive disease should also receive adjuvant endocrine therapy. (See "Adjuvant systemic therapy for HER2-positive breast cancer" and "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer", section on 'Additional considerations for HER2-positive disease'.)

- **Locally advanced breast cancer** – Most patients with locally advanced breast cancer and some with earlier-stage breast cancer (particularly if HER2 positive or triple negative) are treated with neoadjuvant systemic therapy prior to surgery. Neoadjuvant treatment improves the rate of breast conservation without compromising survival outcomes. (See 'Neoadjuvant systemic therapy' above.)

  - For most patients receiving neoadjuvant treatment, we offer chemotherapy rather than endocrine therapy. A HER2-directed agent should be added to the chemotherapy regimen for tumors that are HER2 positive. For select patients with high-risk triple-negative breast cancer, we incorporate immunotherapy with neoadjuvant chemotherapy. (See "Neoadjuvant therapy for patients with HER2-positive breast cancer" and "Neoadjuvant management of newly diagnosed hormone-positive breast cancer", section on 'Selection of treatment' and "General principles of neoadjuvant management of breast cancer".)

  - For patients who received neoadjuvant chemotherapy:

    - Patients with hormone receptor-positive breast cancer should receive adjuvant endocrine therapy. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer", section on 'Indications'.)

- For patients with hormone receptor-negative breast cancer with residual disease after neoadjuvant treatment, adjuvant capecitabine is offered. (See "Approach to the patient following treatment for breast cancer", section on 'Guidelines for post-treatment follow-up' and "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Patients who received neoadjuvant treatment'.)

- Patients with triple-negative disease who initiated pembrolizumab in the neoadjuvant setting should continue it in the adjuvant setting. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer", section on 'Patients who received neoadjuvant treatment'.)

- Patients with HER2-positive breast cancer and a complete response to neoadjuvant treatment receive one year of trastuzumab, with or without pertuzumab, following completion of surgery. If residual disease is present, ado-trastuzumab emtansine is offered, rather than trastuzumab. (See "Adjuvant systemic therapy for HER2-positive breast cancer", section on 'Patients who were treated with neoadjuvant therapy'.)

- **Role of radiation therapy in early and locally advanced disease**

  - Following surgery (with or without neoadjuvant systemic therapy), all patients who undergo breast-conserving surgery should undergo adjuvant RT. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer".)

  - Some patients treated with a mastectomy receive postmastectomy RT. The administration of adjuvant RT is typically based upon the original pretreatment stage, though pathologic response to neoadjuvant therapy may play a role as well. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer".)

- **BRCA carriers** – For select patients with breast cancer susceptibility gene 1 or 2 (*BRCA1/2*) mutations and high-risk early, HER2-negative breast cancer, adjuvant treatment an inhibitor of poly(ADP-ribose) polymerase (PARP), improves disease-free survival outcomes. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer".)

ACKNOWLEDGMENT

The UpToDate editorial staff acknowledges Moataz N El-Ghamry, MD, who contributed to an earlier version of this topic review.

REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin 2023; 73:17.
2. Kesson EM, Allardice GM, George WD, et al. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. BMJ 2012; 344:e2718.
3. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347:1227.
4. Blichert-Toft M, Nielsen M, Düring M, et al. Long-term results of breast conserving surgery vs. mastectomy for early stage invasive breast cancer: 20-year follow-up of the Danish randomized DBCG-82TM protocol. Acta Oncol 2008; 47:672.
5. Litière S, Werutsky G, Fentiman IS, et al. Breast conserving therapy versus mastectomy for stage I-II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. Lancet Oncol 2012; 13:412.
6. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347:1233.
7. van Maaren MC, de Munck L, de Bock GH, et al. 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the Netherlands: a population-based study. Lancet Oncol 2016; 17:1158.
8. Agarwal S, Pappas L, Neumayer L, et al. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. JAMA Surg 2014; 149:267.
9. Hwang ES, Lichtensztajn DY, Gomez SL, et al. Survival after lumpectomy and mastectomy for early stage invasive breast cancer: the effect of age and hormone receptor status. Cancer 2013; 119:1402.
10. Hartmann-Johnsen OJ, Kåresen R, Schlichting E, Nygård JF. Survival is Better After Breast Conserving Therapy than Mastectomy for Early Stage Breast Cancer: A Registry-Based

Follow-up Study of Norwegian Women Primary Operated Between 1998 and 2008. Ann Surg Oncol 2015; 22:3836.

11. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. JAMA 2011; 305:569.
12. Haagensen CD, Stout AP. CARCINOMA OF THE BREAST: II. CRITERIA OF OPERABILITY. Ann Surg 1943; 118:859.
13. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 3.2023. Available at: https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf (Accessed on March 21, 2023).
14. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Breast cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf (Accessed on April 14, 2020).
15. Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 2006; 24:2917.
16. Hamaker ME, Bastiaannet E, Evers D, et al. Omission of surgery in elderly patients with early stage breast cancer. Eur J Cancer 2013; 49:545.
17. Taylor C, McGale P, Probert J, et al. Breast cancer mortality in 500 000 women with early invasive breast cancer diagnosed in England, 1993-2015: population based observational cohort study. BMJ 2023; 381:e074684.
18. Colleoni M, Sun Z, Price KN, et al. Annual Hazard Rates of Recurrence for Breast Cancer During 24 Years of Follow-Up: Results From the International Breast Cancer Study Group Trials I to V. J Clin Oncol 2016; 34:927.
19. Brewster AM, Hortobagyi GN, Broglio KR, et al. Residual risk of breast cancer recurrence 5 years after adjuvant therapy. J Natl Cancer Inst 2008; 100:1179.

Topic 737 Version 70.0

GRAPHICS

Breast carcinoma TNM anatomic stage group AJCC UICC 8th edition

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC

Any T	Any N	M1	IV

- The anatomic stage group table should only be used in global regions where biomarker tests are not routinely available.
- Cancer registries in the US must use the prognostic stage group table for case reporting.

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Graphic 110848 Version 8.0

Breast carcinoma TNM clinical prognostic stage groups AJCC UICC 8th edition

When TNM is…	And grade is…	And HER2 status is…	And ER status is…	And PR status is…	Then the clinical prognostic stage group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB

				Negative	IB
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0 T3 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA

				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0 T3 N0 M0	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
T2 N1[Δ] M0 T3 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G1	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0	G2	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA

T3 N2 M0		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G3	Positive	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB

Any T N3 M0				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC
Any T Any N M1	Any	Any	Any	Any	IV

NOTES:

1. Because N1mi categorization requires evaluation of the entire node, and cannot be assigned on the basis of an FNA or core biopsy, N1mi can only be used with the clinical prognostic staging when clinical staging is based on a resected lymph node in the absence of resection of the primary cancer, such as the situation where sentinel node biopsy is performed prior to receipt of neoadjuvant chemotherapy or endocrine therapy.
2. For cases with lymph node involvement with no evidence of primary tumor (eg, T0 N1, etc) or with breast ductal carcinoma *in situ* (eg, Tis N1, etc), the grade, HER2, ER, and PR information from the tumor in the lymph node should be used for assigning stage group.
3. For cases where HER2 is determined to be "equivocal" by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, the HER2 "negative" category should be used for staging in the clinical prognostic stage group table.
4. The prognostic value of these prognostic stage groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

* T1 includes T1mi.

¶ N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.

Δ N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1, and T4 N1, respectively.

Graphic 110851 Version 11.0

Breast carcinoma TNM pathologic prognostic stage groups AJCC UICC 8th edition

When TNM is…	And grade is…	And HER2 status is…	And ER status is…	And PR status is…	Then the pathological prognostic stage group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB

T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G1	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G2	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G3	Positive	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T2 N1[Δ] M0 T3 N0 M0	G1	Positive	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB

T2 N1[Δ] M0 T3 N0 M0	G2	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0 T3 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIA
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G1	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G2	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB

T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G3	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC

Any T Any N M1	Any	Any	Any	Any	IV

NOTES:

1. For cases with lymph node involvement with no evidence of primary tumor (eg, T0 N1, etc) or with breast ductal carcinoma *in situ* (eg, Tis N1, etc), the grade, HER2, ER, and PR information from the tumor in the lymph node should be used for assigning stage group.
2. For cases where HER2 is determined to be "equivocal" by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, the HER2 "negative" category should be used for staging in the pathological prognostic stage group table.
3. The prognostic value of these prognostic stage groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

Genomic profile for pathologic prognostic staging

When OncotypeDx score is less than 11…

When TNM is…	And grade is…	And HER2 status is…	And ER status is…	And PR status is…	Then the pathological prognostic stage group is…
T1 N0 M0 T2 N0 M0	Any	Negative	Positive	Any	IA

NOTES:

1. Obtaining genomic profiles is NOT required for assigning pathological prognostic stage. However genomic profiles may be performed for use in determining appropriate treatment. If the OncotypeDx test is performed in cases with a T1N0M0 or T2N0M0 cancer that is HER2-negative and ER-positive, and the recurrence score is less than 11, the case should be assigned pathological prognostic stage group IA.
2. If OncotypeDx is not performed, or if it is performed and the OncotypeDx score is not available, or is 11 or greater for patients with T1-2 N0 M0 HER2-negative, ER-positive cancer, then the prognostic stage group is assigned based on the anatomic and biomarker categories shown above.
3. OncotypeDx is the only multigene panel included to classify pathologic prognostic stage because prospective level I data supports this use for patients with a score less than 11. Future updates to the staging system may include results from other multigene panels to assign cohorts of patients to prognostic stage groups based on the then available evidence. Inclusion or exclusion in this staging table of a genomic profile assay is not an endorsement of any specific assay and should not limit appropriate clinical use of any genomic profile assay based on evidence available at the time of treatment.

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

* T1 includes T1mi.

¶ N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.

Δ N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1, and T4 N1, respectively.

Graphic 117141 Version 7.0

Treatments for nonmetastatic breast cancer

	HR-positive/ HER2-negative	HR-positive or HR-negative/ HER2-positive	HR-negative/ HER2-negative
Surgery?	Yes	Yes	Yes
Chemotherapy?	In high risk cases*	Yes¶	Yes¶
Immunotherapy?	No	No	In high-risk cases
Endocrine therapy?	Yes	In HR-positive disease	No
Anti-HER2 therapy?	No	Yes	No
Radiation?	Typically after BCS, sometimes after mastectomyΔ	Typically after BCS, sometimes after mastectomyΔ	Typically after BCS, sometimes after mastectomyΔ

This table provides a broad framework for the management of early breast cancer. Patients with nonmetastatic breast cancer are treated with curative intent. Decisions are typically nuanced, however, and treatments should be individualized and determined in a multidisciplinary setting involving input from surgeons, and medical and radiation oncologists.

HR: hormone receptor; HER2: human epidermal growth factor 2; BCS: breast conserving surgery.

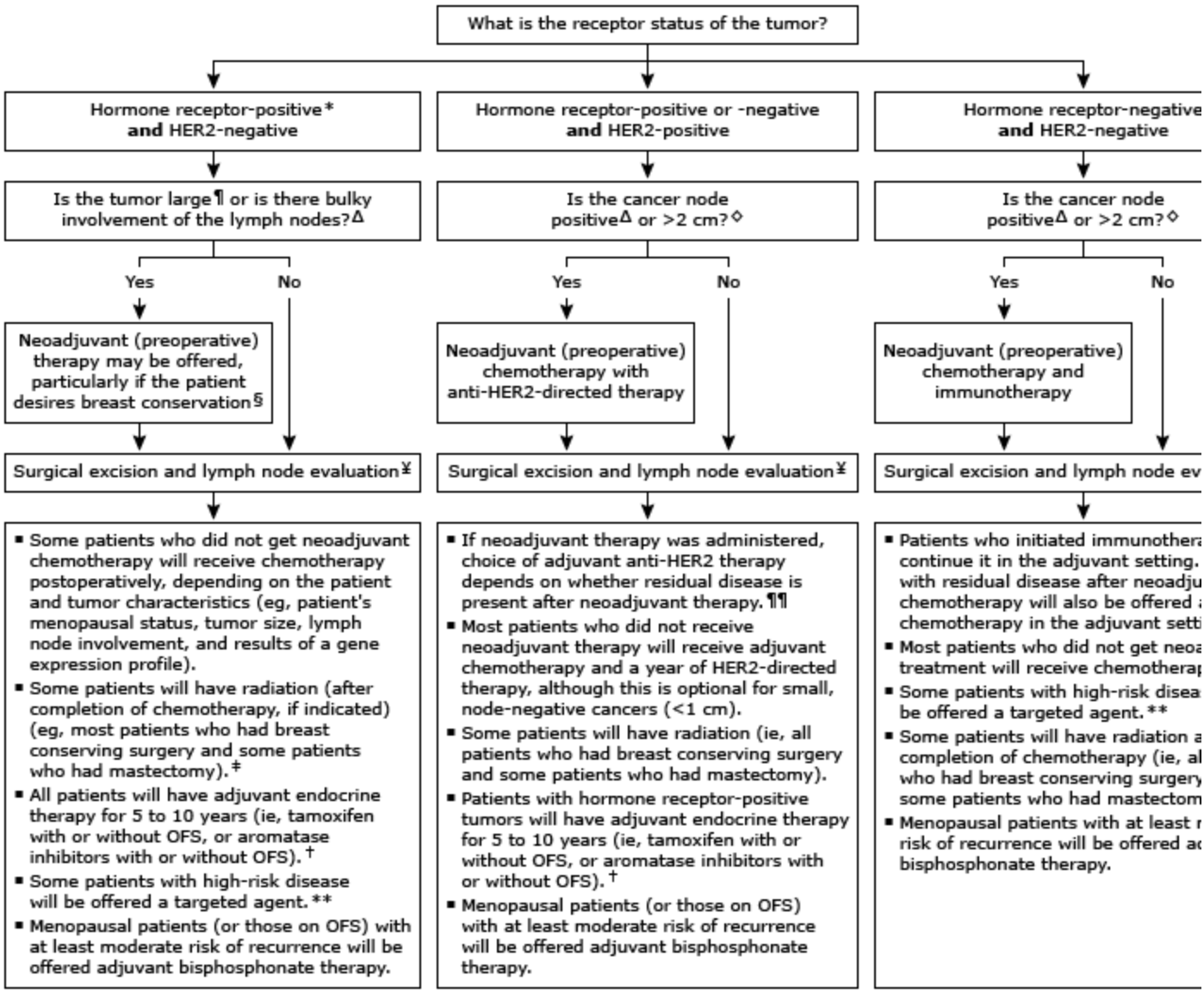
* Most patients proceed directly to surgery, and pathologic findings will influence whether postoperative chemotherapy is administered. However, select patients with larger HR-positive/HER2-negative tumors or bulky lymph nodes will be offered preoperative treatment.

¶ Most cancers that are either HER2-positive (irrespective of hormone receptor status) **or** hormone receptor-negative/HER2-negative will be treated with chemotherapy, although exceptions might be made for very small (a few mm or less) tumors. Typically chemotherapy is administered prior to surgery, as the response to treatment drives postoperative decisions regarding systemic therapy and provides prognostic information. Further chemotherapy may be administered after surgery, depending on the response to treatment.

Δ Most patients receive radiation after BCS. Select older females with small, HR-positive, HER2-negative tumors who will take endocrine therapy may have the option of omitting radiation. For patients who have had mastectomy, reasons for radiation include lymph node involvement or a combination of high-risk features such as young age, lymphovascular invasion, etc.

Graphic 142348 Version 1.0

Approach to patients with nonmetastatic breast cancer



This algorithm provides a broad framework for the management of early breast cancer. Patients with nonmetastatic breast cancer are treated with curative intent. Decisions are typically nuanced, however, and treatments should be individualized and determined in a multidisciplinary setting involving input from surg and medical and radiation oncologists. Many patients with early breast cancer should be offered genetic counseling, given that results of testing may impact treatment decisions, in some cases, as well as personal familial cancer risks.

HER2: human epidermal growth factor 2; OFS: ovarian function suppression; BRCA: breast cancer susceptibi gene.

* Hormone receptors are the estrogen receptor (ER) and progesterone receptor (PR). Threshold for hormon receptor positivity is ER and/or PR expression by immunohistochemistry of at least 1%.

¶ A reasonable cutoff is 5 cm, although it will vary depending on the size of the tumor to the breast and the location, and whether the patient desires breast conservation, all of which influences whether surgical resec

with negative margins is likely. If it is not likely, neoadjuvant therapy may be considered.

Δ Ensure thorough evaluation of axilla. A suspicious node on exam or imaging is typically biopsied.

◇ Preoperative systemic therapy can be considered for triple-negative cancers that are node-negative and b
1 to 2 cm.

§ Most patients receiving neoadjuvant therapy will receive chemotherapy, although endocrine therapy is an
for select patients who wish to avoid the toxicities of chemotherapy.

§ The surgical approach to the primary tumor depends on multiple factors, including:

- The size of the tumor and the breast
- Presence of multifocal disease
- Patient preference

Options include breast-conserving surgery or mastectomy. Sentinel lymph node biopsy and/or axillary disse
done for most patients, with the exception of some older patients with small, hormone receptor-positive, HI
negative cancers.

‡ Select older females with small, hormone receptor-positive, HER2-negative cancers who will take endocrin
therapy may have the option of omitting radiation after breast conserving surgery. For patients who have h
mastectomy, reasons for radiation include lymph node involvement, or a combination of high risk features s
young age, lymphovascular invasion, etc.

† If an aromatase inhibitor is used in a patient with intact ovarian function, it must be administered with ova
suppression.

** Examples of targeted therapy include cyclin dependent kinase inhibitors for hormone receptor-positive, I
negative cancers, or poly(adenosine diphosphate-ribose) polymerase inhibitors for *BRCA1/2* carriers with hig
HER2-negative breast cancer.

¶¶ The antibody drug conjugate trastuzumab emtansine is administered to those with residual disease, whi
trastuzumab with or without pertuzumab is administered to others.

ΔΔ Capecitabine may be utilized in this setting.

Contributor Disclosures

Alphonse Taghian, MD, PhD No relevant financial relationship(s) with ineligible companies to disclose. **Sofia D Merajver, MD, PhD** Equity Ownership/Stock Options: InheRet, LLC [Online tool for patients to enter personal and family health history]. All of the relevant financial relationships listed have been mitigated. **Gary J Whitman, MD** Consultant/Advisory Boards: Siemens [Digital mammography, tomosynthesis, breast cancer]. All of the relevant financial relationships listed have been mitigated. **Claudine Isaacs, MD** Grant/Research/Clinical Trial Support: AstraZeneca [Breast cancer, hereditary breast cancer]; Bristol Myers Squibb [Breast cancer, hereditary breast cancer]; Genentech [Breast cancer, hereditary breast cancer]; Novartis [Breast cancer, hereditary breast cancer]; Pfizer [Breast cancer, hereditary breast cancer]; Seattle Genetics [Breast cancer, hereditary breast cancer]; Tesaro/GSK [Breast cancer, hereditary breast cancer]. Consultant/Advisory Boards: AstraZeneca [Breast cancer, hereditary breast cancer]; Genentech [Breast cancer]; Gilead [Breast cancer]; ION [Breast cancer]; Novartis [Breast cancer]; Pfizer [Breast cancer, hereditary breast cancer]; PUMA [Breast cancer]; Seattle Genetics [Breast cancer]. Other Financial Interest: McGraw Hill [Royalties: Breast cancer]; SideOut Foundation [Medical Director]. All of the relevant financial relationships listed have been mitigated. **Sadhna R Vora, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→