



NCCN Guidelines for Patients™



Version 2010



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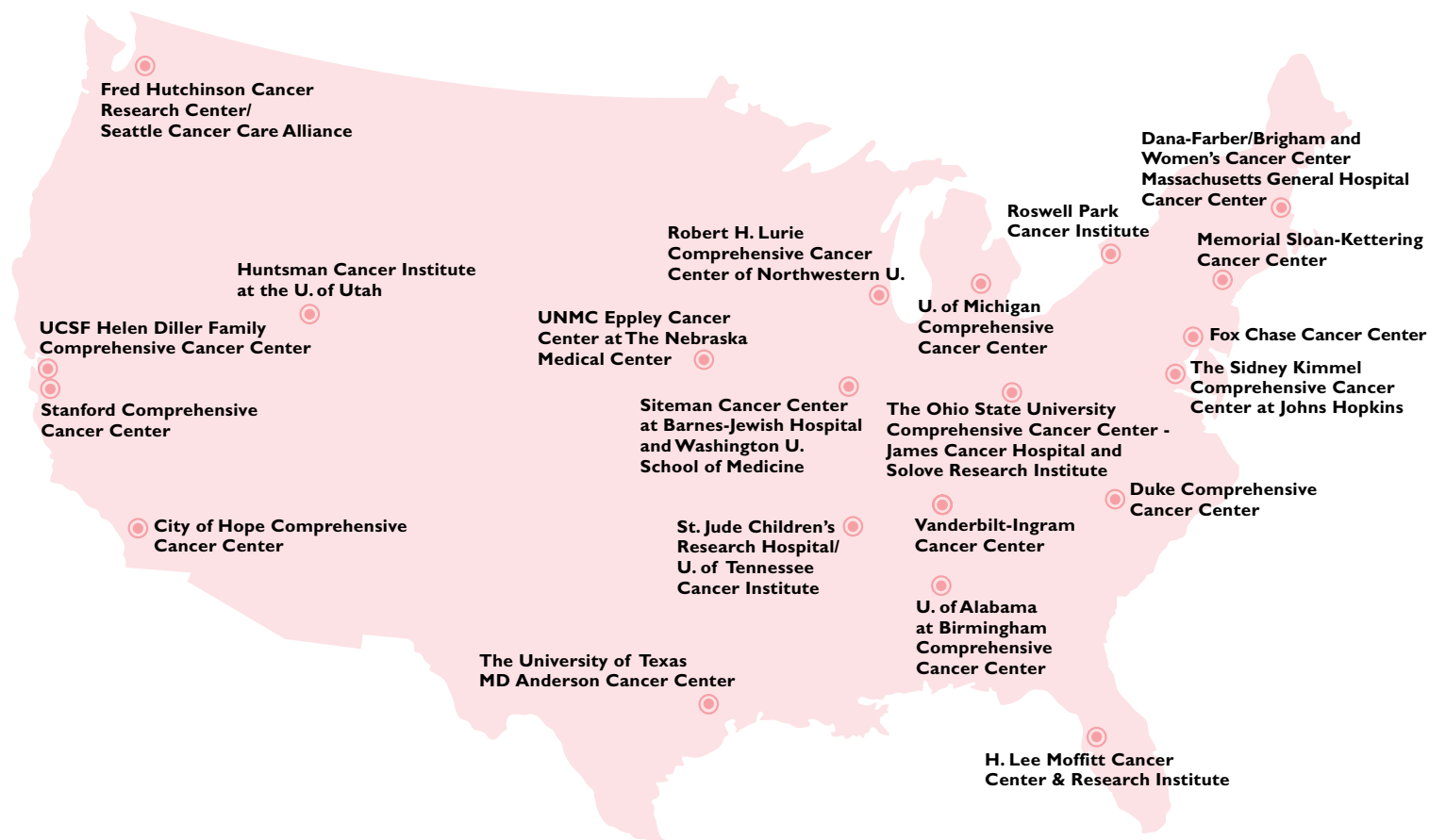
Also available at NCCN.com

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Map of NCCN Member Institutions

The National Comprehensive Cancer Network® (NCCN®), a not-for-profit alliance of 21 of the world's leading cancer centers, is dedicated to improving the quality and effectiveness of care provided to patients with cancer. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. As the arbiter of high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers. The primary goal of all NCCN initiatives is to improve the quality, effectiveness, and efficiency of oncology practice so patients can live better lives.



About the NCCN Guidelines for Patients™

The National Comprehensive Cancer Network® (NCCN®) aims to provide people with cancer and the general public state-of-the-art cancer treatment information in easy-to-understand language. The NCCN Guidelines for Patients™, based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™), are meant to help you when you talk with your doctor about treatment options that are best for you. These guidelines do not replace the expertise and clinical judgment of your doctor.

About the NCCN Guidelines™

The NCCN Guidelines are the most comprehensive and most frequently updated clinical practice guidelines available in any area of medicine. These guidelines provide information that many doctors follow to make sure their decisions for people with cancer are well informed. The NCCN Guidelines are developed by 43 different NCCN Guidelines Panels composed of nearly 900 world-leading experts from each of the NCCN Member Institutions. Cancer is treated by teams of doctors and other health professionals who work together to diagnose and treat cancer. NCCN Guidelines Panels are multidisciplinary, which means they include experts in different fields reflecting the way cancer is treated. These fields include medical oncology, surgical oncology, radiation oncology, pathology, radiology, nursing, and social work. Recommendations in the NCCN Guidelines are based on evaluation of evidence from clinical trials that are published in the medical literature. Most of the panel members who develop the NCCN Guidelines perform both clinical research and treat people with cancer. The members of each NCCN Guidelines Panel specialize in the specific tumors and diseases discussed in that NCCN Guideline. Some NCCN Guidelines Panels also have patient advocates to bring the patient's perspective to the panel discussions. NCCN Guidelines Panel Members volunteer more than 15,000 hours each year to revising and updating the NCCN Guidelines to reflect new data and clinical information.

The NCCN Guidelines are used by doctors in academic centers and community practices to inform their decisions when diagnosing and treating people with cancer. The NCCN Guidelines encompass 97 percent of the tumors encountered in oncology practices, and these guidelines are continually updated as new information becomes available. With the NCCN Guidelines, doctors and patients have access to the same treatment regimens used by NCCN Guidelines Panel Members when they treat their patients. The decisions of the expert panel are based on scientific data coordinated with expert judgment. Community physicians may or may not perform research, but by using the NCCN Guidelines, they have information about the latest evidence from clinical trials and insights to the expertise found at leading cancer centers.

By showing the standard of care, guidelines can reduce variation in how patients are treated and help make sure everyone gets the best care for them. However, no one treatment is right for everyone. Clinical research shows that some treatments are better for a particular disease than others. Similarly, studies have demonstrated that different patients with the same cancer may need different treatments. In many cases, patient preference is important especially when selecting among several effective treatments each with different side effects. Recommendations included in the NCCN Guidelines are those that NCCN doctors feel are most useful based on the evidence published in medical journals and their own experience treating patients. Therefore, even if a treatment is part of the NCCN Guidelines, it may not be the right treatment for all people with cancer or all people with that particular cancer. This is because each patient has a specific medical history and individual circumstances.

On the other hand, not including a particular treatment in the NCCN Guidelines only means that there is not strong enough evidence at this time to support using it as part of standard practice. In some cases, there may be ongoing clinical trials to determine whether the treatment is effective.

Many new treatments are available because patients have participated in clinical trials. Additionally, new treatments that are not yet part of standard practice may only be available in clinical trials. You can discuss whether a clinical trial might be right for you with your doctor.

The NCCN Guidelines for Patients™ translate the information that doctors use to help you and your family understand your treatment options. They empower you to discuss treatment choices with your health care team and make cancer care decisions that are right for you. For the most up-to-date versions of the NCCN Guidelines for Patients™, visit NCCN.com.

A diverse group of experts from NCCN Member Institutions developed the NCCN Guidelines for Breast Cancer. Listed on page 6 are the NCCN Guidelines Panel Members whose recommendations for treatment are featured in these NCCN Guidelines for Patients™.

Breast Cancer Panel

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Benjamin O. Anderson, MD
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& Research Institute

Stephen B. Edge, MD
Roswell Park Cancer Institute

John K. Erban, MD
Massachusetts General Hospital
Cancer Center

William B. Farrar, MD
The Ohio State University Comprehensive
Cancer Center - James Cancer Hospital
and Solove Research Institute

Andres Forero, MD
University of Alabama at Birmingham
Comprehensive Cancer Center

Sharon Hermes Giordano, MD, MPH
The University of Texas MD Anderson
Cancer Center

Lori J. Goldstein, MD
Fox Chase Cancer Center

William J. Gradishar, MD
Robert H. Lurie Comprehensive
Cancer Center of Northwestern University

Daniel F. Hayes, MD
University of Michigan Comprehensive
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Clifford A. Hudis, MD
Memorial Sloan-Kettering Cancer Center

Britt-Marie E. Ljung, MD
UCSF Helen Diller Family Comprehensive
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Duke Comprehensive Cancer Center

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Vanderbilt-Ingram Cancer Center

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Memorial Sloan-Kettering Cancer Center

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University of Michigan Comprehensive
Cancer Center

Elizabeth C. Reed, MD
UNMC Eppley Cancer Center
at The Nebraska Medical Center

Jasjit Sachdev, MD
St. Jude Children's Research Hospital/
University of Tennessee Cancer Institute

Mary Lou Smith, JD, MBA
Consultant

George Somlo, MD
City of Hope Comprehensive Cancer Center

John H. Ward, MD
Huntsman Cancer Institute at the
University of Utah

Eric P. Winer, MD
Dana-Farber/Brigham and Women's Cancer
Center | Massachusetts General Hospital
Cancer Center

Antonio C. Wolff, MD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Richard Zellars, MD
The Sidney Kimmel Comprehensive
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Introduction

These NCCN Guidelines for Patients™: Breast Cancer provide background information about breast cancer and its management, including cancer stage, workup, treatment, and follow up after treatment.

Although breast cancer is a very serious disease, it can be treated. It should be treated by a team of health care professionals working together, each with experience treating women with breast cancer. This team may include a surgeon, radiation oncologist, medical oncologist, diagnostic radiologist, pathologist, oncology nurse, social worker, and others. This team approach is called multidisciplinary care. All NCCN Guidelines are based on this approach, and all of these perspectives were included in the development of these guidelines.

Not all women with breast cancer should receive the same treatment, because clinical situations vary. Therefore, these NCCN Guidelines for Patients™: Breast Cancer can help women and their oncologists decide which choices best meet their medical and personal needs.

Breast cancer can occur in men. However, because the incidence is very low, these guidelines are specific to women with breast cancer. To learn more about breast cancer in men, patients should speak with their doctor. More information is also available on the National Cancer Institute website at www.cancer.gov.

These NCCN Guidelines for Patients™: Breast Cancer are designed to make cancer treatment more understandable. These guidelines apply to most but not all women with breast cancer. Their relevance to you and your treatment will depend on your general health and personal circumstances. The guidelines include several important parts:

- An overview of important questions and issues to discuss with your doctor.
- Staging tables that drive the decisions about the best treatments. Your doctor can tell you which stage applies to your cancer.
- The pathways which outline the step-by-step treatment decisions from diagnosis through all phases of treatment and survivorship. Once you know the stage of your cancer, simply follow the arrows corresponding to that stage to view the treatment recommendations as set forth by the NCCN Guidelines Panel for Breast Cancer. These pathways are simplified versions of the pathways that doctors use in thinking about how to treat breast cancer; however the content is still quite technical.
- Background information is provided to help you understand this complicated information about breast cancer. It includes the tests used in your medical evaluation, factors that lead doctors to recommend one treatment plan over others for a particular patient, description of the treatments themselves and how combinations of treatments are used together to provide the best possible outcomes, and the types of follow up needed after treatment is completed.
- A discussion of each of the pathways is provided, and
- Inevitably, you will encounter unfamiliar words and concepts, either in these guidelines or when talking with your doctor, so a glossary of cancer terms is included. These terms are shown in italics on the first mention in text.

The guidelines are complicated because managing breast cancer is complex. Many users will find that it is convenient to move from one part of the guidelines to another and back again rather than reading from beginning to end. The table of contents can help you navigate from one area to another easily.

Making Decisions about Breast Cancer Treatment

The NCCN Guidelines for Patients™: Breast Cancer will help patients with cancer better understand their disease, the factors that affect the course of the disease, and the characteristics that help determine which treatments are right for them. These NCCN Guidelines for Patients™ also provide information to help patients with cancer discuss the treatment options available to them with their doctors. For example, below are basic questions patients can use as discussion points. We encourage patients to discuss these questions and the rest of the NCCN Guidelines for Patients™ with their doctors.

- How large is my cancer? Do I have more than one tumor in the breast?
- Is my cancer invasive? What is the type of breast cancer do I have?
- Does my cancer express hormone receptors? If so, how will this affect my treatment plan?
- What is the HER2 status of my cancer? How will this affect my treatment plan?
- What is my cancer's grade (how abnormal the cells appear) and cell type as seen under a microscope?
- Do I have any lymph nodes with cancer in them (positive lymph nodes)? If yes, how many?
- Has the cancer spread to any other part of my body?
- What is the stage of my cancer?
- Is breast-conserving treatment an option for me?
- Is reconstruction an option to make my breast look more normal after surgery? When should it be done? Will I need implants? What kind?
- In addition to surgery, what other treatments do you recommend? Radiation? Chemotherapy? Hormone therapy?
- Are there any clinical trials that I should consider?
- How long will each part of my treatment take?
- What is the purpose of each treatment, and what is its goal?
- What are the treatment-related side effects? How long are they likely to last? Is there anything I can do to minimize them?
- If I have questions about any symptoms I might experience, whom should I call? What if it is at night or over the weekend?
- I have young children or grandchildren. Do you have any advice for me about caring for them while I am in treatment?
- Will I be able to go to work during treatment? Will I need to arrange for a reduced schedule?

NCCN Guidelines for Patients™: Breast Cancer

Lobular Carcinoma In Situ (LCIS) (For more detailed information, [see page 64](#))

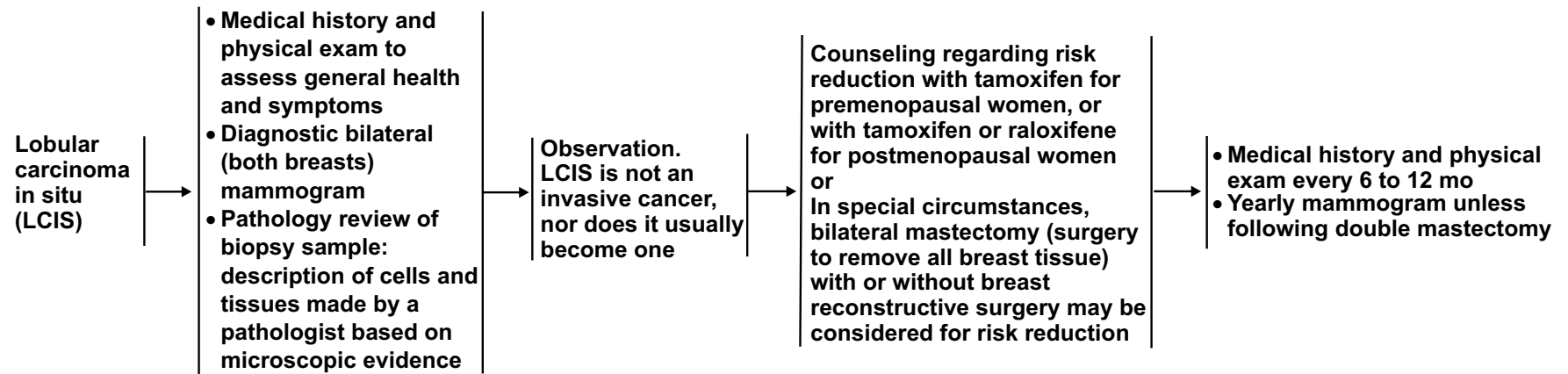
DIAGNOSIS

EVALUATION

TREATMENT

RISK REDUCTION

FOLLOW-UP



NCCN Guidelines for Patients™: Breast Cancer

Ductal Carcinoma In Situ (DCIS) (For more detailed information, [see page 64](#))

DIAGNOSIS

EVALUATION

PRIMARY TREATMENT

Ductal carcinoma in situ (DCIS)
Stage 0
Tis, N0, M0

- Medical history and physical exam to assess general health and symptoms
- Diagnostic bilateral (both breasts) mammogram
- Pathology review of biopsy sample: description of cells and tissues made by a pathologist based on microscopic evidence
- Estrogen receptor test: a lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated
- Genetic counseling if patient is high risk for hereditary breast cancer

Lumpectomy (surgery to remove cancer or other abnormal tissue from your breast. Lumpectomy is also called breast-conserving therapy because only a portion of the breast is removed)^a without lymph node surgery (a surgical procedure in which the lymph nodes are removed and a sample of tissue is checked under a microscope for signs of cancer) followed by whole breast radiation therapy

or

Total mastectomy (surgery to remove all breast tissue) with or without sentinel node biopsy (a surgical procedure used to determine if cancer has spread beyond the initial site) with or without breast reconstruction^b

or

Lumpectomy^a without lymph node surgery without radiation therapy^c

See [Postsurgical Treatment \(page 11\)](#)

^aDuring lumpectomy, a small amount of normal tissue around the lump is also taken to help ensure that all the cancer or other abnormal tissue is removed. If the tumor was removed by lumpectomy but cancer is found in the edges of the specimen, surgery to remove remaining cancer may be done in patients who desire to have breast-conserving surgery. If tumor cannot be completely removed with breast-conserving lumpectomy, the patient should undergo a mastectomy.

^bBreast reconstruction for mastectomy can be performed at the same time as mastectomy (immediate) or at some time following the completion of cancer treatment (delayed). Skin-sparing mastectomy is used to preserve breast skin and allow for a more natural breast appearance following reconstruction. Skin-sparing mastectomy should be performed by an experienced breast surgery team.

^cSome patients may be treated by surgery alone, if the patient and physician view the individual risks as “low”. A number of factors determine the local risk of cancer recurrence, these include: cancer size, low grade, clear margins (edges free of cancer), and patient age.

NCCN Guidelines for Patients™: **Breast Cancer**

Ductal Carcinoma In Situ (DCIS)

TREATMENT AFTER SURGERY

- Consider tamoxifen for 5 years for:
- Patients treated with breast-conserving therapy (lumpectomy) with or without radiation therapy, especially for those with ER-positive DCIS
 - Risk reduction therapy for opposite breast. Counseling regarding consideration of tamoxifen for risk reduction.



FOLLOW UP

- Medical history and physical exam every 6 months for 5 years, then every year
- Mammogram every year or beginning 6-12 months following completion of radiation therapy if treatment included radiation therapy
- Yearly gynecologic assessment for women taking tamoxifen

NCCN Guidelines for Patients™: Breast Cancer

Stage I, II, and some Stage III (For more detailed information, [see page 65](#))

CLINICAL STAGE

WORKUP^a

Stages I and II and Stage IIIA with tumor larger than 5 cm and limited lymph node spread (T3, N1, M0)

- Medical history and physical exam to assess general health and symptoms
 - Complete blood count (CBC) and platelets: a test to check the number of red blood cells, white blood cells, and platelets in a sample of blood
 - Liver function tests and alkaline phosphatase
 - Diagnostic bilateral (both breasts) mammogram, ultrasound as needed
 - Pathology review of biopsy sample: description of cells and tissues made by a pathologist based on microscopic evidence
 - Determination of tumor estrogen/progesterone receptor (ER/PR) status^b and HER2 status^c
 - Genetic counseling if patient is high risk for hereditary breast cancer
- Other studies for breast imaging:
- Breast MRI with dedicated breast coil may be considered for women who have breasts that cannot be adequately imaged with mammography and ultrasound
- Additional studies as directed by symptoms:
- Bone scan - only done if bone pain or tests suggest cancer has spread to the bones
 - Possible abdominal and pelvic CT or ultrasound or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
 - Possible chest imaging if the cancer is large and has spread to 1 or more lymph nodes or there are symptoms of lung disease

[See Treatment Pathway for Locoregional Treatment \(page 13\)](#)

^aThe use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer.

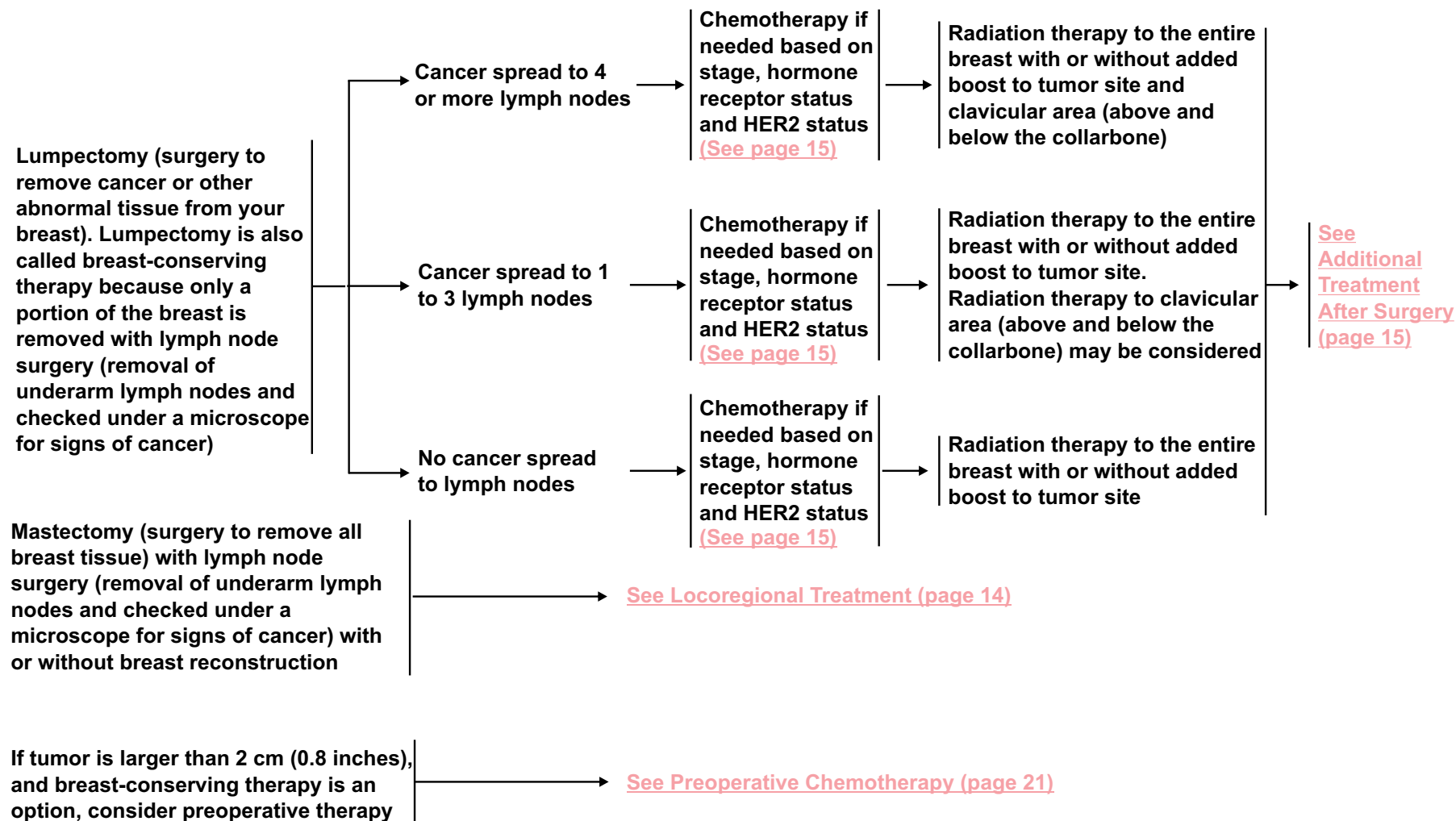
^bEstrogen receptor test: a lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated.

^cHuman epidermal growth factor receptor 2 (HER2) is a protein involved in normal cell growth. It is found on some types of cancer cells, including breast and ovarian cancers. Cancer cells removed from the body may be tested for the presence of HER2 to help decide the best type of treatment. HER2-positive breast cancer is a breast cancer that tests positive for the protein. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. Whenever breast cancer recurs or spreads, the cancer cells should be retested for HER2 when possible as well as for hormone receptor status, as these can change from the original cancer in up to 20% to 30% of cases.

NCCN Guidelines for Patients™: Breast Cancer

Stage I, II, and some Stage III (For more detailed information, [see page 66](#))

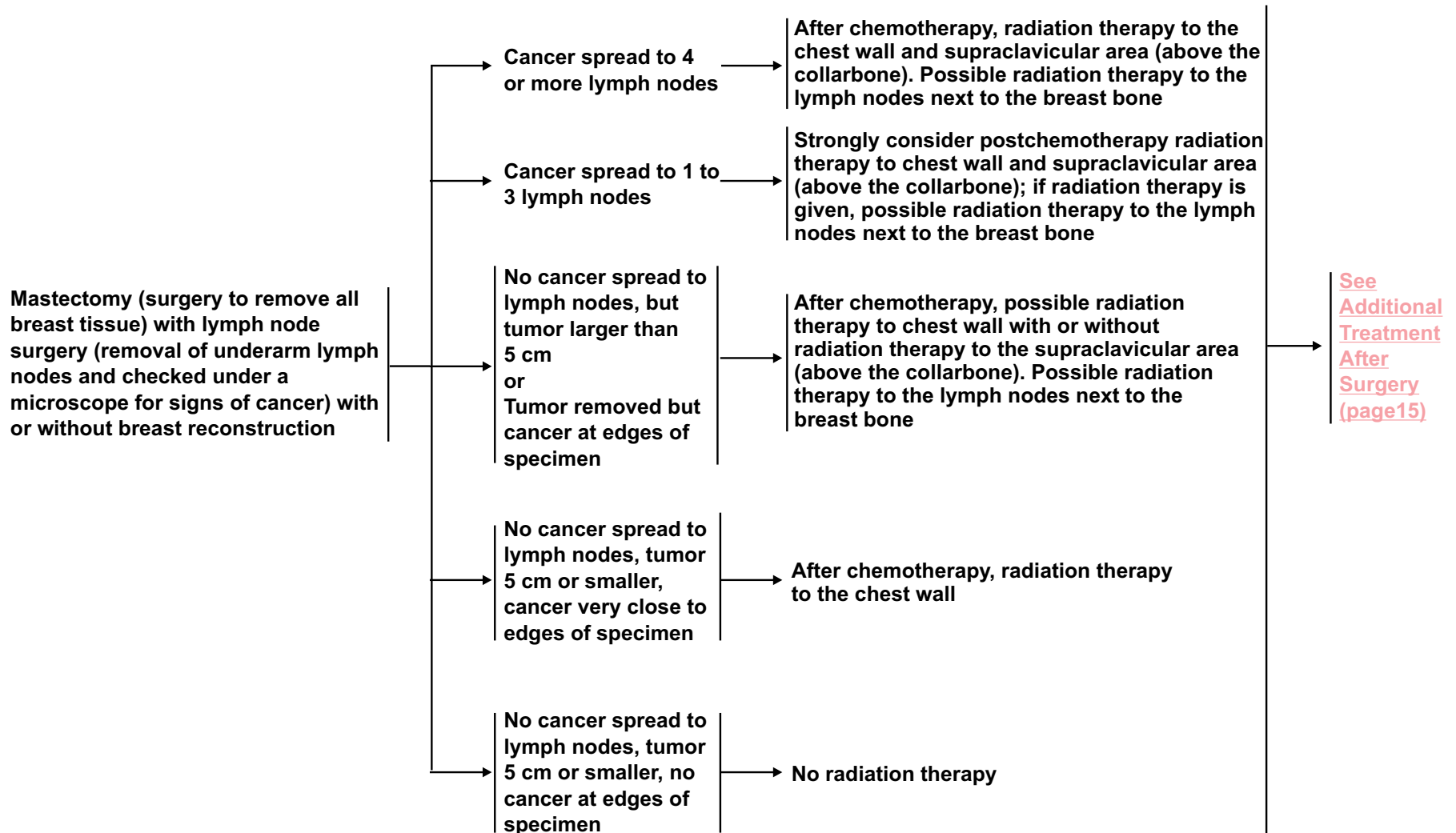
LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



NCCN Guidelines for Patients™: Breast Cancer

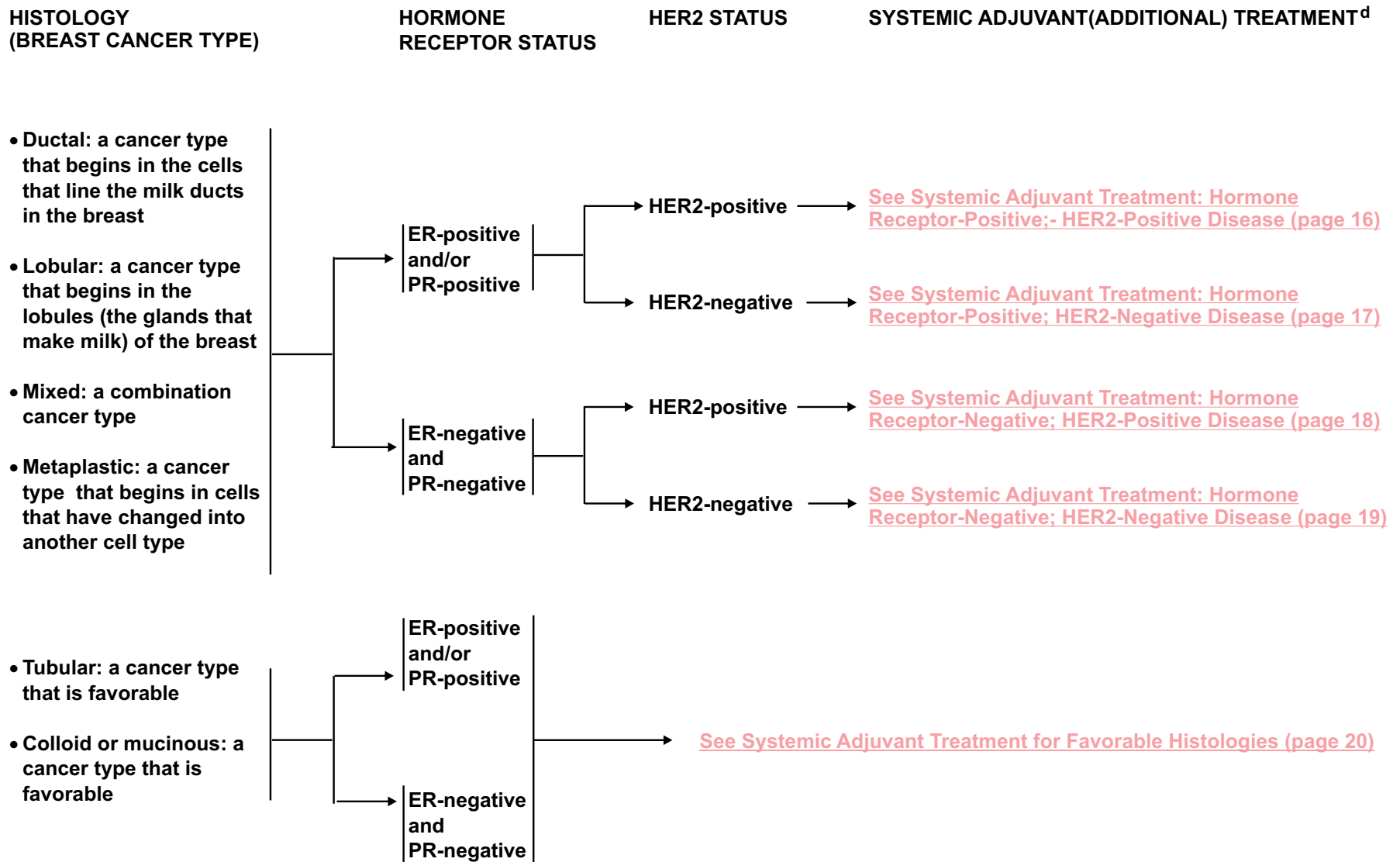
Stage I, II, and some Stage III (For more detailed information, [see page 66](#))

LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



NCCN Guidelines for Patients™: Breast Cancer

Stage I, II, and some Stage III (For more detailed information, [see page 68](#))

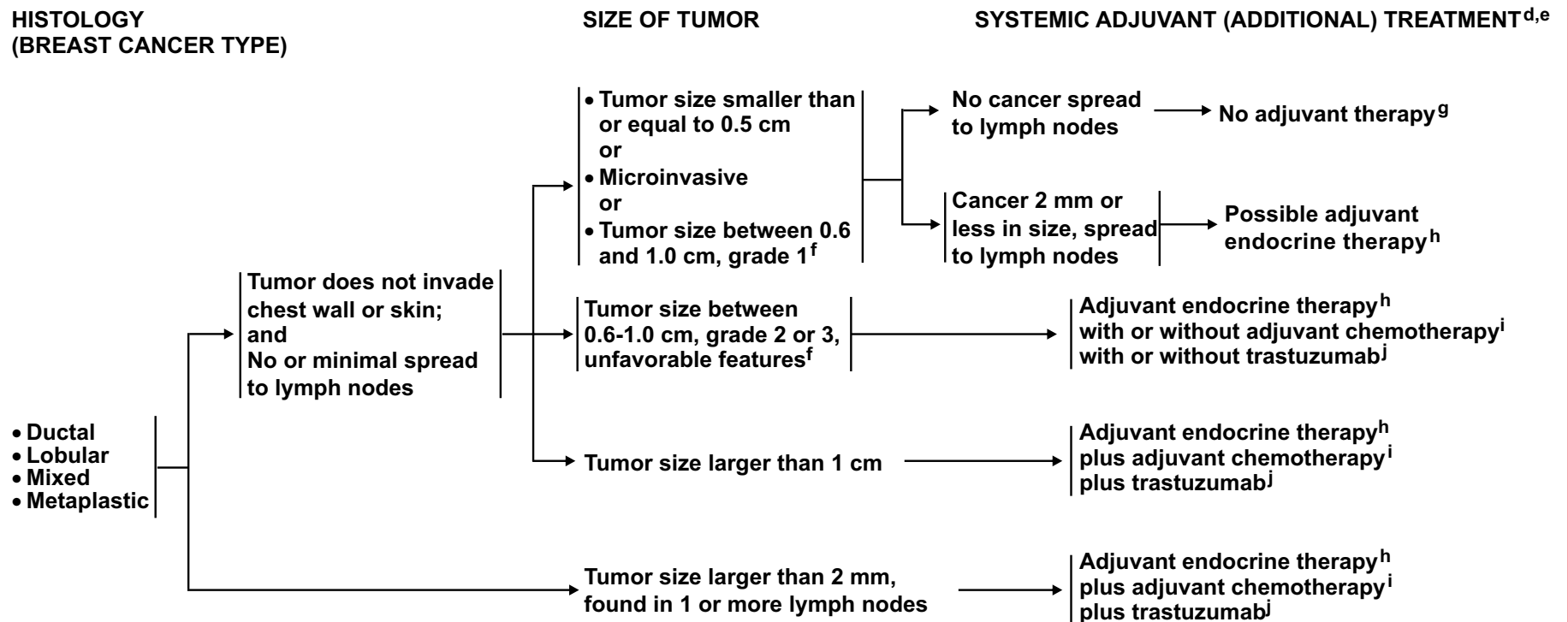


^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biological therapy.

NCCN Guidelines for Patients™: Breast Cancer

Systemic Adjuvant (additional) Treatment Hormone Receptor-Positive; HER2-Positive Disease

(For more detailed information, see page 69)



[See Follow-Up \(page 26\)](#)

^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, or targeted therapy.

^eFor patients who are over 70 years of age, a general health assessment and other medical conditions are considered as factors in deciding whether to give chemotherapy or not. For patients who are between 60 and 70 years of age, with a good prognosis, the benefit from chemotherapy before hormone therapy may be small resulting in some patients to forego chemotherapy and choose to have only radiation therapy and hormone therapy.

^fTumor grade is a description of a tumor based on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grade 1 represents well-differentiated, favorable features; grade 2 is intermediate-differentiated, moderately favorable; and grade 3 is poorly-differentiated, unfavorable features. Poorly-differentiated are tumors that lack the structure and function of normal cells and are likely to grow at a faster rate.

^gIn select circumstances, patients may consider adjuvant endocrine therapy to prevent new breast cancers or to reduce the small risk of disease recurrence.

^hEndocrine therapy is used to slow or stop the growth of cancers in patients with hormone receptor-positive disease. Synthetic hormones or other drugs may be given to block the body's natural hormones. Also called hormonal therapy, hormone therapy, and hormone treatment.

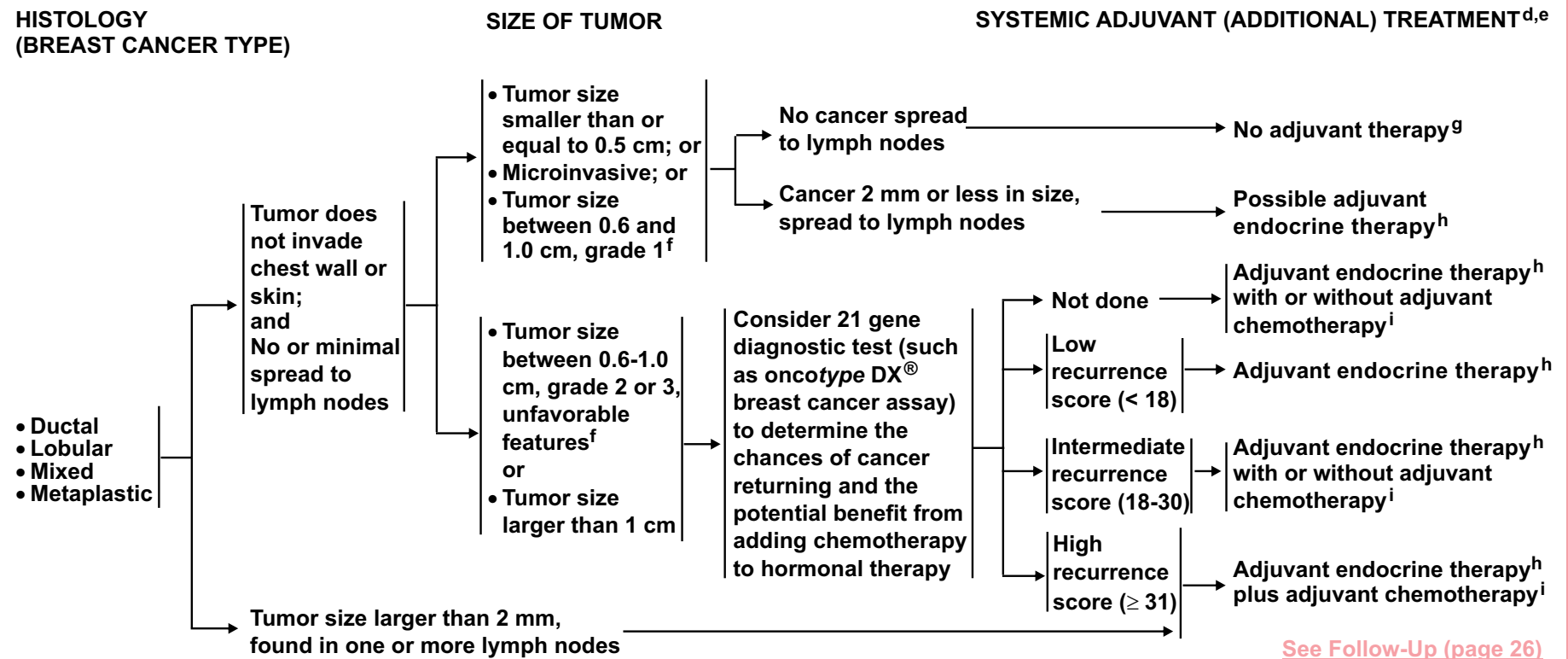
ⁱIf adjuvant therapy consists of chemotherapy and endocrine (hormonal) therapy, chemotherapy is given first followed by endocrine therapy.

^jA monoclonal antibody that binds to HER2 (human epidermal growth factor receptor 2), and can destroy HER2-positive cancer cells. Monoclonal antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Trastuzumab is used to treat breast cancer that is HER2-positive and has spread after treatment with other drugs. It is also used with other anticancer drugs to treat HER2-positive breast cancer after surgery. Also called Herceptin.

NCCN Guidelines for Patients™: Breast Cancer

Systemic Adjuvant (additional) Treatment Hormone Receptor-Positive; HER2-Negative Disease

(For more detailed information, see page 69)



[See Follow-Up \(page 26\)](#)

^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, or targeted therapy.

^eFor patients who are over 70 years of age, a general health assessment and other medical conditions are considered as factors in deciding whether to give chemotherapy or not. For patients who are between 60 and 70 years of age, with a good prognosis, the benefit from chemotherapy before hormone therapy may be small resulting in some patients to forego chemotherapy and choose to have only radiation therapy and hormone therapy.

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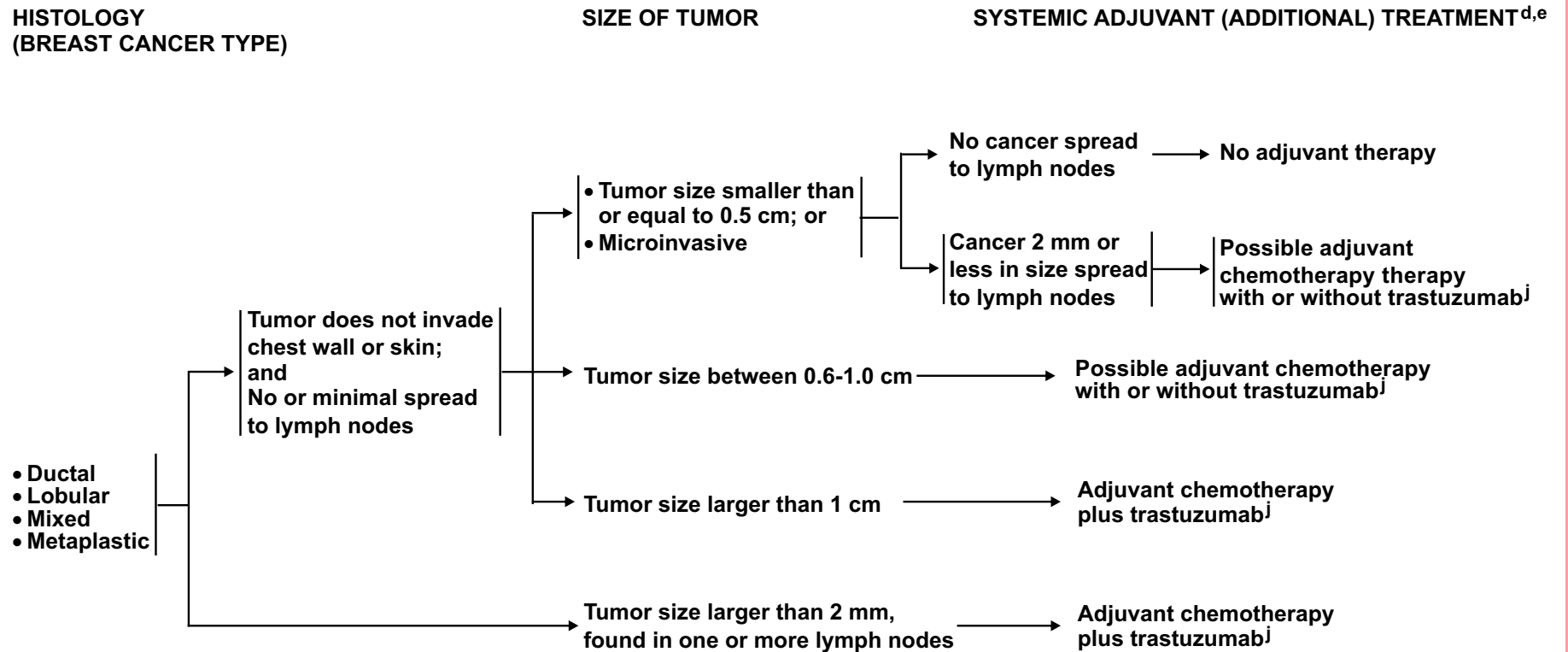
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ⁱIf adjuvant therapy consists of chemotherapy and endocrine (hormonal) therapy, chemotherapy is given first followed by endocrine therapy.

NCCN Guidelines for Patients™: Breast Cancer

Systemic Adjuvant (additional) Treatment Hormone Receptor-Negative; HER2-Positive Disease
 (For more detailed information, see page 70)



[See Follow-Up \(page 26\)](#)

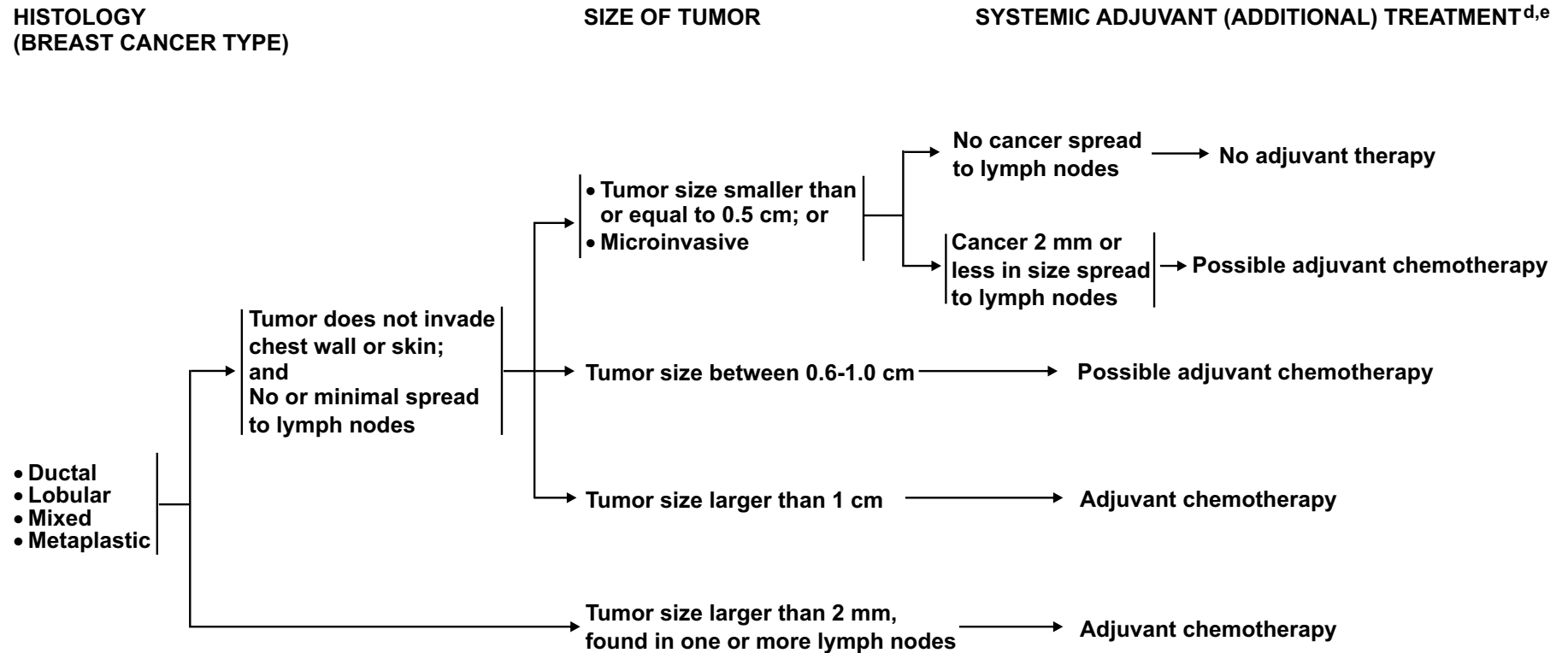
^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, or targeted therapy.

^eFor patients who are over 70 years of age, a general health assessment and other medical conditions are considered as factors in deciding whether to give chemotherapy or not. For patients who are between 60 and 70 years of age, with a good prognosis, the benefit from chemotherapy before hormone therapy may be small resulting in some patients to forego chemotherapy and choose to have only radiation therapy and hormone therapy.

^jA monoclonal antibody that binds to HER2 (human epidermal growth factor receptor 2), and can kill HER2-positive cancer cells. Monoclonal antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Trastuzumab is used to treat breast cancer that is HER2-positive and has spread after treatment with other drugs. It is also used with other anti-cancer drugs to treat HER2-positive breast cancer after surgery. Also called Herceptin.

NCCN Guidelines for Patients™: Breast Cancer

Systemic Adjuvant (additional) Treatment Hormone Receptor-Negative; HER2-Negative Disease
 (For more detailed information, see page 70)



[See Follow-Up \(page 26\)](#)

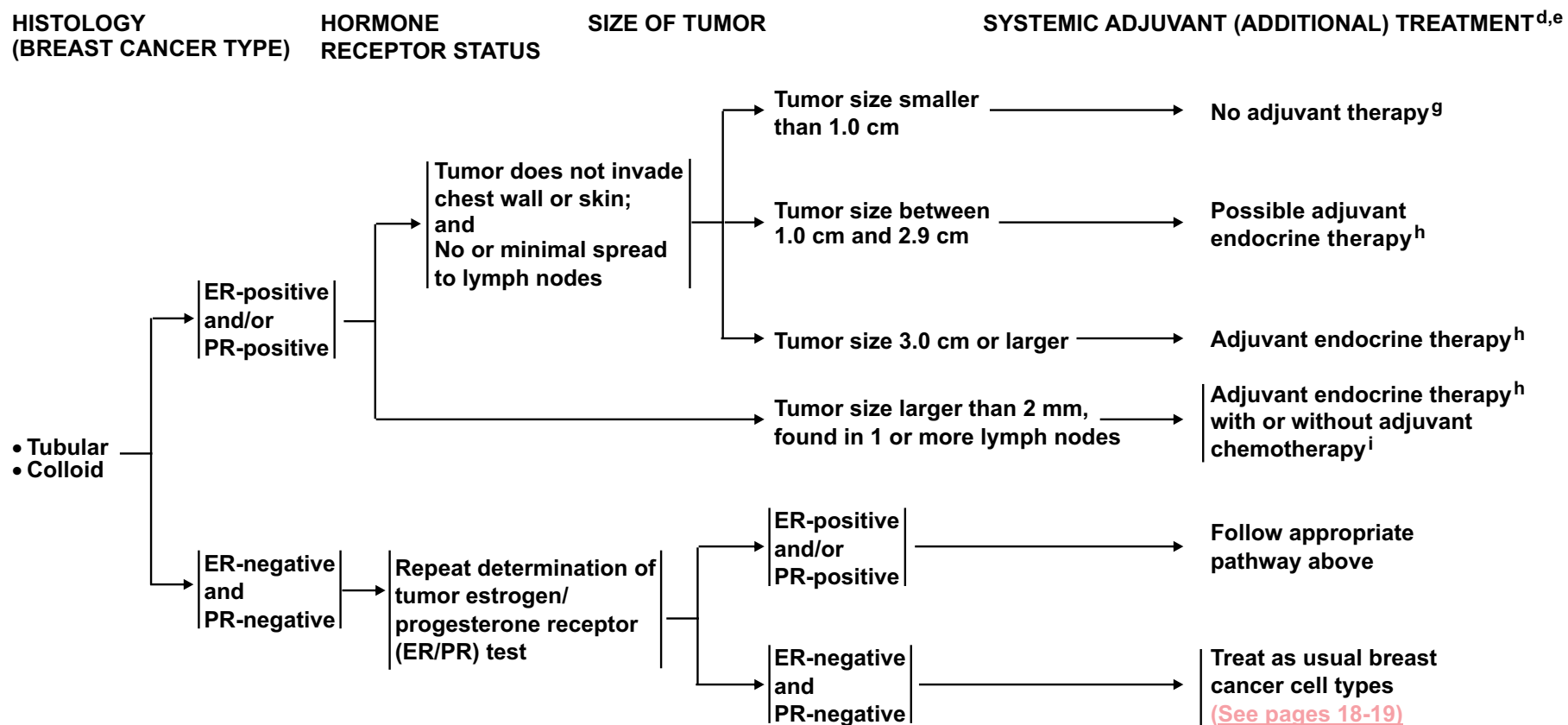
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NCCN Guidelines for Patients™: Breast Cancer

Systemic Adjuvant (additional) Treatment Tubular or Colloid Breast Cancers (Favorable Histologies)

(For more detailed information, see page 70)



[See Follow-Up \(page 26\)](#)

^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, or targeted therapy.

^eFor patients who are over 70 years of age, a general health assessment and other medical conditions are considered as factors in deciding whether to give chemotherapy or not. For patients who are between 60 and 70 years of age, with a good prognosis, the benefit from chemotherapy before hormone therapy may be small resulting in some patients to forego chemotherapy and choose to have only radiation therapy and hormone therapy.

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^hEndocrine therapy is used to slow or stop the growth of cancers in patients with hormone receptor-positive disease. Synthetic hormones or other drugs may be given to block the body's natural hormones. Also called hormonal therapy, hormone therapy, and hormone treatment.

ⁱIf adjuvant therapy consists of chemotherapy and endocrine (hormonal) therapy, chemotherapy is given first followed by endocrine therapy.

NCCN Guidelines for Patients™: Breast Cancer

Large Stage II or Stage IIIA Preoperative Chemotherapy Guideline

(For more detailed information, [see page 71](#))

CLINICAL STAGE

WORKUP^a

Stages IIA, IIB and Stage IIIA (T3, N1, M0)

The cancer is larger than 2 cm and does not invade the chest wall or skin, lymph nodes are movable

Diagnosed by needle biopsy not excision

Breast-conserving therapy not possible because the breast tumor is too large

- Medical history and physical exam to assess general health and symptoms
- Complete blood count (CBC) and platelets: a test to check the number of red blood cells, white blood cells, and platelets in a sample of blood
- Liver function tests and alkaline phosphatase
- Diagnostic bilateral (both breasts) mammogram, ultrasound as needed
- Pathology review of biopsy sample: description of cells and tissues made by a pathologist based on microscopic evidence
- Determination of tumor estrogen/progesterone receptor (ER/PR) status^b and HER2 status^c
- Genetic counseling if patient is high risk for hereditary breast cancer

Other studies for breast imaging:

- Breast MRI

Additional studies if clinical stage IIIA (T3, N1, M0) or as directed by symptoms:

- Bone scan - only done if bone pain or lab tests suggest cancer has spread to the bones
- Possible abdominal ± pelvis CT or ultrasound or MRI if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, abnormal physical examination of the abdomen or pelvis
- Possible chest imaging if the cancer is large and has spread to 1 or more lymph nodes or there are symptoms of lung disease

[See Primary Treatment \(page 22\)](#)

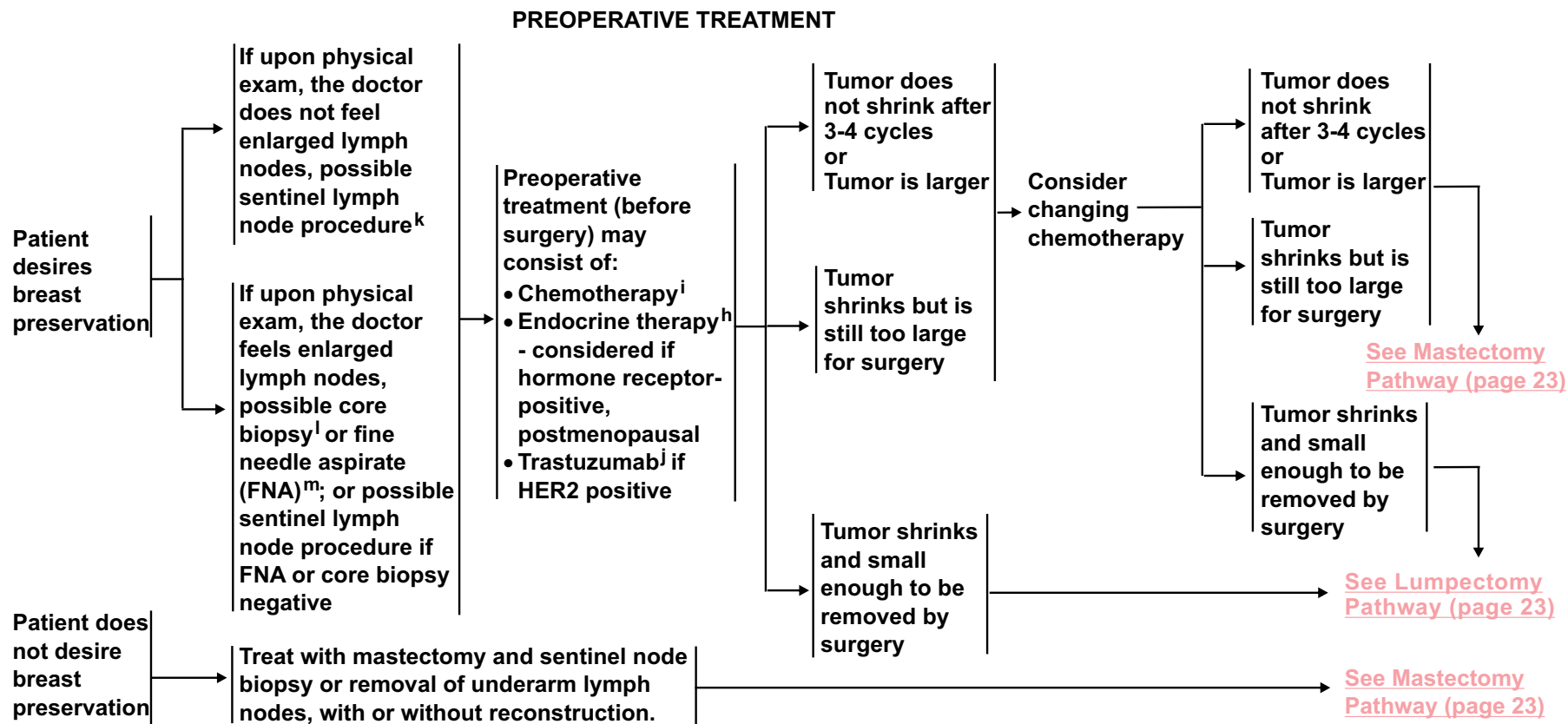
^aThe use of PET or PET/CT scanning is not indicated in the staging of clinical stage I, II, or operable III breast cancer.

^bEstrogen receptor test: A lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated

^cHuman epidermal growth factor receptor 2 (HER2) is a protein involved in normal cell growth. It is found on some types of cancer cells, including breast and ovarian cancers. Cancer cells removed from the body may be tested for the presence of HER2 to help decide the best type of treatment. HER2-positive breast cancer is a breast cancer that tests positive for the protein. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. Whenever breast cancer recurs or spreads, the cancer cells should be retested for HER2 when possible as well as for hormone receptor status, as these can change from the original cancer in up to 20 to 30 % of cases.

NCCN Guidelines for Patients™: Breast Cancer

Large Stage II or Stage IIIA Preoperative Chemotherapy Guideline (For more detailed information, [see page 71](#))



^hEndocrine therapy is used to slow or stop the growth of cancers in patients with hormone receptor-positive disease. Synthetic hormones or other drugs may be given to block the body's natural hormones. Also called hormonal therapy, hormone therapy, and hormone treatment.

ⁱIf adjuvant therapy consists of chemotherapy and endocrine (hormonal) therapy, they should be given sequentially with the chemotherapy first followed by endocrine therapy.

^jA monoclonal antibody that binds to HER2 (human epidermal growth factor receptor 2), and can destroy HER2-positive cancer cells. Monoclonal antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Trastuzumab is used to treat breast cancer that is HER2-positive and has spread after treatment with other drugs. It is also used with other anticancer drugs to treat HER2-positive breast cancer after surgery. Also called Herceptin.

^kSentinel lymph node biopsy: removal and examination of the sentinel node(s) (the first lymph node(s) to which cancer cells are likely to spread from a primary tumor). To identify the sentinel lymph node(s), the surgeon injects a radioactive substance, blue dye, or both near the tumor. The surgeon then uses a probe to find the sentinel lymph node(s) containing the radioactive substance or looks for the lymph node(s) stained with dye. The surgeon then removes the sentinel node(s) to check for the presence of cancer cells.

^lCore biopsy: removal of tissue sample with a wide needle for examination under a microscope. Also called core needle biopsy.

^mFine needle aspiration: removal of tissue or fluid with a thin needle for examination under a microscope. Also called FNA.

NCCN Guidelines for Patients™: Breast Cancer

Large Stage II or Stage IIIA Preoperative Chemotherapy Guideline (For more detailed information, [see pages 71-72](#))

PRIMARY LOCAL TREATMENT

ADJUVANT (ADDITIONAL) TREATMENT^d

Mastectomy with underarm lymph node removal, with or without reconstruction. Removal of underarm nodes may be omitted if sentinel node biopsy done prechemotherapy finds no cancer

→ **Consider additional chemotherapy on a clinical trial**

-
- **Adjuvant radiation therapy post-mastectomy is based on prechemotherapy tumor characteristics as per [page 14](#) and**
 - **Endocrine therapy if ER-positive and/or PR-positive^{h,i}**
 - **Complete up to 1 year of trastuzumab^j therapy if HER2-positive**

→ **See Follow-up ([page 26](#))**

Lumpectomy with lymph node removal, with or without reconstruction. Removal of underarm nodes may be omitted if sentinel node biopsy done and prechemotherapy finds no cancer

→ **Consider additional chemotherapy on a clinical trial**

-
- **Adjuvant radiation therapy post-lumpectomy based on prechemotherapy tumor characteristics as per [page 13](#) and**
 - **Endocrine therapy if ER-positive and/or PR-positive^{h,i}**
 - **Complete up to one year of trastuzumab^j therapy if HER2-positive**

^dAdditional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, or targeted therapy.

^hEndocrine therapy is used to slow or stop the growth of cancers in patients with hormone receptor-positive disease. Synthetic hormones or other drugs may be given to block the body's natural hormones. Also called hormonal therapy, hormone therapy, and hormone treatment.

ⁱIf adjuvant therapy consists of chemotherapy and endocrine (hormonal) therapy, the chemotherapy should be given first followed by endocrine therapy.

^jA monoclonal antibody that binds to HER2 (human epidermal growth factor receptor 2), and can kill HER2-positive cancer cells. Monoclonal antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Trastuzumab is used to treat breast cancer that is HER2-positive and has spread after treatment with other drugs. It is also used with other anticancer drugs to treat HER2-positive breast cancer after surgery. Also called Herceptin.

NCCN Guidelines for Patients™: Breast Cancer

Stage III Locally Advanced Preoperative Chemotherapy Guideline (For more detailed information, [see page 72](#))

CLINICAL STAGE

WORKUP

Tumor growing into chest wall or skin, or enlarged lymph nodes evident on physical exam

Stage IIIA
(except patients who are stage IIIA with T3, N1, M0)

Stage IIIB

Stage IIIC

- Medical history and physical exam to assess general health and symptoms
- Complete blood count (CBC) and platelets - A test to check the number of red blood cells, white blood cells, and platelets in a sample of blood
- Other lab tests
- Chest imaging
- Diagnostic bilateral (both breasts) mammogram, ultrasound as needed
- Pathology review of biopsy sample - Description of cells and tissues made by a pathologist based on microscopic evidence
- Prechemotherapy determination of tumor estrogen/progesterone receptor (ER/PR) status^b and HER2 status^c
- Genetic counseling if patient is high risk for hereditary breast cancer

Additional studies if clinical stage IIIA (T3, N1, M0) or as directed by symptoms or other abnormal staging studies:

- Breast MRI
- Bone scan
- Possible abdominal with or without pelvis CT scan or ultrasound or MRI
- Possible PET/CT scan

[See Preoperative Chemotherapy and Locoregional Treatment \(page 25\)](#)

^bEstrogen receptor test: a lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated

^cHuman epidermal growth factor receptor 2 (HER2) is a protein involved in normal cell growth. It is found on some types of cancer cells, including breast and ovarian cancers. Cancer cells removed from the body may be tested for the presence of HER2 to help decide the best type of treatment. HER2-positive breast cancer is a breast cancer that tests positive for the protein. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. Whenever breast cancer recurs or spreads, the cancer cells should be retested for HER2 when possible as well as for hormone receptor status, as these can change from the original cancer in up to 20% to 30% of cases.

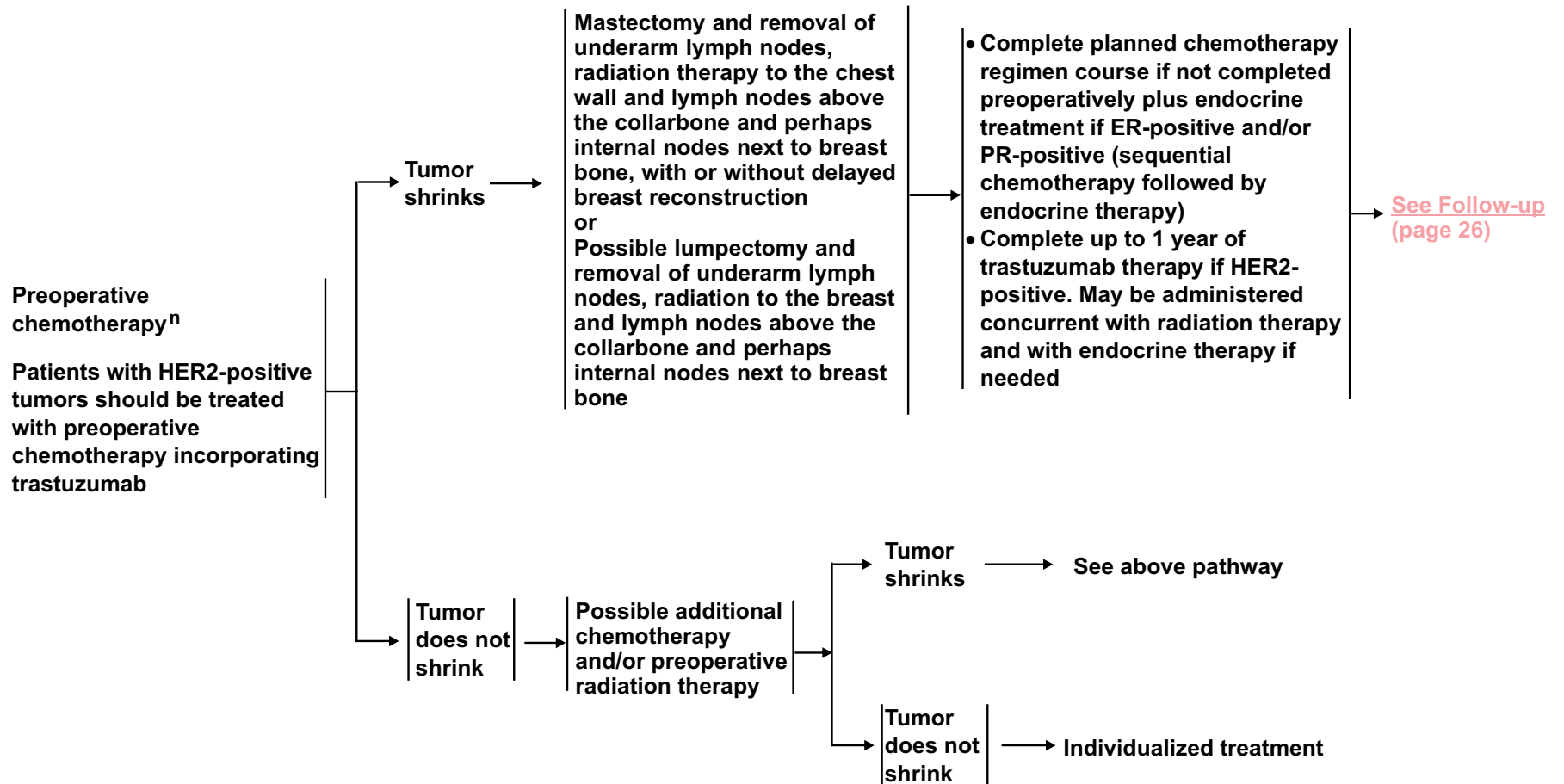
NCCN Guidelines for Patients™: Breast Cancer

Stage III Locally Advanced Preoperative Chemotherapy Guideline (For more detailed information, [see page 72-73](#))

PREOPERATIVE TREATMENT

PRIMARY LOCAL TREATMENT

ADJUVANT (ADDITIONAL) TREATMENT



ⁿA number of combination and single agent chemotherapy regimens have activity in the preoperative setting.

NCCN Guidelines for Patients™: Breast Cancer

Follow-Up, Recurrence Workup or Initial Workup for Stage IV Disease (For more detailed information, [see page 73](#))

FOLLOW-UP

- History and physical exam every 4-6 mo for 5 y, then every 12 mo
- Mammogram every 12 mo (and 6-12 mo post-radiation therapy if breast conserved)
- Women on tamoxifen: annual gynecologic assessment every 12 mo if uterus present
- Women on an aromatase inhibitor or who experience early menopause with treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter
- Assess and encourage adherence to adjuvant endocrine therapy

RECURRENT WORKUP or INITIAL WORKUP FOR STAGE IV DISEASE

- Medical history and physical exam to assess general health and symptoms
- Complete blood count (CBC) and platelets: a test to check the number of red blood cells, white blood cells, and platelets in a sample of blood
- Lab tests
- Chest imaging
- Bone scan
- X-ray of bones that hurt and weight-bearing bones that are abnormal on bone scan
- Abdominal CT or MRI may be recommended
- Biopsy of suspected recurrence if possible
- Determination of tumor estrogen/progesterone receptor (ER/PR) status^b and HER2 status if not known, hormone receptor previously negative, or HER2-negative^c
- Genetic counseling if patient is high risk for hereditary breast cancer

Local recurrence
(cancer came back
in breast, underarm
lymph nodes, or
nearby tissues)

Systemic recurrence
or presenting with
advanced cancer
(Stage IV cancer
spread to other
organs of the body)

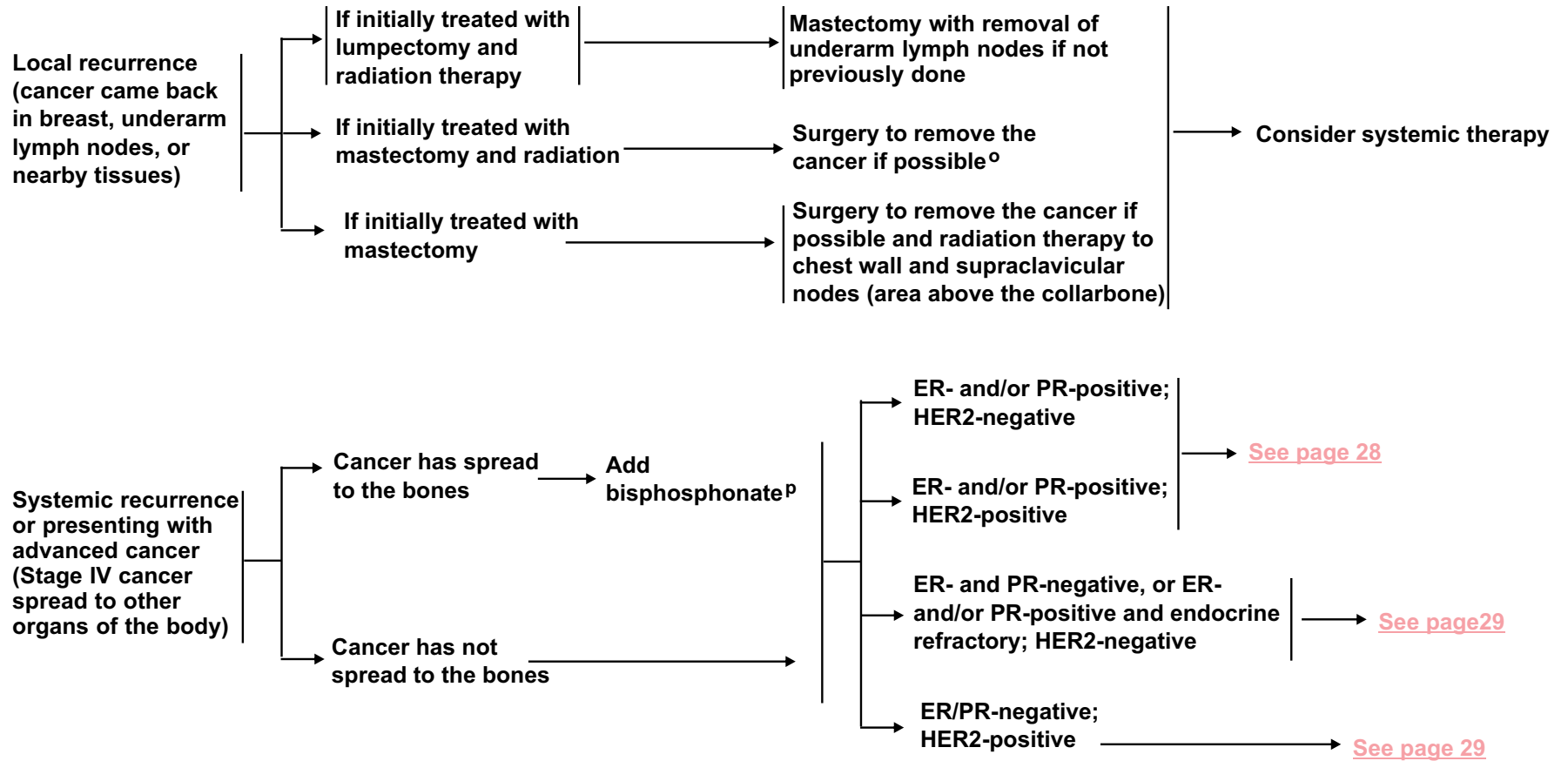
[See Treatment
of Recurrence/
Stage IV Disease
\(page 27\)](#)

^bEstrogen receptor test: a lab test to find out if cancer cells have estrogen receptors (proteins to which estrogen will bind). If the cells have estrogen receptors, they may need estrogen to grow, and this may affect how the cancer is treated.

^cHuman epidermal growth factor receptor 2 (HER2) is a protein involved in normal cell growth. It is found on some types of cancer cells, including breast and ovarian cancers. Cancer cells removed from the body may be tested for the presence of HER2 to help decide the best type of treatment. HER2-positive breast cancer is a breast cancer that tests positive for the protein. HER2-positive breast cancers tend to be more aggressive than other types of breast cancer. Whenever breast cancer recurs or spreads, the cancer cells should be retested for HER2 when possible as well as for hormone receptor status, as these can change from the original cancer in up to 20% to 30% of cases.

NCCN Guidelines for Patients™: Breast Cancer

Treatment of Recurrence or Stage IV Disease (For more detailed information, [see page 73](#))



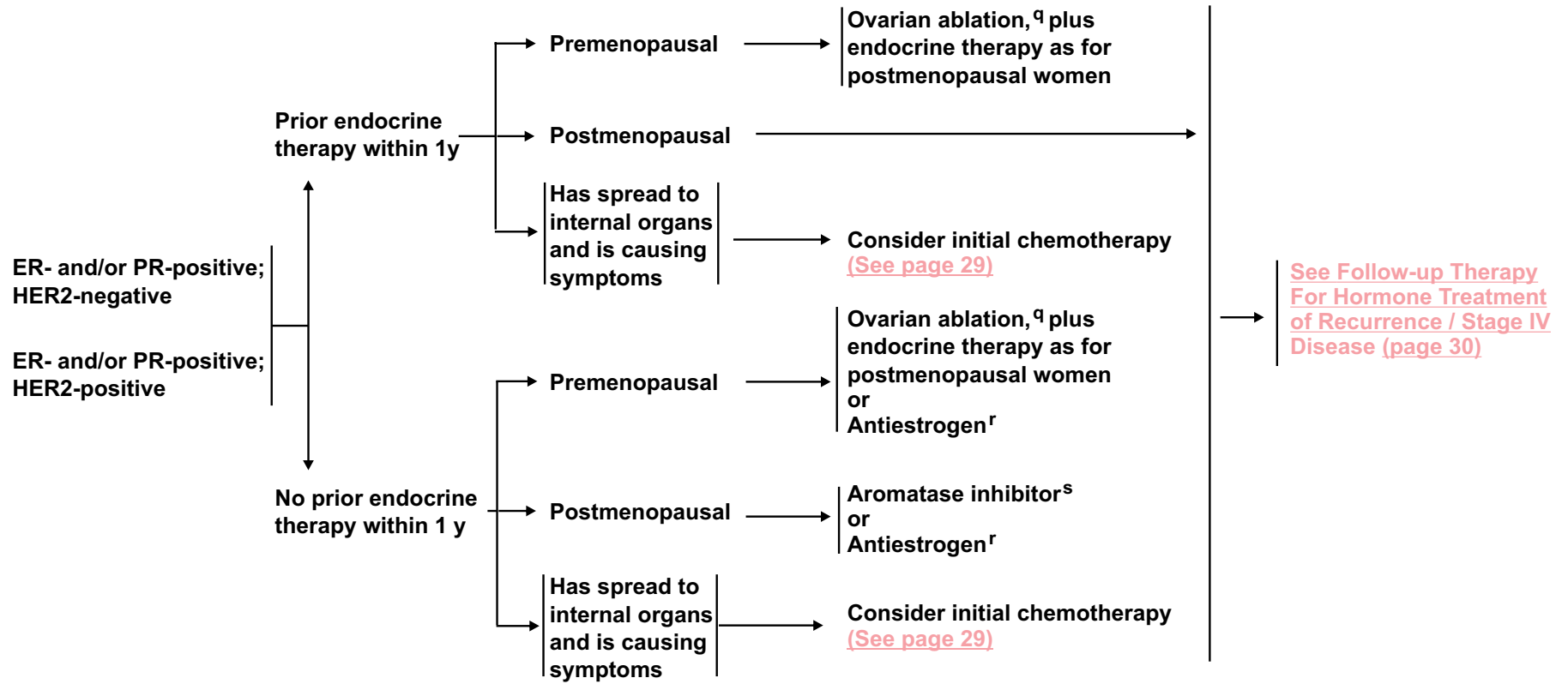
^oIf not technically resectable, consider systemic therapy to best response, then resect if possible.

^PA drug or substance used to treat bone pain caused by some types of cancer. Patients should undergo a dental examination with preventive dentistry prior to initiation of bisphosphonate therapy.

NCCN Guidelines for Patients™: Breast Cancer

Treatment of Recurrence or Stage IV Disease (For more detailed information, [see page 74](#))

ER- and/or PR-POSITIVE; HER2-NEGATIVE OR POSITIVE



^qSurgery, radiation therapy, or a drug treatment to stop the functioning of the ovaries. Also called ovarian suppression

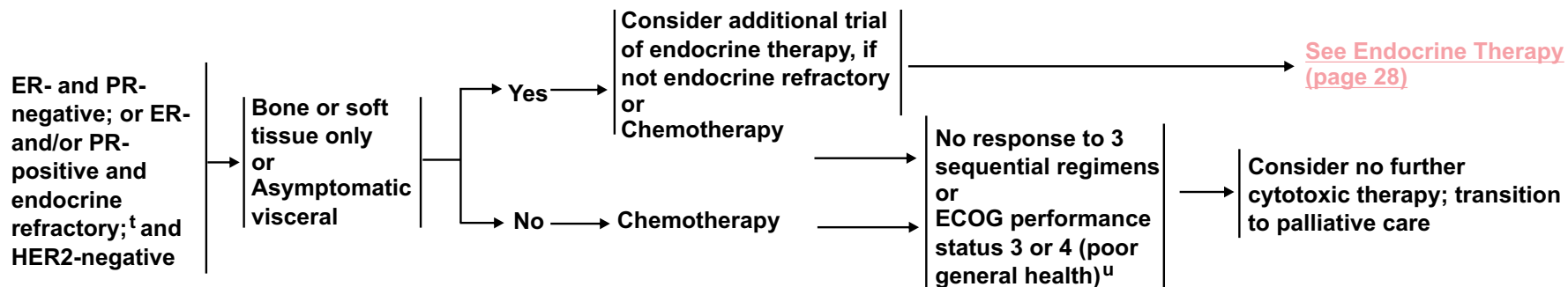
^rAntiestrogens may stop some cancer cells from growing and are used to prevent and treat breast cancer. They are also being studied in the treatment of other types of cancer. An antiestrogen is a type of hormone antagonist. Also called estrogen blocker.

^sAromatase inhibitors are drugs that prevent the formation of estradiol, a female hormone, by interfering with an aromatase enzyme. Aromatase inhibitors are used as a type of hormone therapy for postmenopausal women who have hormone-dependent breast cancer.

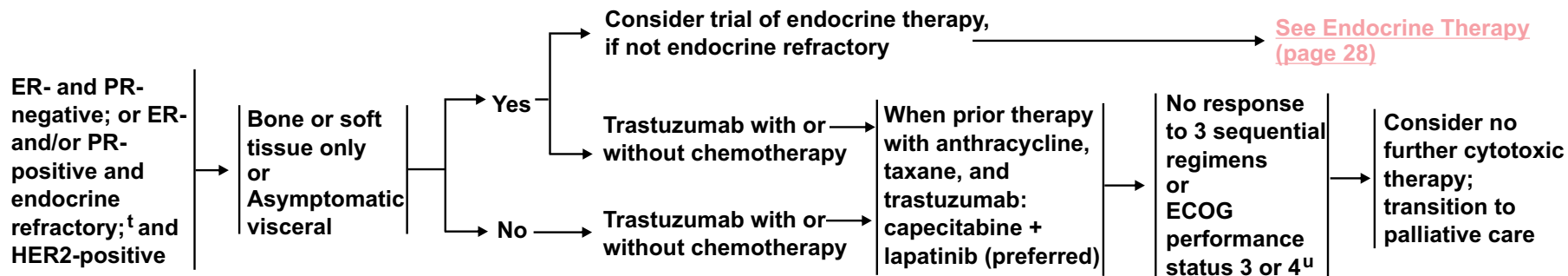
NCCN Guidelines for Patients™: Breast Cancer

Treatment of Recurrence or Stage IV Disease (For more detailed information, [see page 74](#))

ER- and PR-NEGATIVE; or ER- and/or PR-POSITIVE and ENDOCRINE REFRACTORY; HER2-NEGATIVE



ER- and PR-NEGATIVE; or ER- and/or PR-POSITIVE and ENDOCRINE REFRACTORY; and HER2-POSITIVE



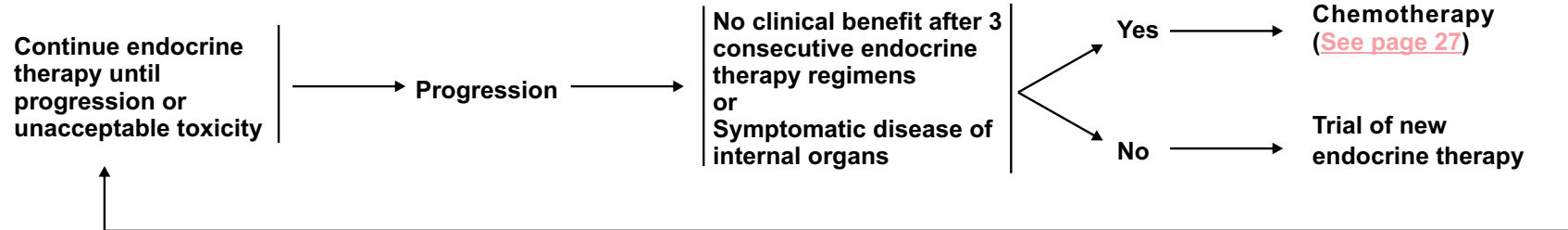
†Cancer that does not respond to endocrine treatment. The cancer may be resistant at the beginning of treatment or it may become resistant during treatment. Also called hormone resistant cancer.

^uECOG performance status 3:Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.

ECOG performance status 4:Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair.

NCCN Guidelines for Patients™: **Breast Cancer**

Follow-Up Therapy for Endocrine Treatment of Recurrence or Stage IV Disease
(For more detailed information, [see page 74](#))



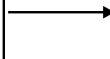
NCCN Guidelines for Patients™: Breast Cancer

Inflammatory Breast Cancer (IBC) (For more detailed information, [see page 76](#))

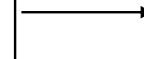
CLINICAL STAGE

WORKUP

Diagnosis of inflammatory breast cancer (IBC)^v
Stage T4, N0-N3, M0



- Medical history and physical exam to assess general health and symptoms
- Complete blood count (CBC) and platelets: a test to check the number of red blood cells, white blood cells, and platelets in a sample of blood
- Lab tests
- Chest imaging if lung symptoms are present
- Diagnostic bilateral (both breasts) mammogram, ultrasound as needed
- Pathology review of biopsy sample: description of cells and tissues made by a pathologist based on microscopic evidence
- Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status
- Breast MRI (optional)
- Bone scan
- Possible abdominal with or without pelvis CT scan or ultrasound or MRI
- Possible PET/CT scan
- Genetic counseling if patient is high risk for hereditary

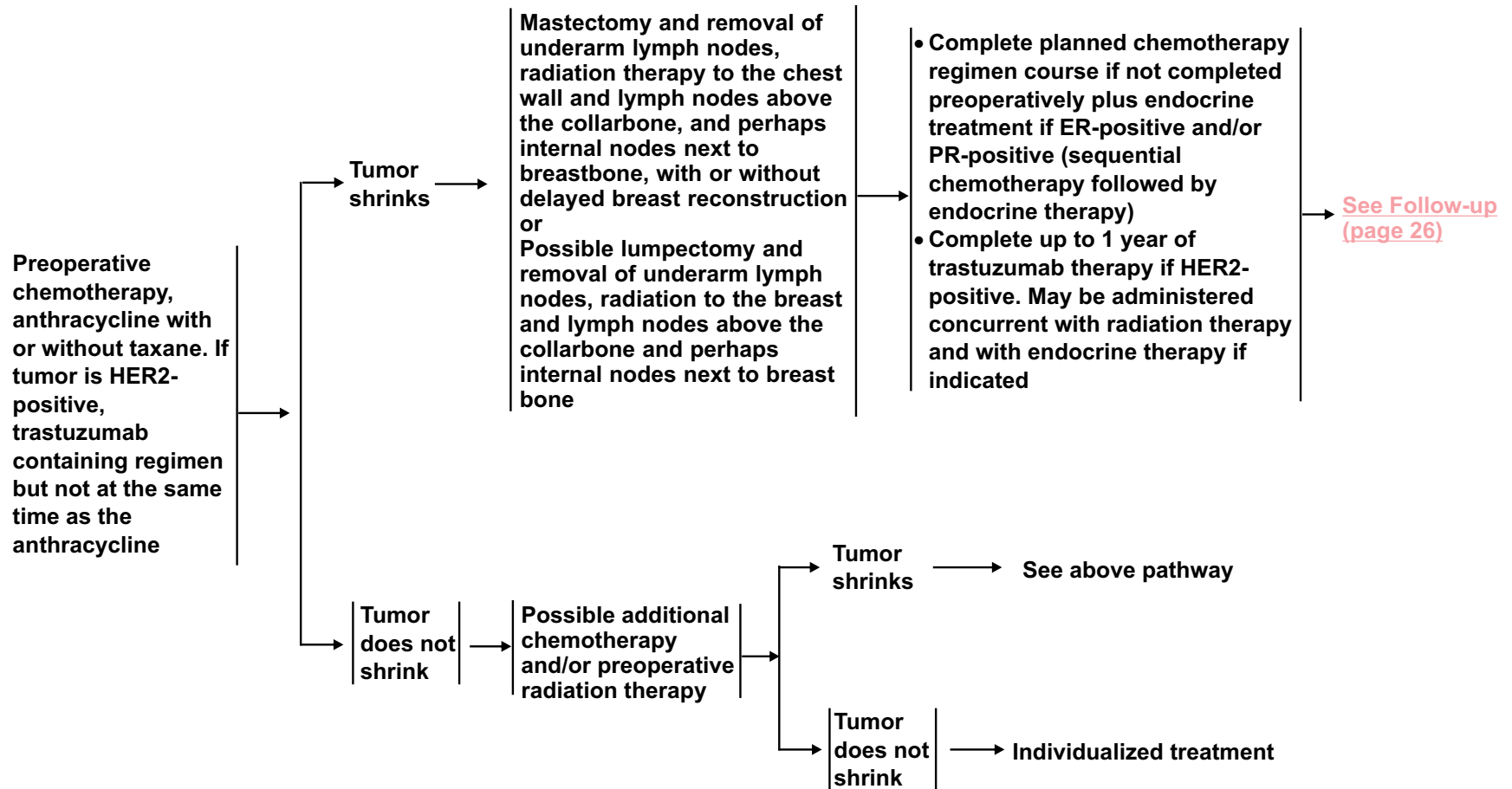


[See Treatment \(page 32\)](#)

^vInflammatory breast cancer is a type of breast cancer in which the breast looks red and swollen, and feels warm. The skin of the breast may also show the pitted appearance called peau d'orange (like the skin of an orange). The redness and warmth occur because the cancer cells block the lymph vessels in the skin.

NCCN Guidelines for Patients™: Breast Cancer

Inflammatory Breast Cancer (IBC) Treatment (For more detailed information, [see page 76](#))



WHAT IS BREAST CANCER?

Breast cancer is the most common cancer in women and is second only to lung cancer as the cause of cancer-related death in women. Although the number of women diagnosed with breast cancer has risen over the past several decades, the number of deaths from the disease has declined because of early diagnosis and better treatments.

Breast cancer begins in the cells of the body. Normal cells in the body “know” to stop growing and dividing when they have developed fully, but cancer cells do not. Normal cells also stay in one part of the body and do not spread to other sites. In breast cancer, cells keep growing and dividing. Thus, abnormal tissue grows in the breast and forms a *tumor*. This abnormal tissue can also spread and invade other organs in the body, a process called *metastasis*. These two characteristics are what make cancer dangerous. Cancer cells may grow and form tumors that can replace or distort normal tissue both in the breast and in other parts of the body, like the liver, lungs, or bone.

Breast cancer usually occurs in the *lobules* of the breast, where milk is produced, or in the *ducts*, which drain milk from the breast. In the United States, breast cancer occurs most frequently in women who have gone through *menopause*; however, it can occur at any age. Breast cancer may occur in men, but it is rare.

The breast also contains blood vessels and *lymphatic vessels*. Blood vessels supply nourishment to the breast tissue and remove waste products. Lymphatic vessels carry a clear fluid, *lymph*, that contains fat, tissue waste products, and immune cells. These small blood vessels and lymph vessels are found throughout the breast. In cancer, some cancer cells can be carried across the vessel walls and spread to other parts of the body.

The lymph vessels transport clear fluid, called *lymphatic fluid*, which may first go to *lymph nodes* located under the arm (*axillary lymph nodes*). Lymph may also go to lymph nodes above the collarbone (*supraclavicular lymph nodes*) and below the breast bone (internal mammary lymph nodes). Lymph nodes are small, bean-shaped collections of immune system cells that are important in fighting infections. Lymph nodes are important in cancer because they are usually the first place where cancer spreads. When breast cancer cells reach the underarm lymph nodes, they can continue to grow, often causing swelling of the lymph nodes in the armpit or elsewhere.

Cancer cells may also enter blood vessels and spread through the bloodstream to other parts of the body (metastasis).

Causes of Breast Cancer

The actual cause of breast cancer is unknown. However, a number of factors are known to increase the risk for breast cancer. The most common risk factors for breast cancer are being a woman and increasing age. Other risk factors are:

- a family history of breast cancer, especially if it was diagnosed at a young age,
- beginning monthly periods at an early age,
- entering menopause at a late age,
- prolonged *hormone replacement therapy*, or
- relatively late childbearing.

Women with a strong family history of breast cancer may wish to discuss evaluating their personal risk and consider starting breast cancer risk reduction therapy. For further information regarding breast cancer risk reduction, see the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Breast Cancer Risk Reduction, available at NCCN.org.

TYPES OF BREAST CANCER

Breast cancer is an abnormal growth in the cells that normally line the ducts that carry milk to the nipple and the lobules where milk is made. Breast cancer is classified by whether the cancer started in the ducts or lobules, whether it has grown or spread through the duct or lobule, and how the cancer cells look under a microscope. Breast cancers are broadly grouped into those that are still in the breast lobules or ducts (called “noninvasive” or “*carcinoma in situ*”) and those that have started to grow and spread beyond the walls of the ducts or lobules (“infiltrating” or “invasive”). It is common for a single breast tumor to have areas with both of these elements; in other words, a mixture of noninvasive and invasive cancer.

Carcinoma In Situ

Carcinoma is another word for cancer; *carcinoma in situ* means that the cancer is a very early cancer, is still confined to the ducts or lobules where it started, and has not spread into surrounding fatty tissues of the breast or to other organs. There are 2 types of breast *carcinoma in situ*:

- **Lobular carcinoma in situ (LCIS):** Also called lobular neoplasia. In LCIS, the cancer began in the lobules and has not grown through the lobule walls. Breast cancer specialists do not think that LCIS becomes an invasive cancer, but women with this condition do run a higher risk of developing an invasive cancer in either breast.
- **Ductal carcinoma in situ (DCIS):** This is the most common type of noninvasive breast cancer. In DCIS, cancer cells inside the ducts do not spread through the ductal walls into the fatty tissue of the breast. DCIS is treated with surgery and sometimes radiation, which usually cures the cancer. If not treated, DCIS will likely progress and become an invasive cancer.

Invasive Breast Cancers

Invasive cancer is cancer that has spread beyond the breast tissue where it started and into surrounding healthy breast tissue. In some cases, it may also have spread to lymph nodes in or near the breast. Invasive breast cancers are divided into different types, depending on the specific type of cells forming the cancer and how the cancer cells look under the microscope. They are also categorized according to how closely they resemble normal cells. This is called the *grade*, which helps predict whether the patient has a good or poor *prognosis* (outlook).

BREAST CANCER WORKUP

Evaluating a Breast Lump or Abnormal Mammogram Finding

An evaluation of a breast lump or an abnormal *mammogram* finding includes a thorough medical history, physical examination, and breast *imaging*, including a mammogram. A *biopsy* is needed for a suspicious finding, though these often prove to be *benign* (i.e., not cancer). If cancer is found, other *x-rays* and blood tests are needed. Exactly which tests will be ordered depends on the type of cancer, and if and where it has spread. These sections provide a summary of the steps, tests, and types of biopsy that may be suggested.

Identification of Breast Cancer

Mammogram: For many women over 40 years of age, an abnormal screening mammogram is the first indication of a possible breast cancer. A mammogram uses x-rays to look at breast tissue. There are two types of mammograms: *screening mammograms* and *diagnostic mammograms*. Screening mammograms usually take two views of the breast and try to identify breast cancer at its earliest, most curable stage. *Radiologists*, doctors with specialized training in evaluating mammography images, review the mammogram and report the findings to the ordering physician using a standardized scale that states whether the radiologist believes the mammogram is normal, uncertain, or cancer. Based on this result, the treating physician may recommend either normal follow up or additional testing.

Only about 90 percent of breast cancers are visible on mammograms. If the doctor is suspicious of an abnormality he or she noticed on examination, additional testing, such as *ultrasound* or *magnetic resonance imaging* (MRI), may be recommended.

Additionally, either the woman or a doctor or nurse may note a change in the breast, such as a lump or thickening. After these findings, the patient will undergo further testing to gather more information.

Clinical Exam: Generally, the physician will examine the patient's breasts in specific ways to see whether there is a lump or thickening that seems different from normal breast tissue. The doctor will also check for enlarged lymph nodes in the armpit and around the collarbone, and check for any obvious signs that the cancer has spread.

Medical History: The doctor will ask questions about the general health of the patient, any symptoms she may have noticed, and whether other family members have a history of cancer. If there is a family history, the physician will ask what types of cancer relatives had and at what ages the diagnosis was made.

Diagnostic Mammogram of Both Breasts: If a screening mammogram or clinical breast exam reveals an abnormality, a diagnostic mammogram will be ordered to visualize the breast more thoroughly and to provide more accurate information about the probable size and other characteristics of the tumor. A diagnostic mammogram will add extra views of the breast by squeezing it in different ways and taking more x-rays. If the diagnostic mammogram does not provide enough information to make a decision about whether a biopsy is needed, other tests may be necessary.

NCCN Guidelines for Patients™: Breast Cancer

Discussion Version 2010

Other Imaging Studies: Ultrasound is a test that uses high-frequency sound waves to construct images of the inside of the breast to evaluate a suspicious area. It is especially useful to differentiate between a solid mass, which is more likely to be cancer, and a fluid filled *cyst*, which is less likely to be cancer.

An MRI uses strong magnets and a computer to look inside the breast to provide more information about the size and extent of a possible breast cancer. MRI is used to evaluate changes in the breast that cannot be seen well in a mammogram either because of the *breast density* or the type of change in the breast is not one that can be seen on mammograms, such as lobular breast cancer. MRI is also used to determine the exact location of a tumor when it is not clear from the mammogram. MRI also serves as a backup imaging technique when the results of the mammogram and ultrasound are not clear.

A breast MRI uses an injection of a *contrast material* so abnormal areas of the breast are easier to see; however, the contrast can also highlight abnormalities that are not cancer. For this reason, MRI is usually reserved for women who either have a very high risk of cancer or who have been diagnosed with cancer.

Breast Biopsy

To determine whether an abnormal area is cancerous, the doctor must do a biopsy for examination by a *pathologist*, a physician who specializes in looking at tissue under a microscope to identify disease. Regardless of the type of biopsy, the doctor will numb the area to make the removal of the sample tissue as painless as possible. The tumor specimen will then be sent to the pathologist for evaluation. The process of preparing the tissue for examination, evaluating it, and reporting back to the doctor usually takes at least 1 or 2 days.

Most often the sample of tissue for the biopsy is removed with a needle placed into the suspicious area through the skin, commonly referred to as a *needle biopsy*. A *core needle biopsy* is the most common technique and extracts a small cylinder of tissue from the mass. A *fine-needle aspiration* is less common and provides a smaller tissue sample and is often used to remove fluid from a cyst to check for cancerous cells in the fluid. The core needle biopsy provides a larger tissue sample for testing and is generally preferred over the surgical *excisional biopsy* because it can be done quickly and with little discomfort. A needle biopsy allows a patient to make informed decisions regarding further treatment before undergoing surgery.

If the doctor can feel a lump, a needle biopsy can be done in the doctor's office. If the area to be biopsied cannot be readily located by touch, the doctor will use an imaging technique such as mammography or ultrasound to help locate the suspicious area. When mammography is used to guide the biopsy, it is called a stereotactic needle biopsy. The image on the mammogram guides the doctor in placing the needle in the right spot. *Ultrasound-guided biopsy* works similarly with the ultrasound image being used to identify where to place the needle.

Sometimes an excisional biopsy surgically removing breast tissue with a scalpel, is used if the doctor feels it is necessary to provide a larger sample of tissue for pathologic analysis. In this case, the surgeon often removes the entire suspicious area along with an area of surrounding normal tissue, called a margin. If the surgeon cannot feel a lump, a wire is inserted into the location of the suspicious area using mammography. This is called a *wire localization biopsy* and is usually done under local anesthesia in an outpatient procedure.

Many women report experiencing anxiety before and after their biopsy while waiting for the results. If the doctors and nurses are aware of their anxiety, they may be able to offer strategies to alleviate it. Some people find physical exercise, talking with family or friends, or activities that distract them helpful; others are helped by medication.

The Pathology Report

Every time a biopsy is taken or surgery is performed, the specimen will be reviewed by a pathologist. The biopsy specimen will be fixed and embedded in a waxy material so that it can be cut into very thin sections, which are then stained to increase the contrast between different parts of the cell and among the cells themselves. These sections are then put on glass slides and examined under a microscope. The pathologist examines the slides and develops a report, called a pathology report, that will be sent to the doctor providing information about the tissue sample.

The report from the pathologist will have several parts. First, and most important, the pathology report will tell whether cancer was present in the specimen and, if so, what type. It will also state whether the cancer is noninvasive or invasive and the cell type where the cancer started. Common types are ductal, lobular, and nipple; each of these has subcategories. The tumor will also be assigned a grade from 1 to 3; grade 1 indicates that the cells are most like those in normal breast tissue, while grade 3 indicates that the cells are least like normal breast tissue. Lobular cancers may not be given a grade. In general, higher-grade tumors are more aggressive than lower-grade tumors. The tumor will also be tested for *estrogen receptors* and *progesterone receptors*, and whether high levels of the HER2 receptor or HER2 gene are present. These *markers* will be used to determine the type of treatment that is most likely to be effective.

It is a good idea to ask for a copy of the pathology report. The patient may also want to discuss it with their doctor or nurse to make sure they understand what it says and how it will be used to help make treatment decisions.

If the biopsy was performed using a needle biopsy, the pathology report will not tell how large the tumor is.

Usually, there are at least two reports: the first evaluating the biopsy specimen and a second examining the tissue removed during surgery for treatment. Additional reports may be added if additional surgery is needed, for example, to make sure that an area of normal tissue was removed all around the tumor.

Other Tests after Cancer Has Been Diagnosed

If the breast biopsy results show that cancer is present, the doctor may decide to order other tests to determine if the cancer has *metastasized* and help determine which treatments would be the most appropriate. Most women with breast cancer do not need extensive testing. However, based on the tumor size, whether lymph nodes appear to be involved, and whether there appears to be any obvious sign of spread, additional tests may be ordered. These tests may include:

Laboratory Tests: Some *laboratory tests* are needed to plan surgery, look for evidence of *metastases*, and plan treatment after surgery. These tests require blood to be taken. They include:

- **Complete blood count.** This test counts the different types of cells in the blood and determines whether the percentage of each type is normal. This test is repeated frequently, particularly if *chemotherapy* is needed because it provides information about whether the patient has enough red blood cells to carry oxygen to the tissues, white blood cells to fight infections, and platelets to make clots needed for wound healing.
- **Blood chemicals and enzyme tests.** These tests are done in patients with invasive breast cancer (not needed with *in situ* cancer) and look for signs of abnormal activity in other organs. Abnormal results may prompt the doctor to order other tests, such as bone scan or *computerized tomography (CT) scan*, to determine whether the cancer has spread to those organs.

Bone Scan: A bone scan may provide information about spread of breast cancer to the bone. However, many changes that appear on a bone scan are not cancer. In early stage disease, this test is used only if there is some reason to think that cancer may have spread to the bone, such as changes in blood chemistry tests or bone pain. A bone scan may be ordered if the cancer is locally advanced, which means that it has spread from where it started into nearby tissues and possibly lymph nodes, and should be done if the cancer has spread to other organs. The test consists of an intravenous injection of a radioactive substance. Several hours later, a scan will be done to determine whether there are areas of new bone formation, indicating possible spread of cancer to the bone.

Computerized Tomography Scans: Computerized tomography (CT) scans are done to determine if cancer has spread to other organs. If the cancer is early stage breast cancer, a CT scan is not needed. However, if the cancer appears more advanced, a CT of the abdomen and/or chest may be done to see whether the cancer has spread. CT scans take multiple x-rays of the same part of the body from different angles to provide detailed pictures of internal organs. Except for the injection of intravenous dye, necessary for most patients, this is a painless procedure.

MRI: MRI uses strong magnets and a computer to look inside the body and produce detailed images of the organs without using x-rays. MRI is useful in looking at the brain and spinal cord and in examining any specific area of the bone. It may also be used if the results of other imaging tests are unclear or if there is concern about exposure to radiation from other scans. Routine MRIs for all patients with breast cancer are not helpful and not needed.

Positron Emission Tomography Scans: *Positron emission tomography* (PET) scans use a form of sugar (glucose) that contains a radioactive atom. A small amount of the radioactive material is injected into an arm. The patient is then put into the PET machine where a special camera can detect the radioactivity. Because of the high amount of energy that breast cancer cells use, areas of cancer in the body absorb large amounts of the radioactive sugar. Newer devices combine PET scans and CT scans. Although this test can find cancer that has metastasized, a number of normal body activities also use large amounts of energy. As a result, false-positive results are common. A positive PET scan result should be verified by other imaging or biopsy.

Tumor Tests: Testing the tumor itself for certain receptors is an important step in deciding what treatment options are best for each woman's particular cancer. The pathology lab tests the cancer tissue that is removed, either from the first biopsy or the final surgery.

Estrogen and Progesterone Receptors: Estrogen and progesterone are hormones that are normally produced in a woman's body and stimulate the growth of normal breast tissue. In some types of breast cancer, these hormones also stimulate the growth of the tumor.

A breast cancer tumor will be tested for estrogen and progesterone receptors that may be found in tumor cells. If these receptors are present, the tumor is called estrogen receptor-positive and/or progesterone receptor-positive (or just hormone receptor-positive), and the hormones estrogen and progesterone can stimulate the growth of breast cancer cells. This is important because there are drugs that can block the effects of these hormones on the cancer cells to help stop tumor growth. Most patients with tumors that are estrogen receptor-positive and/or progesterone receptor-positive will take hormone therapy drugs to reduce the risk that their cancer will recur or progress and to help them live longer. If the tumor does not have these receptors, it is called estrogen receptor-negative and progesterone receptor-negative (or hormone receptor-negative), and hormonal therapies are not likely to be helpful.

In addition, hormone receptor-positive tumors tend to grow more slowly and are less likely to invade the lymph nodes.

Tumor cells are stained to visualize estrogen and progesterone receptors, and the test results are based on the percentage of cells that have the receptors. The higher the percentage of stained cells, the more strongly the tumor is estrogen receptor-positive and/or progesterone receptor-positive, and the more likely it is that the tumor needs hormones to grow.

DCIS and all invasive breast cancers should be tested for hormone receptors at the time of breast biopsy or surgery. Patients should ask their doctor for these test results and keep them for their records.

HER2

Breast cancers can be categorized as being HER2-positive or HER2-negative. HER2-positive breast cancer tends to be faster growing and is considered more aggressive. Studies indicate that the drug *trastuzumab* (Herceptin®) is effective in the treatment of HER2-positive early stage breast cancer and HER2-positive metastatic breast cancer (cancer that has spread to other parts of the body). Trastuzumab is not effective in the treatment of HER2-negative breast cancers.

Trastuzumab has been shown to be a very effective therapy in the treatment of women with HER2-positive early stage and metastatic breast cancer. However, it is a costly therapy which can have serious side effects. Therefore, it is especially important to have tests that accurately determine HER2 tumor status so that trastuzumab is only given to patients likely to benefit from it. If a HER2 test report indicates that a patient's tumor is HER2-positive when it is actually HER2-negative (referred to as a "false-positive"), the patient may be given trastuzumab, which is unlikely to be effective in treating the disease and may cause serious side effects. If a HER2 test report indicates that a patient's tumor is HER2-negative when it is HER2-positive (a "false-negative"), the treatment plan will not include trastuzumab and the treatment may not be as effective.

HER2 Tumor Status

About 15 to 20 percent of women with breast cancer have HER2-positive tumors. The HER2 protein is a receptor on the surface of the cell that sends messages to the cell to grow and divide more frequently. In normal, resting (non-dividing) cells, there are two copies of the HER2 gene. In contrast, in a HER2-positive breast cancer:

- The cell has more than the normal number of copies of the HER2 gene.
- The amount of HER2 protein in the cell increases, or is "overexpressed."
- The increased number of HER2 receptors on the surface of the cell sends more messages for the cell to grow and divide.
- Tumor growth can be very fast and the cancer is considered to be aggressive.

Testing

There are two methods of testing for HER2 tumor status in women with breast cancer: *immunohistochemistry* (IHC) and *fluorescence in situ hybridization* (FISH). Results from both tests are used by doctors to determine whether treatment with trastuzumab might be beneficial.

Immunohistochemistry

IHC is a protein-based test that is used to provide an assessment of the amount of HER2 protein receptors on the surface of the cancer cells. In HER2-positive tumors there is more than a normal amount of HER2 protein on the cell surface (i.e., there is HER2 protein “overexpression”).

The IHC test is done by a pathologist on a sample of a tumor removed during a biopsy, *lumpectomy*, or *mastectomy*.

The scoring for an IHC test ranges from 0 to 3+:

- 0 is HER2-negative
- 1+ is considered HER2-negative
- 2+ is considered a borderline or equivocal result
- 3+ is HER2-positive.

Fluorescence In Situ Hybridization

FISH is a gene-based test used to determine the number of HER2 genes in the cells of the tumor. In HER2-positive breast cancer, if there are too many copies of the HER2 gene, the gene is “amplified.” The FISH test is done by a pathologist on a sample of a tumor removed during a biopsy, lumpectomy, or mastectomy.

Another FISH procedure uses a similar procedure but measures only the average number of HER2 gene copies per cell; tumor samples with an average of more than 4 HER2 gene copies per cell are considered HER2-positive.

HER2 test results are interpreted as follows:

- HER2-positive status is IHC 3+ or FISH-positive
- HER2-negative status is IHC 0, 1+ or FISH-negative
- A borderline IHC result of 2+ should be followed by performing a FISH test.

Genetic Analysis of Tumor

Currently, treatment decisions are based primarily on hormone receptor status, HER2 status, appearance of the cancer under the microscope, size of the tumor, and extent of cancer spread. Recently, there has been interest in studying gene expression in breast cancer to determine if the tumors can be divided into good and poor prognosis tumors. This information has the potential to identify those patients whose breast cancers have not spread to the lymph nodes and who may not need additional chemotherapy. The NCCN Guidelines for Breast Cancer recommend a 21-gene test (onco^{type} DX[®]) because it has been tested and determined to be able to predict which women can safely undergo chemotherapy. This test is helpful for those who have node-negative, hormone receptor-positive tumors that are also HER2-negative; these tumors are the ones with the greatest potential to be at low risk for recurring. The results of the test indicate which patients are most likely to benefit from chemotherapy and which can safely go without.

Hormone receptor-negative tumors and those that are HER2-positive tend to be more aggressive and therefore at a higher risk for recurrence. For all but the very smallest of these tumors, chemotherapy is recommended. Thus, molecular testing adds expense without providing any information that would change treatment.

TYPES OF INVASIVE BREAST CANCER

Invasive Ductal Carcinoma

Invasive ductal carcinoma starts in a duct of the breast but then breaks through the wall of the duct and spreads into the fatty tissue of the breast. The cancer cells are then able to spread into lymphatic channels or blood vessels of the breast and into other parts of the body. About 80 percent of all breast cancers are invasive ductal carcinoma.

Invasive Lobular Carcinoma

Invasive lobular carcinoma starts in the milk-producing glands of the breast. Like invasive ductal carcinoma, this cancer can spread beyond the breast to other parts of the body. About 10 to 15 percent of invasive breast cancers are invasive lobular carcinomas.

Mixed Tumors

Mixed tumors are tumors that contain a variety of cell types, such as invasive ductal breast cancer combined with invasive lobular breast cancer. Mixed tumors are usually treated as an invasive ductal cancer.

Medullary Cancer

Medullary cancer is a special type of invasive ductal cancer that has a fairly well-defined boundary between tumor tissue and normal breast tissue. It also has a number of special features, including the presence of immune system cells at the edges of the tumor. It accounts for about 5% of all breast cancers and can be difficult to distinguish from the more common invasive ductal breast cancer. Most breast cancer specialists believe that medullary cancer is very rare, and that cancers categorized as medullary cancer should be treated as invasive ductal breast cancer.

Metaplastic Tumors

Metaplastic tumors are a very rare type of invasive ductal cancer. These tumors include cells that are normally not found in the breast, such as cells that look like skin cells (squamous cells) or cells that make bone. These tumors are treated similarly to invasive ductal cancer.

Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is a special type of breast cancer in that the cancer cells have spread to the lymph node channels in the skin of the breast. The skin of the affected breast is red, feels warm, and has the appearance of an orange peel. The affected breast may also become larger, firmer, tender, or itchy. IBC is often mistaken for infection in its early stages, and accounts for 1 to 3 percent of all breast cancers.

IBC has a higher chance of spreading and carries a worse prognosis than typical invasive ductal or invasive lobular cancers. IBC is always staged as stage IIIB unless it has already spread to other organs at the time of diagnosis, which would then make it stage IV (see System to Define Breast Cancer Stage, page 43).

Colloid Carcinoma

Colloid carcinoma, also called mucinous carcinoma, is a rare type of invasive ductal breast cancer and is formed by mucus-producing cancer cells. Colloid carcinoma has a better prognosis and a lower chance of metastasis than invasive lobular or invasive ductal cancers of the same size.

Tubular Carcinoma

Tubular carcinoma is a special type of invasive ductal breast carcinoma. About 2 percent of all breast cancers are tubular carcinomas. Women with this type of breast cancer have a better prognosis because the cancer is less likely to spread outside the breast than invasive lobular or invasive ductal cancers of the same size. The majority of tubular cancers are *hormone receptor-positive*, but HER2-negative (see Tumor Tests, page 38).

Breast Cancer Grade

A pathologist looks at the breast cancer cells under a microscope and judges its similarity to normal breast tissue. This determines the grade of the tumor. Cancers that closely resemble normal breast tissue have a lower number grade and tend to grow and spread more slowly. Cancers that do not have the features of normal breast tissue are considered high-grade. In general, a lower grade number indicates a cancer that is slightly less likely to spread, and a higher number indicates a cancer that is slightly more likely to spread.

The tumor grade is most important in patients with small tumors without lymph node involvement. Patients with well-differentiated tumors (meaning the cells in the tumor closely resemble normal cells in the breast) may require no further treatment, while patients with moderately- or poorly-differentiated tumors may receive further genetic testing of the tumor to determine its likelihood of recurring or receive additional hormonal therapy or chemotherapy.

DCIS is graded in a different way; it is given a nuclear grade, which describes how abnormal the nucleus of the cancer cells (the part that contains the genetic material) appears. Sometimes other features of DCIS are also used by the pathologist to determine the grade.

BREAST CANCER STAGES

Cancers are divided into different groups, called stages, based on whether the cancer is invasive or noninvasive, tumor size, how many lymph nodes are involved, and whether there is spread to other parts of the body.

Staging a cancer is the process of determining how far the cancer has spread when it is diagnosed. Medical oncologists determine the stage of a cancer by gathering information from physical examinations and tests on the tumor size, lymph nodes, and distant organs. Staging tables have been developed over time by oncologists examining information regarding thousands of patients with various combinations of disease characteristics and their outcomes. Using this information, staging tables group cancers according to probable outcome. A cancer's stage is therefore an important piece of information to predict the outcome and to select the most appropriate treatments. It is important to note that the stage is based on large numbers of patients and may not predict the prognosis for an individual person with breast cancer. Some people will do better than expected, others will do worse. In addition, other factors, such as age, general state of health, and HER2 and hormone receptor status of the tumor, are very important in determining the likely prognosis for each patient.

A patient should feel as if they can talk frankly with their oncologist about the cancer stage and prognosis, and how the stage and prognosis will affect treatment options.

System to Define Cancer Stage

The system most often used to describe the extent of breast cancer is the *TNM staging system*. In TNM staging, information about the tumor (T-stage), nearby lymph nodes (N-stage), and distant organ metastases (M-stage) is combined and a stage is assigned to specific TNM groupings. The TNM stage groupings are described using Roman numerals from 0 to IV.

The *clinical stage* is determined by what the doctor learns from the physical examination and tests. The *pathologic stage* includes the findings of the pathologist after surgery. Most of the time, pathologic stage is the most important stage since involvement of the lymph nodes can only be accurately determined by examining them under a microscope.

T stands for the size of the cancer (measured in centimeters: 2.54 cm = 1 inch) and whether it is growing directly into nearby tissues. N stands for spread to nearby lymph nodes, and M is for metastasis.

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Categories of T, N, and M

T Categories

T categories are based on the size of the cancer and whether it has spread to nearby tissue.

Tis: Tis is used only for carcinoma in situ or noninvasive breast cancer, such as DCIS or LCIS.

T1: The cancer is 2 cm in diameter (about $\frac{3}{4}$ inch) or smaller.

T2: The cancer is larger than 2 cm but not more than 5 cm in diameter.

T3: The cancer is larger than 5 cm in diameter.

T4: The cancer is any size and has spread to the chest wall or skin.

N Categories

The N category is based on which of the lymph nodes near the breast, if any, are affected by the cancer. There are 2 classifications used: 1) clinical, such as before surgery (what the doctor can feel or see on imaging studies), and 2) pathological, which is what the pathologist can see in lymph nodes removed at the time of surgery.

N0 clinical: The cancer has not spread to lymph nodes, based on clinical exam.

N0 pathological: The cancer has not spread to the lymph nodes, based on examining them under the microscope.

N1 clinical: The cancer has spread to the lymph nodes under the arm on the same side as the breast cancer. Lymph nodes are not attached to one another or to the surrounding tissue.

N1 pathological: The cancer is found in 1 to 3 lymph nodes under the arm.

N2 clinical: The cancer has spread to lymph nodes under the arm on the same side as the breast cancer and are attached to one another or the surrounding tissue, or the cancer has spread to the internal mammary lymph nodes (next to the sternum), but not to the lymph nodes under the arm.

N2 pathological: The cancer has spread to 4 to 9 lymph nodes under the arm.

N3 clinical: The cancer has spread to lymph nodes above or just below the collarbone on the same side as the cancer and may or may not have spread to lymph nodes under the arm. Or the cancer has spread to internal mammary lymph nodes and lymph nodes under the arm, both on the same side as the cancer.

N3 pathological: The cancer has spread to 10 or more lymph nodes under the arm or also involves lymph nodes in other areas around the breast.

M Categories

The M category depends on whether the cancer has spread to any distant tissues and organs.

M0: No distant cancer spread.

M1: Cancer has spread to distant organs.

STAGE GROUPING FOR BREAST CANCER

Once the T, N, and M categories have been assigned, this information is combined to assign an overall stage of 0, I, II, III or IV as seen in Table 1. The stages identify tumor types that have a similar prognosis and thus are treated in a similar way.

TABLE 1. BREAST CANCER STAGING

Overall Stage	T Category	N Category	M Category
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	Any N	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer Science and Business Media LLC, www.springer.com.

BREAST CANCER TREATMENT

Breast cancer treatment includes both *local therapy*, which is treatment of the breast itself, and drug treatment for cancer cells that may have metastasized to other parts of the body. Surgery alone or in combination with *radiation therapy* is used to treat cancer that is contained to the breast. Lymph nodes in the armpit are examined to determine if the breast cancer has spread. Drug treatments for cancer cells that may have spread beyond either of these sites are hormone therapy, chemotherapy, *targeted therapy*, or a combination of these based on how advanced the cancer is (i.e., what the cancer stage is) and the status of hormone and HER2 receptors.

Treatment of the Breast

Most patients with breast cancer will have surgery. Although patients are often anxious to get the surgery completed, it is generally safe to take time to think over the available treatment options and to make arrangements for surgery. This process can take up to 1 to 2 months without serious concern. The 2 common types of surgery patients will undergo are breast-conserving therapy (also known as *breast-conserving surgery*) and mastectomy.

Breast-Conserving Therapy

Lumpectomy removes the entire breast lump and the bordering normal breast tissue from around the tumor to ensure all the diseased tissue has been removed. If cancer cells are present at the outside edge of the specimen (called a positive margin), more surgery is usually needed to remove any remaining cancer. Most often this additional surgery is another lumpectomy but sometimes requires a mastectomy. The surgeon works with the pathologist to ensure that all visible signs of the cancer have been removed; however, small amounts that cannot be seen may be elsewhere in the breast. Following surgery, radiation therapy is used to kill any small amounts of cancer that may remain. Other surgical procedures, such as *partial* (or *segmental*) mastectomy or *quadrantectomy*, remove more breast tissue than a lumpectomy; however, these surgical procedures are still considered breast-conserving therapy and usually require radiation therapy to ensure that all cancer in the breast has been destroyed.

A number of *clinical trials* have demonstrated that breast-conserving therapy (lumpectomy and radiation therapy) is as effective as mastectomy for most women with stage I or II breast cancer; survival rates for these two approaches are the same.

Radiation therapy, as a part of breast-conserving therapy for invasive cancer, can sometimes be omitted. Women who may consider lumpectomy without radiation therapy have all of the following:

- are at least 70 years old;
- have a tumor smaller than 2 cm that has been completely removed;
- have a tumor that contains hormone receptors;
- there is no lymph node involvement; and
- receive treatment with hormone therapy.

However, some women are unable to have breast-conserving therapy. Reasons for having a mastectomy rather than breast-conserving therapy include:

- prior radiation therapy of the affected breast or chest;
- suspicious or malignant-appearing abnormalities that are widespread throughout the breast;
- multiple tumors in the breast that cannot be removed with a single incision;

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- women who have undergone a lumpectomy, including any possible repeat lumpectomies if needed, and whose cancer cannot be completely removed with a satisfactory cosmetic result;
- women with active connective tissue disease involving the skin (especially scleroderma or lupus) that makes body tissues especially sensitive to the side effects of radiation therapy;
- pregnant women who would require radiation therapy while still pregnant; and
- women with tumors larger than 5 cm (2 inches) that cannot be shrunk by treatment before surgery.

Generally, patients with tumors larger than 5 cm are not candidates for lumpectomy. However, those with larger tumors who, nevertheless, want a lumpectomy may first be treated with *preoperative chemotherapy*, sometimes referred to as *neoadjuvant therapy*, to shrink the tumor and to kill any cancer cells that may have spread beyond the tumor. Preoperative chemotherapy refers to cancer drugs that are given before surgery. The *medical oncologist* and surgeon work together to decide the best time for the surgery; this is sometimes a complex decision, and the doctors may suggest that surgery take place before completion of the planned chemotherapy. If this happens, chemotherapy should be completed after surgery. If the cancer does not respond to the first chemotherapy regimen, the medical oncologist may recommend trying a different *regimen* or suggest radiation therapy to the breast. Depending on tumor response to chemotherapy, the surgeon will perform either a lumpectomy or mastectomy. If a lumpectomy is possible, radiation therapy will most likely follow surgery. If a mastectomy is needed, radiation therapy may or may not be required.

Mastectomy

Modified radical mastectomy is the most common type of mastectomy performed today. In this surgery, the entire breast, including the skin, fat, and nipple is removed. However, the chest muscles are not removed so strength is preserved in the arm. Following a mastectomy, the breast is gone and there is a horizontal scar across the chest. Mastectomy is required in some cases, and some women choose mastectomy rather than lumpectomy.

CHOOSING BETWEEN BREAST-CONSERVING SURGERY AND MASTECTOMY

The advantage of breast-conserving surgery (lumpectomy) is that it preserves the appearance of the breast. A disadvantage is the need for several weeks of radiation therapy after surgery. Some women who have a mastectomy will still need radiation therapy. Patients who choose lumpectomy and radiation have the same chance of survival as those who choose mastectomy.

Although most women and their doctors prefer lumpectomy and radiation therapy, the choice depends on a number of factors, such as:

- personal feelings about losing the breast.
- additional time and travel required for radiation therapy.
- whether more surgery to reconstruct the breast after having a mastectomy is wanted.
- a preference for mastectomy as a way to “take it all out as quickly as possible.”

In determining the preference for lumpectomy or mastectomy, consider all the facts. Though a patient may want a mastectomy to “take it all out as quickly as possible,” the fact is that doing so does not provide a better chance of long-term control or a better prognosis in most cases. Large research studies with thousands of women participating and over 20 years of information show that when lumpectomy can be done, mastectomy does not provide a better chance of survival from breast cancer than lumpectomy. It is because of these facts that most women do not have their breast removed.

Reconstructive Surgery

After a mastectomy, the patient may consider having a breast *reconstruction* so that she can have the appearance of a more normal breast. This procedure will require additional surgery to create the appearance of a breast after the tissue removal during a mastectomy. The breast can be reconstructed at the same time the mastectomy is done (immediate reconstruction) or at a later date (delayed reconstruction). Surgeons may use saline-filled implants or tissue from other parts of the body for the breast reconstruction.

Determining the timing and type of reconstruction depends on the patient's personal preferences, breast size and shape, body size and shape, level of physical exercise, details of the patient's medical situation (such as how much skin was removed), and whether the patient needs chemotherapy or radiation. This is a decision that is made by the patient and physician.

If you are thinking about breast reconstruction, it is important to discuss this with your doctor when planning treatment.

Lymph Node Surgery

When cancer metastasizes from the original tumor site, it travels through the blood vessels and lymphatic vessels. The lymph vessels run through the lymph nodes, which act like filters. If cancer cells are caught in a lymph node and begin to grow, this is a sign that the cancer may have started to spread throughout the body. Regardless of whether a woman has breast-conserving surgery or mastectomy, lymph nodes must be examined to determine whether the cancer has spread to them. The only way to accurately determine if lymph nodes are involved is to remove and examine them under the microscope.

In an operation called an *axillary lymph node dissection*, all the lymph nodes in the armpit are removed and examined. While this procedure is effective in identifying whether the cancer has spread to the lymph nodes, some women experienced troublesome swelling in the affected arm. Therefore, researchers looked for a way to get equally reliable information without such extensive surgery.

In recent years, a procedure called *sentinel lymph node biopsy* has become a common way of evaluating whether breast cancer has spread to the lymph nodes for patients who do not exhibit evidence of spread to the lymph nodes. Patients who do have signs that the cancer has spread to the lymph nodes require the full axillary lymph node dissection.

Sentinel lymph node biopsy is based on the way lymph travels through the breast. By using a radioactive substance or dye to track this drainage, the surgeon can identify the first lymph node to which cancer cells would travel. The surgeon then removes that node and sends it to the pathologist for review. A sentinel lymph node biopsy should be considered only if there is a surgical team experienced with this technique. If the sentinel lymph node is cancer free, no additional surgery is needed. However, if cancer is present, the surgeon will remove additional lymph nodes to determine how many are involved, which will help determine the best treatment course. This full axillary lymph node dissection can be performed at the time of the original surgery or several days later.

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For some women with invasive cancer, removing the underarm lymph nodes can be considered optional for:

- women with tumors so small and with such a favorable prognosis that lymph node spread is unlikely;
- instances where the removal would not affect whether adjuvant therapy is given;
- elderly women;
- women with serious medical conditions.

Lymph node surgery is not necessary with pure DCIS or LCIS. A sentinel lymph node biopsy may be done if the patient will be undergoing surgery (such as mastectomy) that would make it impossible to do the sentinel lymph node biopsy procedure if invasive cancer were found in the tissue removed during surgery.

Side Effects of Lymph Node Surgery

Side effects of lymph node surgery can be bothersome to many women and can occur with either the full axillary lymph node dissection or sentinel lymph node biopsy. However, side effects are much less common and less severe with the sentinel lymph node procedure.

Side effects of lymph node surgery include:

- temporary or permanent numbness in the skin on the inside of the upper arm;
- temporary limitation of arm and shoulder movements; and
- swelling of the breast and arm, called lymphedema.

Lymphedema is the most significant of these side effects and may become permanent. Most women who develop lymphedema find it bothersome but not disabling. No one can predict which patients will develop this condition or when it will develop. Lymphedema can develop just after surgery or months to years later. Significant lymphedema occurs in about 10 percent of women who have axillary lymph node dissection and in up to 5 percent of those who have sentinel lymph node biopsy.

With care, patients can take steps to help avoid lymphedema or to at least keep it under control. Some of the steps to help avoid lymphedema include:

- Avoid having blood drawn from or IVs inserted into the arm on the same side as the lymph node surgery.
- Do not allow a blood pressure cuff to be placed on that arm. If you are in the hospital, tell all health care workers about the affected arm.
- If the affected arm or hand feels tight or swollen, don't ignore it. Tell the doctor immediately.
- If needed, wear a well-fitted compression sleeve.
- Wear gloves when gardening or doing other things that are likely to lead to cuts.

Talk to your doctor for more details.

RADIATION THERAPY

Radiation therapy uses a beam of high-energy rays (or particles) to destroy cancer cells left behind in the breast, chest wall, or lymph nodes after surgery. Radiation may also be needed after mastectomy in cases with either a larger breast tumor or when cancer is found in the lymph nodes.

This type of treatment can be given in several ways:

- *External-beam radiation therapy* delivers radiation from a machine outside the body. This type of radiation therapy is most often given after lumpectomy. Radiation is given to the entire breast, with an extra dose (or “boost”) to the site of the tumor. It is usually given 5 days a week for 6 to 7 weeks.
- *Brachytherapy*, also called interstitial radiation, involves the placement of radioactive materials in or near the site from which the tumor was removed. Radioactive material may also be placed in the lumpectomy site to “boost” the radiation dose in external-beam radiation therapy.

Recently, there has been interest in limiting radiation therapy only to the site of the lumpectomy, referred to as partial breast irradiation. This is based on the observation that when breast cancer recurs in the breast, the most common place is the site of the original tumor. The NCCN Guidelines for Patients™: Breast Cancer do not recommend partial breast irradiation outside of a clinical trial because studies demonstrating that it is as effective as whole breast radiation in preventing recurrences elsewhere in the breast are not complete.

The extent of radiation therapy depends on whether a lumpectomy or mastectomy was done and whether or not lymph nodes are involved. If a lumpectomy was done, the entire breast will receive radiation to destroy any cancer cells that are too small to be seen elsewhere in the breast with an extra boost to the area where the cancer was removed to prevent a recurrence.

If the surgery was a mastectomy, radiation is given to the entire area of the skin and muscle where the mastectomy was done if the tumor was larger than 5 cm or if the tumor was close to the edge of the tissue removed during mastectomy.

In patients who have had a lumpectomy or mastectomy, further radiation may be recommended if the cancer has metastasized to the lymph nodes. Radiation may be given to the area just above the collarbone and along the breastbone, depending on the number and location of involved lymph nodes.

Side effects most likely to occur from radiation include swelling and heaviness in the breast, sunburn-like skin changes in the treated area, and *fatigue*. Changes to the breast tissue and skin usually go away in 6 to 12 months. In some women, the breast may become smaller and firmer after radiation therapy. There may also be some aching in the breast, and rarely a rib fracture or second cancer may be caused by the radiation.

SYSTEMIC TREATMENT

To reach cancer cells that may have spread beyond the breast and nearby tissues, doctors use drugs that can be given by pills or injection. This type of treatment is called *systemic therapy*. Examples of systemic treatment include chemotherapy, hormone therapy, and targeted therapy. Hormone therapy is only helpful if the tumor is hormone receptor–positive, and trastuzumab (a targeted therapy) is only effective if the tumor is HER2–positive.

Even in the early stages of disease, cancer cells can break away from the primary breast tumor and spread through the bloodstream. These cells usually don't cause symptoms, don't show up on x-rays, and can't be felt during a physical examination. But if they are allowed to grow, they can establish new tumors in other places of the body. Systemic therapy given to patients with no evidence of metastases, but who are at an increased risk of developing them, is called *adjuvant therapy*. The goal of adjuvant therapy is to kill undetected cells that have traveled from the breast to other places in the body.

Women with invasive breast cancer should receive adjuvant therapy, except those with very small or well-differentiated tumors. For example, patients with hormone receptor–positive disease usually receive hormone therapy, and those with HER2–positive tumors larger than 1 cm in diameter or with involvement of lymph nodes will receive targeted therapy with trastuzumab. Chemotherapy may also be recommended based on the tumor size, grade of the tumor, and presence or absence of lymph node involvement. For women with breast cancer with hormone receptor–negative tumors, hormone therapy is not effective, and in those with HER2–negative tumors, trastuzumab is not effective. For patients with tumors that are hormone receptor– and HER2–negative, the only decision is whether or not to receive chemotherapy.

In most cases, systemic treatment is given soon after surgery, using the results of the surgery and pathology evaluation to determine the best choice of treatment. In some cases, systemic therapy is given to patients after a needle biopsy but before lumpectomy or mastectomy; this is called neoadjuvant treatment. Oncologists give patients neoadjuvant treatment to shrink the tumor enough to make surgical removal easier. This may allow women who would otherwise need mastectomy to have breast-conserving surgery.

For women whose breast cancer has metastasized, systemic treatment is the main treatment. This treatment may be chemotherapy, hormone therapy, trastuzumab, or combined therapy based on the hormone receptor status and the HER2 status of the tumor.

Chemotherapy

Chemotherapy uses drugs that are harmful to cancer cells and are designed to keep them from dividing. Usually these cancer-fighting drugs are given *intravenously* (injected into a vein) or as a pill. Either way, the drugs travel through the bloodstream to the entire body. Sometimes these drugs are used alone (also referred to as a single agent); other times they are used in combination, called a regimen. Since different drugs work in different ways, oncologists design combinations of drugs that work in different ways to increase the probability that more cancer cells will be killed.

There are many drugs that are effective in treating breast cancer which have been tested in clinical trials to show that they are both effective and safe. However, it is important to know that even the most effective drugs do not always work. Similarly, while they are considered safe, some patients who take these drugs will have side effects, sometimes serious ones.

It is also important to know the goal of chemotherapy treatment because it will influence which drugs will be used and whether they will be used alone or in combination.

When chemotherapy is given after surgery for early stage breast cancer, it is called adjuvant chemotherapy. Surgery removes the cancer from the breast, and surgeons always try to remove the entire tumor. However, one of the challenges of breast cancer is its ability to spread to other parts of the body. While removing the breast tumor and performing a sentinel lymph node biopsy can indicate that the cancer probably has

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not spread at the time of surgery, it is impossible to be 100 percent sure. This is the biggest long-term risk for early stage breast cancer, because if the cancer cells that have traveled from the breast tumor are not killed, they can eventually grow and divide and become metastatic breast cancer.

Adjuvant therapy is designed to kill any cancer cells that may have metastasized before surgical removal and to prevent a recurrence. The advantage of using chemotherapy in this way is that relatively few cancer cells exist, so there is a better chance that the drugs can kill them. The disadvantage is that the drugs can have side effects. For this reason, only those combinations that are known to work best with the fewest serious side effects are used as adjuvant therapy. Making the decision about whether to have adjuvant chemotherapy is an important one.

For certain patients with hormone receptor–positive, HER2-negative, node-negative breast cancer, a genetic test can help determine the risk of recurrence based on the specific gene expression profile of the cancer. This test looks at 21 separate genes and provides a score indicating whether the cancer has a high, intermediate, or low risk of recurrence. It is clear what to do if the recurrence score is low or high, but less clear if the score is intermediate. A low recurrence score of below 18 indicates that the cancer is unlikely to recur and a woman can safely omit chemotherapy but must still take adjuvant hormone therapy. A high recurrence score of 31 or higher means that the cancer is likely to recur if untreated, thus chemotherapy should be taken along with hormone therapy. An intermediate score, between 18 and 30, means that the likelihood of recurrence is between low and high. In this case, a woman and her oncologist should carefully discuss whether to take chemotherapy and hormone therapy or omit the chemotherapy. This decision can be based on a number of factors including the woman's age and her personal preferences.

For women with hormone receptor–negative disease, or with positive lymph nodes and either positive or negative receptors, online tools like Adjuvant! Online (available at www.adjuvantonline.com) can help to make decisions about whether or not to undergo chemotherapy. The doctor will input information into a computer program that analyzes a variety of factors specific to that patient and the cancer and then provides an estimate on the benefit of chemotherapy. This program was developed before HER2 status became a significant factor in selecting therapy; thus information about benefits of adjuvant trastuzumab are not included. The tool is currently being updated to include HER2 status.

Sometimes chemotherapy is given before surgery to make it easier to remove the cancer. This is called preoperative or neoadjuvant chemotherapy. In most cases, adjuvant or neoadjuvant chemotherapy is most effective when combinations of drugs are used together. There are several effective chemotherapy combinations. If the cancer is HER2-positive, combinations that include trastuzumab will be used. If the tumor is HER2-negative, trastuzumab will not help and thus will not be included. Every chemotherapy drug has possible side effects, so it is important to take only the ones that are most likely to be effective.

Chemotherapy may also be given to treat breast cancer that has spread to places other than the breast or lymph nodes. Both single drugs and combinations of drugs are often used in the treatment of metastatic breast cancer. In general, chemotherapy is not likely to cure breast cancer that has spread beyond the breast and nearby lymph nodes, so the chemotherapy used is designed to provide the best quality, longest life possible. Since there is a wide variety of chemotherapy drugs that are effective for metastatic breast cancer, treatment with one drug or combination is used to control the cancer and stop its growth; when the cancer begins to grow again, another drug or combination is used. This can continue for years, making breast cancer management much like that of other serious chronic diseases. With continued research, better treatments may be discovered.

TABLE 2. COMMONLY USED CHEMOTHERAPY AND TARGETED THERAPY DRUGS FOR BREAST CANCER

Generic Name	Brand (Trade) Name
Doxorubicin	Adriamycin®
Bevacizumab	Avastin®
Cyclophosphamide	Cytoxan®
Doxorubicin liposomal injection	Doxil®
Epirubicin	Ellence®
Fluorouracil	5-FU
Gemcitabine	Gemzar®
Trastuzumab	Herceptin®
Ixabepilone	Ixempra®
Vinorelbine	Navelbine®
Carboplatin	Paraplatin®
Cisplatin	Platinol®
Paclitaxel	Taxol®
Docetaxel	Taxotere®
Lapatinib	Tykerb®
Etoposide	VePesid®
Vinblastine	-
Capecitabine	Xeloda®

TABLE 3. COMMON COMBINATIONS OF ADJUVANT CHEMOTHERAPY DRUGS

Adjuvant Chemotherapy Options for HER2-Negative Tumors	
Preferred Combinations	
TAC	docetaxel/doxorubicin/cyclophosphamide with filgrastim support
AC	doxorubicin/cyclophosphamide
Dose-dense AC followed by paclitaxel	doxorubicin/cyclophosphamide with paclitaxel every 2 weeks
AC followed by weekly paclitaxel	doxorubicin/cyclophosphamide followed by weekly paclitaxel
TC	docetaxel and cyclophosphamide
Other Combinations	
FAC/CAF	fluorouracil/doxorubicin/cyclophosphamide
FEC/CEF	cyclophosphamide/epirubicin/fluorouracil
CMF	cyclophosphamide/methotrexate/fluorouracil
AC followed by docetaxel every 3 weeks	doxorubicin/cyclophosphamide followed by docetaxel every 3 weeks
EC	epirubicin/cyclophosphamide
A followed by T followed by C weeks with filgrastim support	doxorubicin followed by paclitaxel followed by cyclophosphamide every 2
FEC followed by T	cyclophosphamide/epirubicin/fluorouracil followed by docetaxel
FEC followed by weekly paclitaxel	cyclophosphamide/epirubicin/fluorouracil followed by weekly paclitaxel
Adjuvant Chemotherapy Options for HER2-Positive Tumors	
Adjuvant:	
AC	doxorubicin/cyclophosphamide followed by paclitaxel + concurrent trastuzumab
TCH	docetaxel, carboplatin, trastuzumab
Other Active Combinations	
Docetaxel + trastuzumab followed by FEC	docetaxel + trastuzumab followed by cyclophosphamide/epirubicin/fluorouracil
Chemotherapy followed by trastuzumab	chemotherapy followed by trastuzumab sequentially
AC followed by docetaxel + trastuzumab	doxorubicin/cyclophosphamide followed by docetaxel + trastuzumab
Neoadjuvant:	
T + Trastuzumab followed by CEF + Trastuzumab	paclitaxel plus trastuzumab followed by cyclophosphamide/epirubicin/fluorouracil plus trastuzumab

TABLE 4. CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC BREAST CANCER

Preferred Single Agents	Preferred Combinations
Doxorubicin	CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)
Epirubicin	FEC (fluorouracil/epirubicin/cyclophosphamide)
Pegylated liposomal doxorubicin	AC (doxorubicin/cyclophosphamide)
Paclitaxel	EC (epirubicin/cyclophosphamide)
Docetaxel	AT (doxorubicin/docetaxel or doxorubicin/paclitaxel)
Albumin-bound paclitaxel	CMF (cyclophosphamide/methotrexate/fluorouracil)
Capecitabine	Docetaxel/capecitabine
Gemcitabine	GT (gemcitabine/paclitaxel)
Vinorelbine	
	Other Combinations
	Ixabepilone and capecitabine
Preferred Agents with Bevacizumab	Other Active Agents
Paclitaxel	Cisplatin
	Carboplatin
	Cyclophosphamide
	Mitoxantrone
	Etoposide (in pill form)
	Vinblastine
	Fluorouracil by continuous IV infusion

Preferred Chemotherapy Regimens in Combination with Trastuzumab

(HER2-Positive Metastatic Disease)

- Paclitaxel with or without carboplatin
- Docetaxel
- Vinorelbine
- Capecitabine

Preferred Regimens for HER2-Positive Tumors Already Treated with Trastuzumab (HER2-Positive Metastatic Disease)

Lapatinib and capecitabine

Trastuzumab with different chemotherapy drug than was used before

Trastuzumab and capecitabine

Trastuzumab and lapatinib (with no other chemotherapy)

How Chemotherapy is Given

Doctors give chemotherapy in cycles, with each period of treatment followed by a rest period. These cycles vary in length depending on the specific combination of drugs used. Typically the cycles are 14-, 21-, or 28- day cycles. These cycles, or schedules, give the body a chance to recover from the effects of the chemotherapy before the next cycle. Although the oncologist may recommend that chemotherapy last 3 to 6 months depending on the regimen, the drugs are not given continuously, so patients can plan for rest periods between treatments.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type of drugs used, amount taken, length of treatment, and the individual. Some women have many side effects, while other women have few. Some side effects can be very serious, while others are unpleasant but not serious. Side effects include:

- Heart damage: *doxorubicin* (Adriamycin®) and *epirubicin* (Ellence®) may cause heart damage, but this is uncommon in people who do not have a history of heart disease. The targeted agent, trastuzumab (see Targeted Therapy, page 57), is also known to cause heart damage in some women. If there is concern that you might have heart disease, the oncologist may recommend a heart test before beginning therapy. If the heart is weakened, your doctor may recommend chemotherapy using different drugs that are not known to affect heart function. Fortunately, heart damage, though serious, is uncommon.
- Infections, fevers, low white blood cell counts: many of the commonly used chemotherapy drugs can cause these side effects because they target rapidly dividing cells. White blood cells are among the most rapidly dividing cells in the body, so they are especially vulnerable to chemotherapy. The doctor will check blood counts before each chemotherapy cycle and either delay a dose of therapy or reduce the amount of drugs given if these blood counts are too low. A specific type of white blood cell, the neutrophil, is critical in fighting bacterial infections, and the number of these cells will be monitored during therapy.

There is a delay between giving the treatment and the point at which blood counts are lowest during the cycle. Therefore, patients on chemotherapy should contact their doctor or nurse immediately if they have a fever of 101°F or higher since the body's ability to fight off an infection is weakened during chemotherapy. For some regimens where low white blood cell counts are expected, the doctor may give additional drugs called growth factors that increase the body's production of white blood cells.

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- Bleeding and bruising: a shortage of another type of blood cell, which makes platelets, is also fairly common. Doctors will monitor the numbers of platelets and provide treatment if necessary.
- Nausea and vomiting: these side effects are fairly common; however, doctors can prescribe drugs that minimize these problems. If the doctor recommends these drugs be taken before receiving chemotherapy, it is important to take them. Preventing nausea and vomiting is much easier than stopping it once it starts.
- Temporary side effects often include loss of appetite, fatigue, mouth sores, hair loss, and changes in the menstrual cycle.

Premenopausal women may develop early menopause and infertility from chemotherapy drugs. The older a woman is when she receives chemotherapy, the more likely it is she will stop menstruating or lose her ability to become pregnant; some chemotherapies are more likely to cause this than others. However, women cannot depend on chemotherapy to prevent pregnancy, and becoming pregnant while receiving chemotherapy could lead to birth defects and interfere with treatment. Therefore, premenopausal women should consider using birth control while receiving chemotherapy.

Targeted Therapy

Some treatments are directed toward certain *markers* or processes occurring in tumor cells. For example, drugs like trastuzumab target cancer cells with high quantities of HER2.

The NCCN Guidelines for Patients™: Breast Cancer recommend that trastuzumab be given only as part of chemotherapy regimens; it can be used as part of an adjuvant therapy combination for HER2-positive, early stage breast cancer. Adjuvant trastuzumab is most often given intravenously for one year and is commonly started close to when chemotherapy is first given and continued after it has been completed. Trastuzumab, may also be given as part of a combination of drugs used before surgery to shrink the tumor and make it easier to remove. If trastuzumab and the entire course of chemotherapy is not finished before surgery, it may be completed after surgery.

Trastuzumab may also be used to treat metastatic breast cancer. When treating cancer that has spread, it is used first with one chemotherapy drug or a combination. When the cancer recurs, trastuzumab may be continued with different chemotherapy.

Trastuzumab can affect the heart and should be used with caution when combined with doxorubicin or epirubicin, which can also affect the heart. Patients may need to undergo periodic testing to monitor heart function while taking this drug.

Trastuzumab has not been shown to be effective in women with breast cancer with low HER2 expression. Thus, it is very important that testing for the HER2 tumor marker is accurate.

Lapatinib (Tykerb®) is another targeted therapy used in combination with another anticancer drug to treat HER2-positive breast cancer that has metastasized after it has been treated with other drugs. It is a type of ErbB-2 and EGFR dual *tyrosine kinase inhibitor* that is specially targeted to interfere with specific processes in the cancer cells.

Bevacizumab (Avastin®) is a *monoclonal antibody* that may be used in patients with metastatic breast cancer. It prevents the growth of new blood vessels that supply the tumor with the blood, oxygen, and fuel it needs to grow. It is used in combination with the chemotherapy drug *paclitaxel* (Taxol®). The use of bevacizumab in breast cancer is controversial.

Hormone Therapy

If breast cancer has tested positive for the estrogen receptor and/or progesterone receptor tumor markers, hormone therapy will most likely be part of the treatment plan.

Estrogen is a hormone that is produced mostly by the ovaries but is also produced in small amounts by the *adrenal glands* and fat. It can cause breast cancers that have hormone receptors to grow. Doctors use drugs to either block the effect of estrogen or lower estrogen levels. These drugs include:

- *Antiestrogens*, including the drug *tamoxifen*, block the effect of estrogen on cancer cells but do not decrease estrogen levels. Instead, antiestrogens prevent estrogen from causing the breast cancer cells to grow (see Antiestrogen Drugs, below).
- Other drugs called *aromatase inhibitors* (such as *anastrozole* [Arimidex®], *letrozole* [Femara®], or *exemestane* [Aromasin®]), or treatments such as surgical removal of the ovaries, can lower the production of estrogen in the body so that it is not available to the breast cancer cells.

Aromatase inhibitors are somewhat more effective than tamoxifen in preventing recurrence of breast cancer. Each drug has a different set of likely side effects. Aromatase inhibitors are appropriate only for postmenopausal women because premenopausal women produce much higher amounts of estrogen.

Hormone therapy is typically given after surgery and after chemotherapy has been completed to prevent recurrence of breast cancer. Hormone therapies are usually taken as pills and are often given for at least 5 years. It is important to complete such therapy and not to stop without informing the oncologist, because these drugs are more effective when taken for long periods of time. If the doctor initially recommends tamoxifen, it may be beneficial to switch to an aromatase inhibitor after several years of tamoxifen provided menopause has been reached. Often, both hormone therapy and chemotherapy are used as adjuvant therapy for hormone receptor–positive breast cancer with a significant risk of recurrence.

Hormone therapy may also be used to control cancer that is metastatic on diagnosis (stage IV disease) that recurs following treatment. When used for advanced disease, the oncologist may recommend hormone therapy for hormone receptor–positive or hormone-receptor–negative tumors if the cancer has spread only to the bones or other organs but is not causing severe symptoms. In general, hormone therapy has fewer and milder side effects than chemotherapy; thus, it may provide women with advanced disease a better quality of life, sometimes for several years.

Side effects associated with hormone therapies include hot flashes, a slightly increased risk for blood clots and cancer of the uterus (a rare event associated with tamoxifen), and decreased bone mass and pain in the joints (with aromatase inhibitors). If any of these side effects are troublesome, the oncologist may be able to switch to an alternate drug that provides similar benefits. While there may be small differences between the effectiveness of one type of hormone therapy and another, the big difference is between hormone therapy and no hormone therapy. Accordingly, it is worth the effort to work with the oncologist to find one that works best.

Strategies for early detection of these side effects include monitoring of bone health through periodic measurements of *bone mineral density*; prompt investigation of abnormal uterine bleeding; and prompt investigation of symptoms or signs of venous thromboembolism (blood clot in a vein), such as swelling and pain in a leg or arm.

Hormone therapy has not been shown to be effective as adjuvant therapy in estrogen and/or progesterone receptor–negative tumors. Thus, it is very important that testing for these tumor markers is evaluated by laboratories experienced in reading these tests. Ask the oncologist about the laboratory where the tests will be evaluated.

Treatment to stop the production of estrogen may also be accomplished by removing the ovaries, which make estrogen.

Antiestrogen Drugs

Tamoxifen is the antiestrogen drug used most often to treat hormone receptor–positive tumors and is most commonly used for women who have not reached menopause. Taking tamoxifen as adjuvant therapy after surgery, usually for 5 years, reduces the chance of a recurrence. Tamoxifen is also used to treat metastatic breast cancer.

In many women, tamoxifen causes the symptoms of menopause, including hot flashes, vaginal discharge, and mood swings. Tamoxifen has two rare but more serious side effects: 1) a slight increased risk of developing cancer of the lining of the uterus (endometrial cancer) and uterine sarcoma, and 2) a slightly increased risk of developing blood clots. For most women with breast cancer, the benefits of taking the drug far outweigh the risks.

Toremifene (Fareston®) is another antiestrogen closely related to tamoxifen. It may be an option for postmenopausal women with metastatic breast cancer.

Fulvestrant (Faslodex®) is a newer drug that reduces the number of estrogen receptors. It is often effective in postmenopausal women even if the breast cancer is no longer responding to tamoxifen. Hot flashes, mild nausea, and fatigue are the major side effects of fulvestrant.

Drugs that Lower Estrogen Levels—Aromatase Inhibitors

Aromatase inhibitors stop estrogen production in postmenopausal women. Three drugs in this category have been approved for treatment of breast cancer: anastrozole, letrozole, and exemestane. These drugs work by blocking an enzyme that makes estrogen in postmenopausal women. They cannot stop the ovaries of premenopausal women from making estrogen. For this reason, they are only effective in postmenopausal women. For premenopausal women, tamoxifen remains the best drug to use.

The aromatase inhibitors have been compared with tamoxifen as adjuvant hormone therapy. They have fewer side effects than tamoxifen because they don't cause uterine cancer and very rarely cause blood clots. They can, however, cause osteoporosis and bone fractures because they remove all estrogen from the body of a postmenopausal woman. They also cause hot flashes and sometimes joint pain. Although these are considered less serious side effects, some women find them severe enough to consider discontinuing therapy. These women should talk with their oncologists to determine whether a switch to another drug may provide similar benefit with more tolerable side effects.

Aromatase inhibitors are at least as effective as tamoxifen in preventing breast cancer from recurring in postmenopausal women. Based on recent studies, many oncologists recommend including an aromatase inhibitor in the adjuvant hormone therapy of postmenopausal women with hormone receptor–positive breast cancer.

Hormone Therapy and Menopause

As discussed in the previous section, aromatase inhibitors are not recommended for premenopausal women. Therefore, determining whether the woman is menopausal is important as a basis for making treatment decisions. This is not as simple as it may sound, because menstrual periods can stop as a side effect of treatment while the ovaries continue to make estrogen. Additionally, sometimes chemotherapy stops the ovaries from making estrogen for a period of time, but after they recover from chemotherapy they may begin to make estrogen again. Therefore, if the use of an aromatase inhibitor is considered, monitoring the levels of hormones such as estradiol and FSH may be required to ensure that a woman is truly postmenopausal.

Ovarian Ablation

The ovaries are the source of most of the estrogen in premenopausal women. Destroying the ability of the ovaries to produce estrogen (ablation) may be an effective hormone therapy to treat premenopausal women with cancers that are positive for estrogen or progesterone receptors. Destruction of the ovaries production of estrogen can be done in a number of ways:

- The ovaries can be removed by surgery (i.e., *oophorectomy*).
- Radiation therapy can be given to the ovaries.
- Drugs called *luteinizing hormone-releasing hormone* (LHRH) agonists or *antagonists* block estrogen production by the ovaries.

BISPHOSPHONATES

Bisphosphonates are used in breast cancer treatment to strengthen bones that have been weakened by the spread of cancer cells. The most commonly used bisphosphonates in breast cancer treatment are *pamidronate* and *zoledronate*. These are usually given with calcium and vitamin D supplements.

Adjuvant hormonal therapy with aromatase inhibitors may also weaken the bones by causing loss of calcium from the bone (called osteoporosis) and thus increase the risk for a fracture. Therefore, patients treated with an aromatase inhibitor should have their bone strength tested (called a bone density test) to determine if medication to strengthen their bones would be appropriate. Some patients may enter menopause early due to the side effects of chemotherapy. Because menopause itself is associated with bone loss, these patients also may undergo a bone density test to evaluate the presence of osteoporosis. There are a number of medications, including some oral forms of bisphosphonates, to treat the loss of calcium from bone that is not caused by direct breast cancer in the bone.

When breast cancer has spread to the bones, bisphosphonates are frequently given on a regular basis to reduce the risk of bone fracture, the need for radiation to bones, and other skeletal events. Bisphosphonates are associated with an unusual complication, osteonecrosis (or bone death) of the jaw. Before a bisphosphonate is given, your dentist should evaluate your dental health. In most cases, the benefits of bisphosphonates dramatically outweigh the risk for this rare event.

TREATMENT OF PAIN AND OTHER SYMPTOMS

The greater part of the NCCN Guidelines for Patients™: Breast Cancer discusses ways to remove, destroy, or slow the growth of breast cancer cells. However, helping patients feel well and continue to do the things they enjoy is also an important goal. If you are a woman with breast cancer, do not hesitate to discuss your symptoms or how you feel with your cancer care team. There are effective and safe ways to treat pain, other symptoms of breast cancer, and most of the side effects caused by breast cancer treatment. If you don't tell your health care team, they have no way of knowing about your problems.

OTHER THINGS TO CONSIDER DURING AND AFTER TREATMENT

During and after treatment for breast cancer, you may be able to speed up your recovery and improve your quality of life by taking an active role in your care. Learning about the benefits and risks of each of your treatment options and asking your cancer care team questions can help you feel more in control of your care. Learning about which side effects of treatment are likely to occur will help you; then report them right away to your cancer care team so they can take steps to ease them.

Your body and how it responds to cancer and its treatment is as unique as your personality and fingerprints. Although understanding your cancer's stage and learning about your treatment options can help predict what health problems you may face, no one can say for sure how you will respond to cancer or its treatment. All prognostic information is based on large numbers of patients with similar disease, stage, and treatments, but it does not predict what will happen to the individual.

Everyone has strengths and capabilities. Use yours to help you cope with cancer and its treatments. Maintain good nutrition, physical activity, and warm relationships with family and friends. If you are a person of faith, your religion can help you during this time. There are also experienced professionals in mental health services, *social work services*, and pastoral services who are able to assist you in coping with your illness.

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You can help in your own recovery by making healthy lifestyle choices. For example, if you use tobacco, quit now. Quitting will improve your overall health, and the full return of your sense of smell may help you enjoy a healthy diet during recovery. If you use alcohol, limit how much you drink

to no more than one drink per day. Good nutrition can also help you get better after treatment. Eat a nutritious and balanced diet with plenty of fruits, vegetables, and whole grain foods.

If you are being treated for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy add to the fatigue caused by the disease itself. To help with the fatigue, plan your daily activities around when you feel best, and get plenty of sleep at night. Ask your cancer care team about a daily exercise program to help you feel better. But also remember that there are many enjoyable activities that do not require you to expend much energy. Working puzzles, visiting with friends, reading books, watching TV or movies, even sitting in the sunshine on a nice day can all help to improve the quality of your life while you cope with cancer treatment.

A woman's choice of treatment will likely be influenced by her age, body image, hopes and fears, and stage in life. For example, many women select breast-conserving surgery with radiation therapy over a mastectomy for body image reasons. On the other hand, some women who choose mastectomy may want the affected area removed, regardless of the effect on their body image. Still others may be more concerned about the side effects of radiation therapy than body image.

Other issues that concern women include hair loss from chemotherapy and the changes in the breast from radiation therapy. Women on chemotherapy may gain weight, so it is important to continue to eat a healthy diet and exercise as much as your energy level will permit. In addition to these body changes, women may also be concerned about the outcome of their treatment. These are all factors that affect treatment decisions, how you view yourself, and how you feel about your treatment.

Concerns about sexuality are often very worrisome to a woman with breast cancer. In addition to changes in appearance, some treatments for breast cancer change hormone levels that may affect sexual interest or response. Young women with breast cancer may find this especially difficult since they may not yet have entered into a stable relationship or may have concerns about bearing children. The diagnosis of cancer is distressing to both the woman with cancer and her partner. Partners are usually concerned about how to express their love physically and emotionally during and after treatment. Discussing ways to be most supportive can help both partners.

Friends and family often are not sure what to do to help. Make a list of things that would make things easier for you ranging from simple visits or phone calls to helping with life chores, driving to appointments, helping you care for others you are responsible for, lending books or music you might enjoy, or cooking foods you feel like eating. Most would be delighted to get some guidance from you about what you need.

Suggestions that may help a woman adjust to changes in her body image include looking at and touching her body; seeking the support of others, preferably before surgery; involving her partner as soon as possible after surgery; and openly talking about the feelings, needs, and wants created by her changed image.

A cancer diagnosis and its treatment are a major life challenge, with an impact on you and everyone who cares for you. Consider attending a local support group meeting so that you can interact with others who have similar concerns and experiences. If you need help in other ways, contact your hospital's social service department. Other resources are also available; visit the NCCN's resources page (NCCN.com) for more information.

CLINICAL TRIALS

The Purpose of Clinical Trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only planned and begun when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used currently. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment. NCCN is strongly committed to clinical trials and believes that the best management for any patient with cancer is in a clinical trial.

Clinical trials can focus on many things, such as:

- New uses of drugs that are already approved by the U.S. Food and Drug Administration (FDA). For example, drugs that are used in one type of cancer may be tested in another type of cancer, or different drugs may be combined together.
- Different ways of administering chemotherapy, such as using oral drugs instead of IVs.
- New drugs that have not yet been approved by the FDA, where research is being done to determine the best dosage that balances the side effects with effectiveness.
- Different types of radiation therapy, designed either to decrease the side effects of radiation therapy or allow higher, more effective doses of radiation or both.
- Different types of surgery, some designed to be more "minimally invasive" to permit a faster recovery or to use different tools to destroy tumors, such as lasers.
- Medicines or procedures to relieve symptoms or improve comfort.

Phases of Clinical Trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV, and are described below, using the example of a drug therapy.

Phase I Clinical Trials: The purpose of a phase I study is to find the best way to give a new treatment to patients safely. The cancer care team will closely watch patients for any harmful side effects. In phase I studies, the drug has already been tested in lab and animal studies, but the drug needs to be tested in humans to understand the optimal dose balanced against the potential side effects. Most patients in these trials have not been successfully treated with other "standard" chemotherapies. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase II Clinical Trials: These studies are designed to determine if the drug works for a specific type of cancer. Frequently, phase II trials involve new combinations of drugs. Patients are closely watched for an effect on the cancer. The cancer care team also looks for side effects. If a drug or combination of drugs is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III Clinical Trials: Phase III studies involve large numbers of patients. Often, these are randomized clinical trials, which means that patients are randomly put in 1 of 2 (or more) treatment groups. One group (called the control group) receives the standard, most accepted treatment. Other groups get the new treatment or treatments being studied. Neither the patient nor physician can pick which group they want to be in. However, the doctor will explain the exact rationale for the clinical trial and the risks and benefits of being assigned to either group. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others. Phase III clinical trials are usually needed before the FDA will approve a new drug for use by the general public.

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Phase IV Clinical Trials: Once a new drug has been approved by the FDA and is available for all patients, it may be studied in phase IV studies in very large numbers of patients with different types of cancer. In this setting, more can be learned about short-term and long-term side effects and safety of the drug. For example, some rare side effects may only become apparent in phase IV studies. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways, such as in combination with other treatments.

Deciding to Enter a Clinical Trial

If you have breast cancer and are interested in taking part in a clinical trial, you should begin by asking your doctor if the clinic or hospital participates in clinical trials. In order to interpret the results of a clinical trial, all the participants must be similar in terms of the tumor status and general health, so the physician can be certain that any improvement in outcome is the result of treatment and not due to different patient or tumor characteristics. Therefore, you will need to meet certain requirements in order to take part in any clinical trial. However, whether or not you enroll in a clinical trial is completely up to you.

Anyone participating in a clinical trial will need to sign a document called an “informed consent.” This informed consent describes the study in detail and outlines the potential risk and benefits. Your signature on the informed consent document means that you understand the risk and benefits and agree to participate in the clinical trial. However, the informed consent does not mean that you must stay committed to the clinical trial; you can leave the clinical trial whenever you want for any reason. It is also important to understand that participating in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Among the questions you should ask are:

- Is there a clinical trial that I could take part in? What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before? Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily activities? What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow up care is part of the study?
- Has the treatment been used to treat other types of cancers?

People interested in clinical trials can also get a list of current trials by calling the National Cancer Institute’s Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

EXPLANATION OF TREATMENT PATHWAYS

Stage 0 Lobular Carcinoma in Situ (based on page 9)

The workup for LCIS includes a complete medical history and physical examination (see page 9). A diagnostic mammogram of both breasts (also known as *bilateral*) is done to determine if there are any other abnormal areas in either breast. A pathology review is suggested to make certain the correct diagnosis is LCIS and not invasive breast cancer or another condition.

LCIS is usually not treated with surgery other than the initial biopsy procedure. *Observation* is the preferred option for most women who are diagnosed with LCIS because neither is it an invasive cancer, nor does it normally become one. Nonetheless, women with LCIS have an increased risk of developing invasive breast cancer in either breast. Ways to reduce the individual risk of breast cancer have become an important option, and women should discuss these options with their oncologist.

One way to lower the risk for developing an invasive breast cancer is to take tamoxifen, an antiestrogen drug. There is evidence that, when used as hormone therapy (also known as endocrine therapy), it can lower this risk when taken for a full 5 years (see page 57).

A preventive mastectomy of both breasts may be an option for women with LCIS who have a very high risk for developing invasive breast cancer. Those determined to be very high risk are women who have many family members with breast cancer. An oncologist can help each patient decide whether to consider this treatment. Patients at high risk should also consider *genetic counseling* to find out if they have a gene that increases the risk for developing breast cancer before they decide to have a preventive mastectomy (also known as *prophylactic* mastectomy). Breast reconstruction is an option that may be done at the same time as the mastectomy or at a later date.

For patients who decide with their doctor on observation as the primary treatment for LCIS, follow up includes a medical history and physical exam every 6 to 12 months. These patients should have a mammogram every year unless they choose a bilateral mastectomy. Because tamoxifen increases endometrial cancer risk in postmenopausal women, women taking this drug should have a pelvic exam each year, and postmenopausal women should report any vaginal bleeding right away. These precautions are not needed if the uterus has been removed (hysterectomy).

Ductal Carcinoma in Situ, Stage 0 (based on page 10)

The workup (or evaluation) for DCIS begins with a complete medical history and physical examination.

Diagnostic mammograms of both breasts (bilateral) should be done to help estimate how far DCIS has spread within the ducts of the breast and to check whether the opposite breast contains any abnormal areas. NCCN recommends a pathology review to confirm a diagnosis of DCIS. The tumor should also be tested for hormone receptors. If any evidence of invasive breast cancer is seen in the biopsy, treatment should be according to the treatment pathways for invasive breast cancer (see page 12). For patients with a family history of breast cancer, especially if it occurred at a young age, the oncologist may recommend genetic counseling to determine whether the woman has a high risk of developing an invasive breast cancer at some point and whether other family members (daughters or sisters) may be at increased risk.

The NCCN recommends that the margin of normal tissue removed around the tumor should be more than 1 mm. If DCIS is present in only 1 area and no cancer is found at the edges of the first surgical *excision*, the surgical options are either a total mastectomy or lumpectomy. Lymph node surgery (lymph node dissection or sentinel lymph node biopsy) is generally not done with DCIS. If a lumpectomy is chosen, then radiation therapy to the whole breast with a boost (extra dose) to the tumor site may or may not be performed depending on several factors, such as age, other health problems, certain characteristics of the tumor, and the woman's preference. The NCCN Guidelines recommend that women interested in partial breast irradiation (*irradiation* is also known as radiation therapy) participate in a clinical trial.

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Mastectomy provides the most certain local control of DCIS. Studies have shown that women with DCIS who are treated with lumpectomy and radiation therapy are in no greater danger of dying from breast cancer than those who have a mastectomy. They do, however, have a risk of the cancer coming back in the breast, which would require a mastectomy. Mastectomy is recommended if the margins of the specimen contain cancer and if after repeat surgery the cancer cannot be completely removed. Radiation is not needed if a mastectomy is done unless the DCIS is at the margin of the mastectomy. If the mammogram, physical examination, or biopsy results show that two or more separate areas of the breast contain DCIS, mastectomy is recommended. With mastectomy, sentinel lymph node biopsy may be performed in case an area of invasive cancer is found on pathologic evaluation.

After lumpectomy, a mammogram is suggested to ensure that the entire tumor has been removed.

Women with DCIS who undergo a mastectomy can choose to have either immediate or delayed breast reconstruction. Those treated with lumpectomy with or without radiation and who have estrogen receptor–positive tumors should consider taking tamoxifen for 5 years. Regardless of whether mastectomy or breast-conserving surgery is used, 5 years of tamoxifen can reduce the risk of breast cancer developing in the other breast.

Follow-up for women with DCIS includes a medical history and physical exam every 6 months for 5 years, then every year thereafter, as well as yearly mammograms. Again, because tamoxifen increases the risk for endometrial cancer in postmenopausal women, women taking tamoxifen should have a pelvic exam every year and should promptly report any abnormal vaginal bleeding. These precautions are not needed if the uterus was removed.

Stage I and II and Some Stage III Breast Cancer (based on page 12)

The treatment pathways for women with stage I and II tumors, and those stage IIIA tumors larger than 5 cm (2 inches) with cancer in the lymph nodes but not attached to each other (T3, N1, M0), recommend:

- Medical history and physical examination
- Complete blood count, platelet count, and liver function tests
- Chest x-ray
- Diagnostic mammograms of both breasts
- Breast ultrasound and MRI if needed
- Pathology review of biopsy sample
- Test for the presence of hormone receptors
- HER2 test.

A bone scan may be ordered and is recommended if there is bone pain or abnormal blood tests. Chest imaging may also be recommended if the cancer is large, has spread to 1 or more lymph nodes, or if there are symptoms of lung disease, such as a persistent cough or shortness of breath.

Abdominal CT scan, ultrasound, or MRI may be ordered for stage II disease and is recommended if the blood tests are abnormal or the cancer is stage IIIA (T3, N1, M0).

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For patients with stage I or II breast cancer, surgical options are either a lumpectomy (see page 13) or mastectomy (see page 14). Lumpectomy is possible in most women with stage I or II breast cancer. If the tumor is large (i.e., more than 2 cm in diameter), breast-conserving surgery is sometimes done after chemotherapy (see page 13). Adjuvant chemotherapy is given after surgery but before radiation therapy if needed (see page 15). Radiation therapy to the whole breast is recommended following lumpectomy in most cases. Extra radiation should be given to the area of the breast where the tumor was removed. Breast irradiation may be omitted in some patients over 70 years old with small, hormone receptor–positive tumors that do not have lymph node involvement and who are treated with hormone therapy. The NCCN Guidelines recommend that patients interested in partial breast irradiation should participate in a clinical trial.

After the cancer is removed by lumpectomy or mastectomy, the lymph nodes under the arm are examined to determine if they are cancerous. There are 2 choices for examining the lymph nodes: complete axillary lymph node dissection or sentinel lymph node biopsy. Some women do not need lymph node evaluation, including women with good prognosis tumors, where selection of additional treatment will not be based on lymph node involvement, or in patients with other serious medical conditions. Women should discuss their specific circumstances with their doctor. If the cancer has spread to lymph nodes, radiation to these areas may be given, depending on the number of involved nodes.

In choosing between lumpectomy and mastectomy, women must understand that as long as lumpectomy can be done satisfactorily (based on the factors that follow), the chances of successful treatment and survival are the same with lumpectomy and radiation, as with mastectomy. The reasons for choosing lumpectomy and mastectomy are discussed on page 46. Lumpectomy and radiation therapy are not appropriate in the following women:

- Prior radiation therapy to the affected breast or chest.
- Suspicious or malignant-appearing abnormalities that are widespread throughout the breast.
- 2 or more tumors that cannot be removed through a single incision.
- Women whose lumpectomy, including any possible repeat lumpectomy, cannot completely remove the cancer with a satisfactory cosmetic result.
- Women with active connective tissue disease involving the skin (especially scleroderma or lupus) that makes body tissues especially sensitive to the side effects of radiation.
- Pregnant women who would require radiation while pregnant.
- Women with tumors larger than 5 cm (2 inches) that can't be shrunk by treatment before surgery.

Axillary Lymph Node Surgery

In addition to surgery for breast cancer, lymph nodes under the arm are examined in most cases. Examining the lymph nodes provides information that can guide further treatment and is usually done at the same time as the breast surgery.

Types of surgery for lymph nodes under the arm are fully discussed on page 46 and include axillary lymph node dissection or sentinel lymph node biopsy. In a mastectomy, lymph nodes are removed through the same incision. In a lumpectomy, it is usually done through an incision separate from the lumpectomy incision.

Sentinel lymph node biopsy is not appropriate for all women, and should only be used when the nodes are not enlarged and are not cancerous at the time of diagnosis. Use of sentinel lymph node biopsy is controversial when undergoing preoperative chemotherapy because the chemotherapy may change a positive sentinel node to a negative one. Some oncologists remove the sentinel node before chemotherapy; others will perform an axillary lymph node dissection. If a suspicious node is found on physical exam, it can be first assessed with a needle biopsy and examined under the microscope. If the biopsy shows no evidence of cancer, a sentinel lymph node biopsy is still considered appropriate. Recovery following a sentinel lymph node biopsy may be easier, but it should only be done by a team of doctors with proven experience in this procedure.

If mastectomy is chosen as a treatment option instead of lumpectomy (see page 14), the NCCN Guidelines recommend radiation after surgery in the following situations:

- If the cancer has spread to 4 or more lymph nodes, radiation should be given to the area that the breast was removed from (the chest wall), the area above the collarbone, and perhaps the part of chest near the breast bone.
- If the cancer has spread to 1 to 3 lymph nodes, radiation should be given to the chest wall, the area above the collarbone, and the part of chest near the breastbone may be considered.
- If there is no spread to lymph nodes and the tumor is larger than 5 cm or the margins are positive, radiation may be given to the chest wall, the area above the collarbone, and possibly the area near the breastbone. If the tumor is less than 5 cm, the cancer has not spread to the lymph nodes, and the margins are very close, radiation should be given to the chest wall.

No radiation is needed if the tumor is smaller than 5 cm, with good margins, and no spread to lymph nodes.

In all cases where both radiation and chemotherapy are used, radiation is given after chemotherapy unless the chemotherapy regimen is CMF; CMF and radiation can be given together.

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Invasive Ductal, Lobular, Mixed, or Metaplastic Cancers with Small Tumors (based on page 15)

Additional Treatment (Adjuvant Therapy) After Surgery

Decisions about adjuvant chemotherapy or hormonal therapy for most common types of cancer (with the exception of tumors with good prognosis cell types, such as tubular or colloid) are based on the status of the hormone receptors and whether or not the tumor is HER2-positive. This creates 4 different groups of tumors based on the hormone receptor and HER2 status:

- hormone receptor–positive and HER2-positive tumors
- hormone receptor–negative and HER2-positive tumors
- hormone receptor–positive and HER2-negative tumors
- hormone receptor–negative and HER2-negative tumors

In general, hormone therapy is used only in tumors that are hormone receptor–positive; trastuzumab is used only for tumors that are HER2-positive. Chemotherapy is used when there is a higher risk of metastasis based on tumor stage and grade, or if the tumor is hormone receptor–negative. Patients are often treated with combinations of hormone therapy, trastuzumab, and chemotherapy, depending on the status of the hormone receptors, HER2 status, and the risk for recurrence.

The decisions regarding adjuvant chemotherapy for women over the age of 70 are complex because few clinical trials have included large numbers of older women. Decisions regarding chemotherapy for women over 70 are difficult because of several factors:

- Breast cancer can take a long time to recur and threaten the well-being of an older woman.
- The older or less healthy a woman is, the smaller the likelihood that chemotherapy will prevent a life-threatening recurrence.
- Depending on a patient’s general health status, other health problems may be more serious.

Because breast cancers in older women tend to be less aggressive, the risks of chemotherapy side effects may outweigh the benefits of reducing the small probability of a life-threatening recurrence. Decisions regarding chemotherapy in women over 70 should take into consideration the age of the patient, her personal preferences, and other health conditions.

Estrogen Receptor–Positive and/or Progesterone Receptor–Positive and HER2-Positive Tumor (based on page 16)

The top treatment pathway describes care after surgery for women with invasive ductal, lobular, mixed, or metaplastic cancer that measures up to 1 cm in diameter. The tumor has not spread to the chest wall or skin and either the lymph nodes are not involved or only one lymph node shows a very small deposit of cancer:

- If the tumor is smaller than 0.5 cm, or is a well-differentiated tumor and is no larger than 1 cm, or the tumor is considered microinvasive, then no adjuvant treatment is needed. If there is lymph node spread smaller than 2 mm, hormone therapy may be given.
- If the tumor measures 0.6 to 1 cm, is moderately or poorly differentiated, or has unfavorable features (such as appearing to be aggressive under the microscope), hormone therapy with or without chemotherapy is recommended. Trastuzumab may also be recommended. Whenever chemotherapy is given, it should be given before hormone therapy.
- If the tumor is larger than 1 cm, adjuvant chemotherapy, hormone therapy, and trastuzumab are all recommended. Chemotherapy is given before hormone therapy.
- If cancer larger than 2 mm is found in one or more lymph nodes, adjuvant chemotherapy, trastuzumab, and hormone therapy are recommended.

Estrogen Receptor–Positive and/or Progesterone Receptor–Positive and HER2-Negative Tumor (based on page 17)

The top treatment pathway describes care after surgery for women with hormone receptor–positive, HER2-negative invasive ductal, lobular, mixed, or metaplastic cancer that does not invade the chest wall or skin and has no more than 2 mm spread to one lymph node. Recommendations for adjuvant therapy depend on the size and characteristics of the tumor:

- If the tumor is smaller than 0.5 cm, is a well-differentiated tumor no larger than 1 cm, or is considered microinvasive, with no spread to the lymph nodes, no adjuvant treatment is needed. If a similarly sized tumor has lymph node spread smaller than 2 mm, hormone therapy may be given.
- If the tumor measures 0.6 to 1 cm, is moderately or poorly differentiated, or has unfavorable features (such as appearing aggressive microscopically), or the tumor is larger than 1 cm, a 21 gene test may be performed to determine the risk that the cancer will recur. Results of this test indicate the likelihood that chemotherapy will be helpful. If the resulting recurrence score is less than 18, only adjuvant endocrine therapy is necessary. If the score is between 18 and 30, adjuvant endocrine therapy is needed, and chemotherapy may or may not be given based on discussions with the doctor and the woman's preferences. If the recurrence score is 31 or higher, adjuvant chemotherapy and hormone therapy are needed. If the test is not performed, adjuvant endocrine therapy with or without chemotherapy is recommended.
- If cancer larger than 2 mm is found in one or more lymph nodes, adjuvant chemotherapy and hormone therapy are recommended. Chemotherapy is given before hormone therapy.

Estrogen Receptor–Negative and Progesterone Receptor–Negative and HER2-Positive Tumor (based on page 18)

The top treatment pathway describes care following surgery for women with hormone receptor–negative, HER2-positive invasive ductal, lobular, mixed, or metaplastic cancer that does not invade the chest wall or skin and has no more than 2 mm spread to one lymph node. Recommendations for adjuvant therapy depend on the size and characteristics of the tumor:

- If the tumor is 0.5 cm or smaller or is considered microinvasive, with no spread to the lymph nodes, no adjuvant treatment is needed. If a similarly sized tumor has lymph node spread smaller than 2 mm, chemotherapy with or without trastuzumab may be given.
- If the tumor measures 0.6 to 1 cm, chemotherapy with or without trastuzumab may be given.
- If the tumor is larger than 1 cm or if cancer larger than 2 mm is found in one or more lymph nodes, adjuvant chemotherapy with trastuzumab is recommended.

Estrogen Receptor–Negative and Progesterone Receptor–Negative and HER2-Negative Tumor (based on page 19)

The top treatment pathway describes care following surgery for women with hormone receptor–negative, HER2-negative invasive ductal, lobular, mixed, or metaplastic cancer that does not invade the chest wall or skin and has no more than 2 mm spread to one lymph node. Recommendations for adjuvant therapy depend on the size and characteristics of the tumor:

- If the tumor is 0.5 cm or smaller or is considered microinvasive, with no spread to the lymph nodes, no adjuvant treatment is needed. If a similarly sized tumor has lymph node spread smaller than 2 mm, chemotherapy may be given.
- If the tumor measures 0.6 to 1 cm, chemotherapy may be given.
- If the tumor is larger than 1 cm or if cancer larger than 2 mm is found in one or more lymph nodes, adjuvant chemotherapy is recommended.

Tubular or Colloid Breast Cancers (based on page 20)

The treatment pathways address tubular or colloid breast cancers, which have a more favorable prognosis than other types of breast cancer. Hormone receptor status is an important factor in deciding treatment for these tumors, but HER2 status is not, since these tumors are usually HER2-negative. In fact, the diagnosis of tubular cancer should be questioned if the tumor is either hormone receptor–negative or HER2-positive. Treatment options for tubular and colloid tumors are based on the size of tumor and lymph node status, as well as the status of hormone receptors. The NCCN Guidelines for Patients™ recommend the following:

- For tumors smaller than 1 cm with no or a minimal spread to the lymph nodes, no treatment is needed after surgery.
- Hormone therapy may be considered for women with hormone receptor–positive disease if the tumor is between 1 and 2.9 cm in size and there is no cancer in lymph nodes or very small spread to 1 lymph node. If the tumor is larger than 3 cm, hormone therapy is recommended.
- Hormone therapy with or without chemotherapy is recommended for hormone receptor–positive tumors that have spread to the lymph nodes. The benefits of chemotherapy and hormone therapy are additive. However, the benefit of chemotherapy may be minimal in patients over the age of 60 with good prognosis tumors who are already receiving hormone therapy. In these patients, the decision to add chemotherapy to hormone therapy should be individualized.
- If the tumor is hormone receptor-negative the test should be repeated because it is uncommon for this particular type of breast cancer to be hormone receptor negative. If ER and PR negative status is confirmed, the cancer should be treated like other ER and PR negative cell types.

Evaluation Treatment of Large Stage II or IIIA Breast Cancers (based on page 21)

Breast-conserving treatment is usually not recommended for women with large tumors. However, chemotherapy may shrink the tumor enough to permit a lumpectomy that completely removes the main tumor and still keeps the size and shape of the breast acceptable. Preoperative chemotherapy (neoadjuvant chemotherapy) is an option that allows some women with large tumors (larger than 2 cm) that have not spread to the skin or chest wall to have breast-conserving treatment if they want it.

The recommended workup before starting preoperative chemotherapy includes:

- Medical history and physical examination
- Blood counts and chemical tests
- CT scan of the chest or chest x-ray
- Diagnostic mammography of both breasts
- Breast ultrasound and MRI if needed
- Pathology review of biopsy sample
- Hormone receptor test of the tumor
- HER2 test of the tumor
- Bone scan and CT, MRI, or ultrasound of the abdomen if the tumor is larger than 5 cm (2 inches) with lymph node spread, or if there are symptoms of tumor spread to other parts of the body, such as pain or abnormal blood tests
- Genetic testing may be recommended if other members of the family have had breast cancer or ovarian cancer especially at a young age.

If there are enlarged lymph nodes, a needle biopsy can be done before chemotherapy. If the lymph nodes are not enlarged, a sentinel lymph node biopsy may be done before chemotherapy. It is recommended that the tumor be marked before chemotherapy so that the area can be located in the event that the tumor completely disappears on physical examination and mammogram. While complete disappearance of the tumor is a good thing, surgery is still required to remove the site of the tumor from the breast. Marking the site helps the surgeon to know which part of the breast to remove.

The same drugs used for adjuvant treatment in stage I or II breast cancer are also used before surgery to shrink the tumor for a mastectomy or lumpectomy. If the tumor is HER2-positive, trastuzumab should be added to the chemotherapy. If the tumor is hormone receptor-positive, then hormone therapy is sometimes used instead of chemotherapy. If hormone therapy is used instead of chemotherapy, the preferred hormone therapy is an aromatase inhibitor in postmenopausal women.

If the tumor shrinks from the chemotherapy or hormone therapy, the next step is lumpectomy (see page 23) and removal of underarm lymph nodes unless a sentinel lymph node biopsy is performed before chemotherapy and showed no evidence of cancer.

If the tumor doesn't shrink enough to permit a lumpectomy, another type of chemotherapy may be given, but a mastectomy will be needed if there isn't enough tumor shrinkage to allow a lumpectomy (see page 22). Mastectomy may be followed by breast reconstruction. The underarm lymph nodes should be removed unless a sentinel lymph node biopsy is done before the chemotherapy and found no cancer.

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After mastectomy or lumpectomy, more chemotherapy may be recommended to complete all the originally planned chemotherapy (see page 23) or as part of a clinical trial depending on the tumor size and number of positive lymph nodes. If the tumor was hormone receptor–positive, hormone therapy should be given. If a lumpectomy was done, it should be followed by radiation therapy to the whole breast and sometimes to the surrounding lymph nodes. The decision to treat the lymph nodes with radiation or to treat the skin after mastectomy is based on the same principles as in stage I and II cancers above.

Stage III Locally Advanced Breast Cancers (based on pages 24-25)

Stage III cancers are advanced cancers growing into the skin of less than one third of the skin of the breast or chest wall, or have enlarged lymph nodes that are matted together. There is no evidence of spread anywhere else in the body. The recommended workup for stage III breast cancer includes:

- Medical history and physical examination
- Blood counts and blood tests to measure liver function
- Chest CT scan and perhaps chest x-ray
- Diagnostic mammograms of both breasts
- Breast ultrasound test and/or breast MRI (if needed)
- Pathology review
- Hormone receptor test
- HER2 test of the biopsy sample

Other tests may be required if blood tests are abnormal, if there are other signs or symptoms of the cancer spreading, or to get more information about the breast tumor itself. These tests include:

- Breast MRI
- Bone scan
- CT, MRI, or ultrasound of the abdomen
- PET/CT scan if other tests are suspicious but unclear

The treatment for locally advanced breast cancer starts with chemotherapy given before surgery. The chemotherapy regimen should contain an *anthracycline* (doxorubicin or epirubicin) with or without a *taxane* (paclitaxel or *docetaxel* [Taxotere®]) and should include trastuzumab if the tumor is HER2-positive. Patients whose tumors shrink enough to be surgically removed may undergo either:

- Mastectomy and removal of underarm lymph nodes. This is followed by radiation therapy to the chest wall, above the collarbone, and, if they are enlarged, internal nodes next to the sternum or breastbone. Breast reconstruction can be done later if desired.
- Possible lumpectomy with removal of underarm lymph nodes, if the cancer has shrunk enough, followed by radiation therapy to the breast and above the collarbone, and, if they are enlarged, internal nodes next to the sternum or breastbone.

For these women the NCCN Guidelines recommend adding more chemotherapy after surgery. If the cancer is hormone receptor–positive, hormone therapy is recommended. If the tumor is HER2-positive, trastuzumab is also recommended.

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Women with stage IIIA or IIIB breast cancer that doesn't shrink after their first treatment can be treated with another chemotherapy regimen and/or radiation therapy. If the tumor shrinks, the patient can be treated as outlined above. If the tumor does not shrink, the patient should discuss specific treatment for the medical situation with her doctor.

Follow-Up, Recurrence Workup, or Initial Workup for Stage IV Disease (based on page 26)

Routine follow-up for all patients with invasive breast cancer includes the following:

- A medical history and physical exam every 4 to 6 months for 5 years, then once a year.
- Women who have had a lumpectomy should have a mammogram of the treated breast 6 months after radiation therapy, and mammograms of both breasts every year.
- Women who have had a mastectomy should have a yearly mammogram of the remaining breast after the surgery.
- Because tamoxifen increases a woman's risk of developing uterine cancer, women taking this drug should have a yearly pelvic exam and should promptly tell their doctor if there is any abnormal bleeding from the vagina.
- Women on an aromatase inhibitor or who went through early menopause on treatment should have their bones tested for strength using a test called a bone mineral density test.

If there is a suspected recurrence or if the cancer had already spread on diagnosis, the workup includes:

- Complete medical history and physical examination
- Blood counts and chemistry tests
- Liver function tests
- Chest imaging
- Bone scan

Weight-bearing bones that are painful or show abnormalities on the bone scan should also be x-rayed, and CT or MRI scans of the abdomen, chest, or head should be done if there are symptoms or blood tests suggesting a recurrence in these areas. Another option is a PET scan.

A biopsy should be performed to confirm the first recurrence whenever possible. If HER2 testing was not done on the original cancer or was negative, it should be performed on a new biopsy specimen if possible. Likewise, if hormone receptor tests were not done or were negative, testing for these should be done. Genetic counseling should be considered if there is a strong family history of breast or ovarian cancer.

Treatment of Recurrence or Stage IV Disease (based on pages 27 and 28)

A recurrence may be local, meaning that cancer has returned to the area of the breast, underarm lymph nodes, or nearby tissue. Or it may be systemic, which means that cancer has spread to distant organs. If the recurrence is local and the woman had a lumpectomy and radiation therapy, she will need a mastectomy with lymph node removal. If mastectomy was already done, the recurrent cancer should be removed by surgery, if possible. The area of the recurrence and surrounding tissues should receive radiation therapy, if it has not been given before. If the cancer cannot be removed with surgery, the woman should have radiation therapy if it was not given before. In either case, the NCCN recommends considering chemotherapy, hormone therapy, or trastuzumab. If the woman was first treated with lumpectomy and radiation and the recurrence is in the breast, a mastectomy should be done, and then chemotherapy, hormone therapy, or trastuzumab therapy should be considered.

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If the recurrence is in areas outside the breast or lymph nodes around the breast, or it is first diagnosed as stage IV, treatment options are based on whether or not the tumor is hormone receptor–positive and whether the tumor has limited or extensive spread. Hormone therapy with or without ovarian ablation is appropriate for the following patients:

- The tumor is hormone receptor–positive;
- The tumor is hormone receptor–positive or –negative, and there is spread only to the bones or soft tissues; or
- The tumor is hormone receptor–positive or –negative, and the cancer has spread to other organs, such as the liver or lungs, but the organs are still working well.

These last two options seem inconsistent with other recommendations regarding using hormone therapy only in women with hormone receptor–positive tumors. However, hormone therapy has many fewer side effects than chemotherapy and can sometimes help in these situations. Since chemotherapy does not cure the cancer once it has spread outside the breast, NCCN recommends the treatments that cause the fewest side effects and still can control the cancer. If one treatment stops working or does not work at all, the oncologist will recommend changing to a different treatment. In breast cancer that has spread, women often take a series of different treatments over time.

The specific treatment is based on what type of treatment the patient has received before and whether or not the woman is premenopausal or postmenopausal (see page 28). For example, if an antiestrogen, such as tamoxifen, has been given within the past year, then a different hormone therapy should be offered. If the patient has not received an antiestrogen within the past year, treatment options are based on whether the patient is pre- or postmenopausal. For postmenopausal women, an aromatase inhibitor or antiestrogen would be the first choice. Premenopausal women may be treated with an antiestrogen alone. Another treatment option for premenopausal women is to block the ovaries from making estrogen (see page 28) and then use hormone therapy similar to postmenopausal patients. The ovaries may be blocked with a medicine that decreases estrogen production in the ovary, with radiation therapy to the ovary, or by surgically removing the ovaries. If there is spread to bone, either pamidronate or zoledronate, along with calcium and vitamin D, should be given to strengthen the bones.

In patients whose tumor is hormone receptor–negative and causing symptoms, treatment options depend on whether or not the tumor is HER2–positive. If the tumor is HER2–positive (see page 29), then trastuzumab may be given, either alone or combined with chemotherapy. If the cancer grows after trastuzumab treatment, it may be continued with a different chemotherapy drug. Another option is to try a combination with lapatinib either with more trastuzumab or with a chemotherapy drug.

If the tumor is HER2–negative, chemotherapy alone is recommended (see page 29).

If the tumor does not shrink after 3 different chemotherapy regimens, stopping chemotherapy and providing supportive care to relieve symptoms should be considered.

If hormone therapy causes the cancer to shrink or at least not grow for a while, it should be continued until the cancer begins to grow again (see page 30). At that time another hormone treatment may be tried. NCCN recommends trying at least 3 different hormone treatments until there is no longer any benefit or the cancer has spread extensively to internal organs with associated symptoms. At that point chemotherapy is recommended.

Hormone therapy is not recommended when the tumor has not responded to 3 hormone therapies in a row; or when the tumor has spread extensively to organs, such as the lungs or liver, and is causing the organs to not work well.

Adjuvant Hormone Treatment

This section describes the options for adjuvant hormonal treatment after breast surgery in women whose cancer contained hormone receptors.

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In the past, tamoxifen has been the standard therapy. Results of recent clinical trials have pointed to new treatments, particularly the use of aromatase inhibitors (anastrozole, letrozole, or exemestane) either alone or after tamoxifen in post-menopausal women. Although all aromatase inhibitors are probably equally effective, they are specifically named in this treatment pathway, based on the results of clinical trials.

In general, tamoxifen is recommended for premenopausal patients. Treatment with tamoxifen followed by an aromatase inhibitor, or an aromatase inhibitor alone is recommended for postmenopausal women. Treatment with tamoxifen followed by an aromatase inhibitor is an option for premenopausal women who become postmenopausal during tamoxifen treatment.

If use of an aromatase inhibitor is considered later in therapy for a woman who was premenopausal at the time of her diagnosis of breast cancer, she should be monitored for hormone levels such as estradiol and FSH to ensure that she is truly postmenopausal.

For premenopausal women, tamoxifen for 2 to 3 years is recommended. While tamoxifen alone is often recommended, another option is to combine tamoxifen with efforts to decrease ovarian production of estrogen using surgery, radiation, or LHRH agonist or antagonist. If the woman becomes postmenopausal during treatment, the tamoxifen may be continued for a total of 5 years and followed by 5 years of letrozole. Another option would be stopping the tamoxifen after 2 to 3 years and taking exemestane or anastrozole for the remaining 2 to 3 years. If the woman remains premenopausal during treatment with tamoxifen, tamoxifen should be continued for a total of 5 years. If she then becomes postmenopausal, the tamoxifen should be stopped and letrozole, for 5 years, could be added.

For women who are postmenopausal at the beginning of therapy, one choice is an aromatase inhibitor, either anastrozole or letrozole, for 5 years. A second option is to take tamoxifen for 2 to 3 years and then complete 5 years of treatment with either anastrozole or exemestane. A third choice is to take tamoxifen for 4.5 to 6 years and then take letrozole for 5 years. If a patient can't take an aromatase inhibitor, then tamoxifen for 5 years is an acceptable option. Aromatase inhibitors may weaken bones. Therefore, women taking these drugs may have periodic checks of their bone strength to determine if they would benefit from bone strengthening drugs.

If you have side effects that cause you to consider discontinuing treatment, talk to your doctor first. Often a different drug can be substituted that will also reduce the risk of recurrence without the troublesome side effects.

Complementary and Alternative Therapies

Complementary and alternative medicines are a group of different types of health care practices, systems, and products that are not part of your usual medical treatment. They may include Chinese herbs, special supplements, acupuncture, massage, and a host of other types of treatment. Patients may hear and learn about different treatments from family and friends. People may offer all sorts of things, such as vitamins, herbs, stress reduction, and more, as a treatment for cancer or to help patients feel better.

Complementary medicines are methods that are used in addition to regular medical care, and may add to a patient's comfort and well-being. Alternative medicines are defined as those that are used instead of regular medical care. Some of these medicines have been proven harmful but are still promoted as "cures." If a patient chooses to use these alternatives, they may reduce the chance of fighting cancer by delaying or replacing regular cancer treatment.

There is a great deal of interest today in complementary and alternative treatments for cancer. Many are being studied to find out if they are truly helpful to patients with cancer.

Before changing treatment or adding any of these methods, it is important to discuss this openly with the oncologist or nurse. Some methods can be safely used along with standard medical treatment. Others, however, can interfere with standard treatment or cause serious side effects.

Inflammatory Breast Cancer (based on page 31)

Inflammatory breast cancer (IBC) is a very aggressive type of breast cancer in which the skin of a third or more of the breast is red and it usually feels warm; there is no evidence of spread anywhere else in the body. The breast may also be swollen, and the skin of the breast may look dimpled, like the skin of an orange. IBC can be mistaken for a breast infection, but the redness and swelling of the breast is caused by small pieces of tumor that interfere with the flow of lymphatic fluid through the breast tissue. With IBC, the physician may not always be able to feel a lump inside the breast.

Only a biopsy of the breast tissue or skin can be used to confirm or rule out IBC. In addition to confirming a diagnosis of cancer, the biopsy provides the oncologist with information about whether tumor markers are present in high amounts on the tumor cells. Before treatment begins, a variety of tests will be performed to find out whether the cancer has spread to other parts of the body and to help to identify the treatments that are likely to be most effective.

In the case of IBC, tumor size is not always the main consideration in determining the stage of the disease; in some cases, no tumor mass will be detected and staging depends on how widespread the cancer is in the breast, the number of lymph nodes involved, and whether the cancer has spread to other parts of the body. If there is no spread to distant organs, it is considered to be stage IIIB. In stage IV, breast cancer cells have spread to other organs (metastasized) and it is treated like other metastatic breast cancer (see page 32).

For stage IIIB, tumor stage, estrogen and progesterone receptor tumor status, and HER2 tumor status will help determine the best treatment.

Treatment for a woman with IBC is highly individualized; no single treatment plan is right for everyone. Because IBC is a fast-growing, aggressive cancer, the treatment plan is likely to involve chemotherapy, surgery, and radiation therapy, as well as other possible treatments. Usually, chemotherapy is the first treatment given including either doxorubicin or epirubicin, and perhaps paclitaxel or docetaxel. If the tumor is HER2-positive, trastuzumab will likely be added. If the tumor shrinks, the next step is a mastectomy with radiation to the chest and lymph nodes around the collarbone. Reconstruction, if desired, is performed at a later date. Following surgery, chemotherapy will be completed if not all the planned cycles were completed before surgery, and if the tumor has hormone receptors, hormone therapy will be started. If the tumor is HER2-positive, a full year of trastuzumab will be completed.

If the tumor did not shrink with the preoperative chemotherapy, a different chemotherapy regimen, radiation therapy, or both will be tried. If the tumor responds to this second treatment, surgery will take place as described above. If not, the doctor will recommend treatment based on the woman's individual situation.

Glossary

Ablation

In medicine, the removal or destruction of a body part or tissue or its function. Ablation may be performed by surgery, hormones, drugs, radiofrequency, heat, or other methods.

Adjuvant therapy

Additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biological therapy, and is added after surgery.

Adrenal gland

A small gland that makes steroid hormones, adrenaline, and noradrenaline. These hormones help control heart rate, blood pressure, and other important body functions. There are two adrenal glands, one on top of each kidney. Also called suprarenal gland.

Anastrozole

An anticancer drug that is used to decrease estrogen production and suppress the growth of tumors that need estrogen to grow. It is a type of nonsteroidal aromatase inhibitor. The trade name for anastrozole is Arimidex®.

Anthracycline

A type of antibiotic that comes from certain types of Streptomyces bacteria. Anthracyclines are used to treat many types of cancer. Anthracyclines damage the DNA in cancer cells, causing them to die. Doxorubicin and epirubicin are anthracyclines.

Antiestrogen

A substance that keeps cells from making or using estrogen (a hormone that plays a role in female sex characteristics, the menstrual cycle, and pregnancy). Antiestrogens may stop some cancer cells from growing and are used to prevent and treat breast cancer. They are also being studied in the treatment of other types of cancer. An antiestrogen is a type of hormone antagonist. Also called estrogen blocker. Tamoxifen is an antiestrogen. In breast cancer, antiestrogens are used to treat tumors that depend on estrogen for growth.

Aromatase inhibitors

A drug that prevents the formation of estradiol, a female hormone, by interfering with an aromatase enzyme. Aromatase inhibitors are used as a type of hormone therapy for postmenopausal women who have hormone-dependent breast cancer. Examples are anastrozole, letrozole, and exemestane.

Assay

A laboratory test to find and measure the amount of a specific substance.

Glossary

Asymptomatic

Having no signs or symptoms of disease.

Axillary lymph node

A lymph node in the armpit region that drains lymph from the breast and nearby areas.

Axillary lymph node dissection

A surgical procedure in which the lymph nodes in the armpit (axillary nodes) are removed. This is also done to remove any cancerous lymph nodes.

Benign

Not cancerous. Benign tumors may grow larger but do not spread to other parts of the body. Also called nonmalignant.

Bevacizumab

A drug used to treat several types of cancer, including certain types of colorectal, lung, breast, and kidney cancers and glioblastoma. It is also being studied in the treatment of other types of cancer. Bevacizumab binds to vascular endothelial growth factor (VEGF) and may prevent the growth of new blood vessels that tumors need to grow. It is a type of antiangiogenesis agent and a type of monoclonal antibody. The trade name for bevacizumab is Avastin®.

Bilateral

Affecting both the right and left sides of the body.

Biological therapy

Treatment to boost or restore the ability of the immune system to fight cancer, infections, and other diseases. Also used to lessen certain side effects that may be caused by some cancer treatments. Agents used in biological therapy include monoclonal antibodies, growth factors, and vaccines. These agents may also have a direct antitumor effect. Also called immunotherapy.

Biopsy

The removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy, in which only a sample of tissue is removed; (2) excisional biopsy, in which an entire lump or suspicious area is removed; and (3) needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

Glossary

Bisphosphonates

A drug or substance used to treat hypercalcemia (abnormally high blood calcium) and bone pain caused by some types of cancer. Forms of bisphosphonates are also used to treat osteoporosis and for bone imaging. Bisphosphonates inhibit a type of bone cell that breaks down bone, thus help strengthen bones weakened by cancer by encouraging the deposition of calcium. These include pamidronate and zoledronate.

Bone mineral density

A measure of the amount of minerals (mostly calcium and phosphorous) contained in a certain volume of bone. Bone mineral density measurements are used to diagnose osteoporosis (a condition marked by decreased bone mass), to see how well osteoporosis treatments are working, and to predict how likely the bones are to break. Low bone mineral density can occur in patients treated for cancer. Also called BMD, bone density, and bone mass.

Bone scan

A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner.

Brachytherapy

A type of radiation therapy in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near a tumor. Also called implant radiation therapy, internal radiation therapy, and radiation brachytherapy.

Breast-conserving surgery

An operation to remove the breast cancer but not the breast itself. Types of breast-conserving surgery include lumpectomy (removal of the lump), quadrantectomy (removal of one quarter, or quadrant, of the breast), and segmental mastectomy (removal of the cancer as well as some of the breast tissue around the tumor and the lining over the chest muscles below the tumor). Also called breast-sparing surgery.

Breast density

Describes the relative amount of different tissues present in the breast. A dense breast has less fat than glandular and connective tissue. Mammogram films of breasts with higher density are harder to read and interpret than those of less dense breasts.

Breast reconstruction

Surgery that rebuilds the breast contour after mastectomy. A breast implant or the woman's own tissue provides the contour. If desired, the nipple and areola may also be recreated. Reconstruction can be done at same time as the mastectomy or any time later.

Glossary

Capecitabine

A drug used to treat stage III colon cancer in patients who had surgery to remove the cancer. It is also used to treat metastatic breast cancer that has not improved after treatment with certain other anticancer drugs. Capecitabine is being studied in the treatment of other types of cancer. It is taken up by cancer cells and breaks down into 5-fluorouracil, a substance that kills tumor cells. Capecitabine is a type of antimetabolite. Its trade name is Xeloda®.

Carcinoma

Cancer that begins in the skin or in tissues that line or cover internal organs.

Carcinoma in situ

A group of abnormal cells that remain in the place where they first formed. They have not spread. These abnormal cells may become cancer and spread into nearby normal tissue. Also called stage 0 disease. Most in situ carcinomas are highly curable.

CBC

See complete blood count.

Chemotherapy

Treatment with drugs to destroy cancer cells. Chemotherapy is often used in addition to surgery or radiation to treat cancer when spread (metastasis) is proven or suspected, when the cancer has come back (recurred), or when there is a strong likelihood that the cancer could recur.

Chest wall

The muscles, bones, and joints that make up the area of the body between the neck and the abdomen.

Clavicle

One of a pair of bones at the base of the front of the neck. The clavicles connect the breastbone to the shoulder blades. Also called collarbone.

Clinical stage

Stage includes evaluation of the size and extent of the cancer, the presence or absence of spread to lymph nodes, and the presence or absence of spread to other body organs. Clinical stage is the stage determined only by physical examination and x-ray or other imaging studies. This includes determination of the size of the cancer and evaluation of lymph nodes by the doctor's examination of the armpit. The final stage is the pathological stage which is determined from microscopic examination of the tumor and lymph nodes. Clinical stage is used for initial treatment planning.

Clinical trial

A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease.

Glossary

Complete blood count

Also known as CBC. A test to check the number of red blood cells, white blood cells, and platelets in a sample of blood. Also called blood cell count.

Computerized tomography scan

Also known as a CT scan. A series of detailed pictures of areas inside the body taken from different angles. The pictures are created by a computer linked to an x-ray machine. Also called CAT scan and computed tomography scan.

Contrast material

A dye or other substance that helps show abnormal areas inside the body. It is given by injection into a vein, by enema, or by mouth. Contrast material may be used with x-rays, CT scans, MRI, or other imaging tests.

Core Biopsy

See core needle biopsy.

Core Needle Biopsy

The removal of a tissue sample with a wide needle for examination under a microscope. Also called core biopsy.

CT

See computerized tomography scan.

Cyst

A fluid-filled mass that is usually not cancer (benign). The fluid can be removed for testing.

Cytotoxic chemotherapy

Anticancer drugs that kill cells, especially cancer cells.

DCIS

See ductal carcinoma in situ.

Diagnostic mammogram

X-ray of the breasts used to check for breast cancer after a lump or other sign or symptom of breast cancer has been found.

Glossary

Docetaxel

A drug used together with other drugs to treat certain types of breast cancer, stomach cancer, prostate cancer, and certain types of head and neck cancer. It is also being studied in the treatment of other types of cancer. Docetaxel is a type of mitotic inhibitor. Its trade name is Taxotere®.

Doxorubicin

A drug that is used to treat many types of cancer and is being studied in the treatment of other types of cancer. Doxorubicin comes from the bacterium *Streptomyces peucetius*. It damages DNA and may kill cancer cells. It is a type of anthracycline antitumor antibiotic. Its trade name is Rubex®.

Duct

A hollow passage for gland secretions. In the breast, a passage through which milk passes from the lobule (which makes the milk) to the nipple. These ducts are the starting point for most breast cancers.

Ductal carcinoma in situ

A noninvasive condition in which abnormal cells are found in the lining of a breast duct. The abnormal cells have not spread outside the duct to other tissues in the breast. In some cases, ductal carcinoma in situ may become invasive cancer and spread to other tissues, although it is not known at this time how to predict which lesions will become invasive. Also called DCIS.

EGFR

See epidermal growth factor receptor.

Endocrine therapy

See hormone therapy.

Epidermal growth factor receptor

The protein found on the surface of some cells and to which epidermal growth factor binds, causing the cells to divide. It is found at abnormally high levels on the surface of many types of cancer cells, so these cells may divide excessively in the presence of epidermal growth factor. Also called EGFR, ErbB1, and HER1.

Epirubicin

A drug used together with other drugs to treat early breast cancer that has spread to lymph nodes. It is also being studied in the treatment of other types of cancer. Epirubicin is a type of anthracycline antibiotic. Also called Ellence and epirubicin hydrochloride.

ER

See estrogen receptor.

Glossary

Estradiol

A form of the hormone estrogen.

Estrogen

A type of hormone made by the body that helps develop and maintain female sex characteristics and the growth of long bones. Estrogens can also be made in the laboratory. They may be used as a type of birth control and to treat symptoms of menopause, menstrual disorders, osteoporosis, and other conditions. In breast cancer, estrogen may help the growth of breast cancer cells.

Estrogen receptor

A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone estrogen will bind to the receptors inside the cells and may cause the cells to grow. Also called ER.

Excision

Removal by surgery.

Excisional biopsy

A surgical procedure in which an entire lump or suspicious area is removed for diagnosis. The tissue is then examined under a microscope.

Exemestane

A drug used to treat advanced breast cancer and to prevent recurrent breast cancer in postmenopausal women who have already been treated with tamoxifen. It is also being studied in the treatment of other types of cancer. Exemestane causes a decrease in the amount of estrogen made by the body. It is a type of aromatase inhibitor. The trade name for exemestane is Aromasin®.

External-beam radiation therapy

A type of radiation therapy that uses a machine to aim high-energy rays at the cancer from outside of the body. Also called external radiation therapy.

Fatigue

A condition marked by extreme tiredness and inability to function due lack of energy. Fatigue may be acute or chronic.

Fine-needle aspiration

The removal of tissue or fluid with a thin needle for examination under a microscope.

FISH

See fluorescence in situ hybridization.

Glossary

Fluorescence in situ hybridization

Also called FISH. A laboratory technique used to look at genes or chromosomes in cells and tissues. Pieces of DNA that contain a fluorescent dye are made in the laboratory and added to cells or tissues on a glass slide. When these pieces of DNA bind to specific genes or areas of chromosomes on the slide, they light up when viewed under a microscope with a special light.

FNA

See fine-needle aspiration.

FSH

A hormone made in the pituitary gland. In females, it acts on the ovaries to make the follicles and eggs grow. Also called follicle-stimulating hormone and follitropin.

Fulvestrant

A drug used to treat certain types of breast cancer in postmenopausal women. It is also being studied in the treatment of other types of cancer. Fulvestrant blocks estrogen activity in the body and is a type of antiestrogen. Its trade name is Faslodex®

Gene expression

The process by which a gene gets turned on in a cell to make RNA and proteins. Gene expression may be measured by looking at the RNA, or the protein made from the RNA, or what the protein does in a cell.

Genetic counseling

A communication process between a specially trained health professional and a person concerned about the genetic risk of disease. The person's family and personal medical history may be discussed, and counseling may lead to genetic testing.

Grade

A description of a tumor based on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grade 1 (also called well-differentiated) means the cancer cells look like the normal cells. Grade 3 (poorly-differentiated) cancer cells do not look like normal cells at all. Grade 1 cancers aren't considered aggressive and tend to grow more slowly and metastasize slower. Grade 3 cancers are more likely to grow fast and metastasize. A cancer's grade, along with its stage, is used to determine treatment.

Growth factors

A substance made by the body that functions to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy.

Glossary

HER2

A protein involved in normal cell growth. It is found on some types of cancer cells, including breast and ovarian. Cancer cells removed from the body may be tested for the presence of HER2/neu to help decide the best type of treatment. Breast cancer cells with too many HER2 receptors tend to be fast-growing and may respond to treatment with a monoclonal antibody, trastuzumab.

Histology

The way the cancer cells look under the microscope (described as type and arrangement of tumor cells).

Hormone

One of many chemicals made by glands in the body. Hormones circulate in the bloodstream and control the actions of certain cells or organs. Some hormones can also be made in the laboratory.

Hormone receptor

These are the cells' "welcome mat" for hormones circulating in the blood. The receptor is a protein that binds to a hormone, and may be on the surface of the cell or inside the cell. Many changes take place in a cell after a hormone binds to its receptor.

Hormone replacement therapy

Hormones (estrogen, progesterone, or both) given to women after menopause to replace the hormones no longer produced by the ovaries. Also called HRT.

Hormone therapy

Treatment that adds, blocks, or removes hormones. For certain conditions (such as diabetes or menopause), hormones are given to adjust low hormone levels. To slow or stop the growth of certain cancers (such as prostate and breast cancer), synthetic hormones or other drugs may be given to block the body's natural hormones. Sometimes surgery is needed to remove the gland that makes a certain hormone. The most common hormone therapy for breast cancer is the drug tamoxifen. Other hormonal therapies include aromatase inhibitors, androgens, and surgical removal of the ovaries (oophorectomy). Also known as endocrine therapy.

Human epidermal growth factor receptor 2

See HER2.

IHC

See immunohistochemistry.

Glossary

Imaging

In medicine, a process that makes pictures of areas inside the body. Imaging uses methods such as x-rays (high-energy radiation), ultrasound (high-energy sound waves), and radio waves.

Immunohistochemistry

Also called IHC. A technique used to identify specific molecules in different kinds of tissue. The tissue is treated with antibodies that bind the specific molecule. These are made visible under a microscope by using a color reaction, a radioisotope, colloidal gold, or a fluorescent dye. Immunohistochemistry is used to help diagnose diseases, such as cancer, and to detect the presence of microorganisms. It is also used in basic research to understand how cells grow and differentiate (become more specialized).

In situ

In its original place. For example, in carcinoma in situ, abnormal cells are found only in the place where they first formed. They have not spread. This describes a very early stage of cancer.

Inflammatory breast cancer

A type of breast cancer in which the breast looks red and swollen and feels warm. The skin of the breast may also show the pitted appearance called *peau d'orange* (like the skin of an orange). The redness and warmth occur because the cancer cells block the lymph vessels in the skin.

Internal mammary lymph nodes

Lymph nodes located inside the chest, next to where the sternum (breastbone) and ribs meet.

Intravenous

Into or within a vein. Intravenous usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein. Also called IV.

Invasive

Cancer that has spread from where it started in the breast into surrounding, healthy tissue. In breast cancer, most start in the ducts (tubes that carry milk from the lobules to the nipple). Invasive breast cancer can spread to other parts of the body through the blood and lymph systems. Also called infiltrating breast cancer.

Irradiation

See radiation therapy.

Glossary

Laboratory test

A medical procedure that involves testing a sample of blood, urine, or other substance from the body. Tests can help determine a diagnosis, plan treatment, check to see if treatment is working, or monitor the disease over time.

Lapatinib

A drug used with another anticancer drug to treat breast cancer that is HER2 positive and has advanced or metastasized (spread to other parts of the body) after treatment with other drugs. Lapatinib is also being studied in the treatment of other types of cancer. It is a type of ErbB-2 and EGFR dual tyrosine kinase inhibitor. The trade name for lapatinib is Tykerb®.

LCIS

See lobular carcinoma in situ.

Letrozole

A drug used to treat advanced breast cancer in postmenopausal women. Letrozole causes a decrease in the amount of estrogen made by the body. It is a type of aromatase inhibitor. The trade name for letrozole is Femara®.

LHRH agonists or antagonists

A drug that inhibits the secretion of sex hormones. In men, luteinizing hormone-releasing hormone agonist causes testosterone levels to fall. In women, luteinizing hormone-releasing hormone agonist causes the levels of estrogen and other sex hormones to fall. Also called LH-RH agonist.

Liver function test

A blood test to measure the blood levels of certain substances released by the liver. A high or low level of certain substances can be a sign of liver disease.

Lobe

A portion of an organ, such as the liver, lung, breast, thyroid, or brain.

Lobular carcinoma in situ

A condition in which abnormal cells are found in the lobules of the breast. Lobular carcinoma in situ seldom becomes invasive cancer; however, having it in one breast increases the risk of developing breast cancer in either breast. Also called LCIS.

Glossary

Lobule

A small lobe or a subdivision of a lobe.

Local therapy

Treatment that affects cells in the tumor and the area close to it.

Lumpectomy

Surgery to remove the breast tumor and a small amount of surrounding normal tissue. It is a type of breast-sparing surgery.

Luteinizing hormone-releasing hormone agonists or antagonists

See LHRH agonists or antagonists.

Lymph

The clear fluid that travels through the lymphatic system and carries cells that help fight infections and other diseases. Also called lymphatic fluid.

Lymph node

A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph (lymphatic fluid), and they store lymphocytes (white blood cells). They are located along lymphatic vessels. Also called lymph gland.

Lymph node dissection

A surgical procedure in which the lymph nodes are removed and a sample of tissue is checked under a microscope for signs of cancer. For a regional lymph node dissection, some of the lymph nodes in the tumor area are removed; for a radical lymph node dissection, most or all of the lymph nodes in the tumor area are removed. Also called lymphadenectomy.

Lymph vessel

See lymphatic vessel.

Lymphadenectomy

See lymph node dissection.

Lymphatic fluid

See lymph.

Glossary

Lymphatic vessel

A thin tube that carries lymph (lymphatic fluid) and white blood cells through the lymphatic system. Also called lymph vessel.

Lymphedema

A possible complication after breast cancer treatment. A condition in which extra lymph fluid builds up in tissues and causes swelling. It may occur in an arm or leg if lymph vessels are blocked, damaged, or removed by surgery.

Magnetic resonance imaging

Also called MRI. A procedure in which radio waves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. These pictures can show the difference between normal and diseased tissue. Magnetic resonance imaging makes better images of organs and soft tissue than other scanning techniques, such as computed tomography (CT) or x-ray. Magnetic resonance imaging is especially useful for imaging the brain, the spine, the soft tissue of joints, and the inside of bones.

Malignant

Cancerous. Malignant tumors can invade and destroy nearby tissue and spread to other parts of the body.

Mammogram

An x-ray of the breast.

Mammography

The use of film or a computer to create a picture of the breast.

Margin

The edge or border of the tissue removed in cancer surgery. The margin is described as negative or clean when the pathologist finds no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. The margin is described as positive or involved when the pathologist finds cancer cells at the edge of the tissue, suggesting that all of the cancer has not been removed.

Marker

A diagnostic indication that disease may develop.

Glossary

Mastectomy

Removal of the entire breast. In a simple or total mastectomy surgeons do not cut away any lymph nodes or muscle tissue; in a modified radical mastectomy, surgeons remove the breast and some armpit lymph nodes; in a radical mastectomy (now rarely performed) surgeons remove the breast, armpit lymph nodes, and chest wall muscles under the breast.

Medical oncologist

A doctor who specializes in diagnosing and treating cancer using chemotherapy, hormonal therapy, biological therapy, and targeted therapy. A medical oncologist often is the main health care provider for someone who has cancer. A medical oncologist also gives supportive care and may coordinate treatment given by other specialists.

Menopause

The time of life when a woman's ovaries stop producing hormones and menstrual periods stop. Natural menopause usually occurs around age 50. A woman is said to be in menopause when she hasn't had a period for 12 months in a row. Symptoms of menopause include hot flashes, mood swings, night sweats, vaginal dryness, trouble concentrating, and infertility. Menopause can also be caused by surgical removal of both ovaries (oophorectomy), or by chemotherapy, which often destroys ovarian function.

Metastases

The plural form of metastasis.

Metastasis

The spread of cancer from one part of the body to another. A tumor formed by cells that have spread is called a "metastatic tumor" or a "metastasis." The metastatic tumor contains cells that are like those in the original (primary) tumor.

Metastasize

To spread from one part of the body to another. When cancer cells metastasize and form secondary tumors, the cells in the metastatic tumor are like those in the original (primary) tumor.

Modified radical mastectomy

Surgery for breast cancer in which the breast, most or all of the lymph nodes under the arm, and the lining over the chest muscles are removed. Sometimes the surgeon also removes part of the chest wall muscles.

Glossary

Monoclonal antibody

A type of protein made in the laboratory that can bind to substances in the body, including tumor cells. There are many kinds of monoclonal antibodies. Each monoclonal antibody is made to find one substance. Monoclonal antibodies are being used to treat some types of cancer and are being studied in the treatment of other types. They can be used alone or to carry drugs, toxins, or radioactive materials directly to a tumor.

MRI

See magnetic resonance imaging.

National Cancer Institute

The National Cancer Institute, part of the National Institutes of Health of the United States Department of Health and Human Services, is the Federal Government's principal agency for cancer research. The National Cancer Institute conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. The website is available at www.cancer.gov. Also called NCI.

NCI

See National Cancer Institute.

Needle biopsy

The removal of tissue or fluid with a needle for examination under a microscope. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

Neoadjuvant therapy

Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.

Noninvasive

In medicine, it describes a procedure that does not require inserting an instrument through the skin or into a body opening. In cancer, it describes disease that has not spread outside the tissue in which it began.

Observation

In medicine, watching a patient's condition but not giving treatment unless symptoms appear or change.

Glossary

Oncologist

A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation.

Oophorectomy

Surgery to remove one or both of the ovaries.

Ovarian ablation

Surgery, radiation therapy, or a drug treatment to stop the functioning of the ovaries. Also called ovarian suppression.

Paclitaxel

A drug used to treat breast cancer, ovarian cancer, and AIDS-related Kaposi sarcoma. It is also used together with another drug to treat non-small cell lung cancer. Paclitaxel is also being studied in the treatment of other types of cancer. It blocks cell growth by stopping cell division and may kill cancer cells. It is a type of antimetabolic agent. Its trade name is Taxol®.

Palliative care

See supportive care.

Pamidronate

A drug that is used to treat hypercalcemia (too much calcium in the blood) and cancer that has spread to the bones. It belongs to the family of drugs called bisphosphonates.

Partial mastectomy

The removal of cancer as well as some of the breast tissue around the tumor and the lining over the chest muscles below the tumor. Usually some of the lymph nodes under the arm are also taken out. It is also called a segmental mastectomy or a quadrantectomy.

Pathologic stage

A method used to determine the stage of cancer. Tissue samples are removed during surgery or a biopsy. The stage is determined based on how the cells in the samples look under a microscope. Most of the time, pathologic stage is the most important stage since involvement of the lymph nodes can only be accurately evaluated by examining them under a microscope.

Pathologist

A doctor who identifies diseases by studying cells and tissues under a microscope.

Glossary

Pathology report

The description of cells and tissues made by a pathologist based on microscopic evidence, and sometimes used to make a diagnosis of a disease.

Performance status

A measure of how well a patient is able to perform ordinary tasks and carry out daily activities.

PET scan

See positron emission tomography scan.

Positron emission tomography scan

A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is used. Because cancer cells often use more glucose than normal cells, the pictures can be used to find cancer cells in the body. Also called PET scan.

PR

See progesterone receptor.

Preoperative chemotherapy

Chemotherapy given before surgery to shrink some breast tumors, so they can be removed with less extensive surgery than would otherwise be needed. Also called neoadjuvant chemotherapy.

Preventative mastectomy

See prophylactic mastectomy.

Primary tumor

The original tumor.

Progesterone

A type of hormone made by the body that plays a role in the menstrual cycle and pregnancy. Progesterone can also be made in the laboratory. It may be used as a type of birth control and to treat menstrual disorders, infertility, symptoms of menopause, and other conditions.

Progesterone receptor

A protein found inside the cells of the female reproductive tissue, some other types of tissue, and some cancer cells. The hormone progesterone will bind to the receptors inside the cells and may cause the cells to grow. Also called PR.

Glossary

Prognosis

The likely outcome or course of a disease; the chance of recovery or recurrence. For example, women with breast cancer whose tumor is small, and does not involve the lymph nodes, and receive prompt treatment have a good prognosis.

Prophylactic mastectomy

Surgery to reduce the risk of developing breast cancer by removing one or both breasts before disease develops. Also called preventive mastectomy.

Quadrantectomy

Surgical removal of the region of the breast (approximately one quarter) containing cancer. This type of breast-conserving surgery removes more breast tissue than a lumpectomy. It is also called a partial or segmental mastectomy.

Radiation

Energy released in the form of particle or electromagnetic waves. Common sources of radiation include radon gas, cosmic rays from outer space, medical x-rays, and energy given off by a radioisotope (unstable form of a chemical element that releases radiation as it breaks down and becomes more stable). This treatment is used to kill or shrink cancer cells. The radiation may come from outside of the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation called brachytherapy).

Radiation oncologist

A doctor who specializes in using radiation to treat cancer.

Radiation therapy

The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that travels in the blood to tissues throughout the body. Also called irradiation and radiotherapy.

Radiologist

A doctor who specializes in creating and interpreting pictures of areas inside the body. The pictures are produced with x-rays, sound waves, or other types of energy.

Glossary

Raloxifene

The active ingredient in a drug used to reduce the risk of invasive breast cancer in postmenopausal women who are at high risk of the disease or who have osteoporosis. It is also used to prevent and treat osteoporosis in postmenopausal women. It is also being studied in the prevention of breast cancer in certain premenopausal women and in the prevention and treatment of other conditions. Raloxifene blocks the effects of the hormone estrogen in the breast and increases the amount of calcium in bone. It is a type of selective estrogen receptor modulator (SERM).

Recur

To come back or to return.

Regimen

A treatment plan that specifies the dosage, the schedule, and the duration of treatment.

Screening mammogram

X-rays of the breasts taken to check for breast cancer in the absence of signs or symptoms.

Segmental mastectomy

See partial mastectomy.

Selective estrogen receptor modulator

A drug that acts like estrogen on some tissues but blocks the effect of estrogen on other tissues. Tamoxifen and raloxifene are selective estrogen receptor modulators. Also called SERM.

Sentinel lymph node biopsy

Removal and examination of the sentinel nodes (the first lymph nodes to which cancer cells are likely to spread from a primary tumor). To identify the sentinel lymph nodes, the surgeon injects a radioactive substance, blue dye, or both near the tumor. The surgeon then uses a probe to find the sentinel lymph nodes containing the radioactive substance or looks for the lymph nodes stained with dye. The surgeon then removes the sentinel nodes to check for the presence of cancer cells.

Side effect

A problem that occurs when treatment affects healthy tissues or organs. Some common side effects of cancer treatment are fatigue, pain, nausea, vomiting, decreased blood cell counts, hair loss, and mouth sores.

Social worker

A professional trained to talk with people and their families about emotional or physical needs, and to find them support services.

Glossary

Stage

The extent of a cancer in the body. Staging is usually based on the size of the tumor, whether lymph nodes contain cancer, and whether the cancer has spread from the original site to other parts of the body.

Stereotactic needle biopsy

A method of needle biopsy that is useful in some cases in which calcifications or a mass can be seen on mammogram, but cannot be located by touch. Computerized equipment maps the location of the mass and this is used as a guide to place the needle.

Supportive care

Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of supportive care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment. Also called palliative care and symptom management.

Supraclavicular lymph nodes

Lymph nodes located in the area just above the collarbone.

Systemic therapy

Treatment using substances that travel through the bloodstream, reaching and affecting cells all over the body. An example is chemotherapy.

Tamoxifen

A drug used to treat certain types of breast cancer in women and men. It is also used to prevent breast cancer in women who have had ductal carcinoma in situ (abnormal cells in the ducts of the breast) and in women who are at a high risk of developing breast cancer. Tamoxifen is also being studied in the treatment of other types of cancer. It blocks the effects of the hormone estrogen in the breast. Blocking estrogen is desirable in some cases of breast cancer because estrogen promotes their growth. Tamoxifen is a type of antiestrogen. Recent research suggests that tamoxifen may lower the risk of developing breast cancer in women with certain risk factors.

Targeted therapy

A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to identify and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

Taxane

A type of drug that blocks cell growth by stopping mitosis (cell division). Taxanes interfere with microtubules (cellular structures that help move chromosomes during mitosis). They are used to treat cancer. A taxane is a type of mitotic inhibitor and a type of antimicrotubule agent.

Glossary

TKI

See tyrosine kinase inhibitor.

TNM staging system

A system for describing the extent of cancer in a patient's body. T describes the size of the tumor and whether it has invaded nearby tissue, N describes any lymph nodes that are involved, and M describes metastasis (spread of cancer from one body part to another).

Toremifene

An anticancer drug that belongs to the family of drugs called antiestrogens. Toremifene blocks the effect of the hormone estrogen in the body. It may help control some cancers from growing, and it may delay or reduce the risk of cancer recurrence.

Total mastectomy

Removal of the breast. Also called simple mastectomy.

Toxic

Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects.

Toxicity

The extent to which something is poisonous or harmful.

Trastuzumab

A monoclonal antibody that binds to HER2 (human epidermal growth factor receptor 2), and can kill HER2-positive cancer cells. Monoclonal antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Trastuzumab is used to treat breast cancer that is HER2-positive and has spread after treatment with other drugs. It is also used with other anticancer drugs to treat HER2-positive breast cancer after surgery. Trastuzumab is also being studied in the treatment of other types of cancer. The trade name for trastuzumab is Herceptin®.

Tumor

An abnormal mass of tissue that results when cells divide more than they should or do not die when they should. Tumors may be benign (not cancer), or malignant (cancer). Also called neoplasm.

Tyrosine kinase inhibitor

A drug that interferes with cell communication and growth and may prevent tumor growth. Some tyrosine kinase inhibitors are used to treat cancer.

Glossary

Ultrasound

A procedure in which high-energy sound waves are bounced off internal tissues or organs and make echoes. The echo patterns are shown on the screen of an ultrasound machine, forming a picture of body tissues called a sonogram. Also called ultrasonography or US.

Ultrasound-guided biopsy

The removal of tissue or fluid with a needle for examination under a microscope. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

US

See ultrasound.

Visceral

Having to do with the viscera, which are the soft internal organs of the body, including the lungs, the heart, and the organs of the digestive, excretory, reproductive, and circulatory systems.

Wire localization biopsy

A procedure used to mark a small area of abnormal tissue so it can be removed by surgery. An imaging device is used to guide a thin wire with a hook at the end through a hollow needle to place the wire in or around the abnormal area. Once the wire is in the right place, the needle is removed and the wire is left in place so the doctor will know where the abnormal tissue is. The wire is removed when a biopsy is done.

X-ray

A type of high-energy radiation. In low doses, x-rays are used to diagnose diseases by making pictures of the inside of the body. In high doses, x-rays are used to treat cancer.

Zoledronic Acid

A drug used to treat patients with hypercalcemia (high blood levels of calcium) caused by cancer. It is also used together with other drugs to treat multiple myeloma and to prevent bone fractures and reduce bone pain in people who have cancer that has spread to the bone. It is a type of bisphosphonate. Also called zoledronic acid. The trade name for zoledronic acid is Zometa®.

For a more comprehensive glossary, visit the NCI website at www.cancer.gov.

NCCN Member Institutions

City of Hope Comprehensive Cancer Center

Los Angeles, California
800.826.4673
www.cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center

Boston, Massachusetts
800.320.0022
www.dfbwcc.org • www.massgeneral.org/cancer

Duke Comprehensive Cancer Center

Durham, North Carolina
888.275.3853
www.cancer.duke.edu

Fox Chase Cancer Center

Philadelphia, Pennsylvania
888.369.2427
www.fccc.edu

Huntsman Cancer Institute at the University of Utah

Salt Lake City, Utah
877.585.0303
www.huntsmancancer.org

Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance

Seattle, Washington
206.288.7222 • www.seattlecca.org
206.667.5000 • www.fhcrc.org

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Chicago, Illinois
866.587.4322
www.cancer.northwestern.edu

Memorial Sloan-Kettering Cancer Center

New York, New York
800.525.2225
www.mskcc.org

H. Lee Moffitt Cancer Center & Research Institute

Tampa, Florida
800.456.3434
www.moffitt.org

The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Columbus, Ohio
800.293.5066
www.jamesline.com

Roswell Park Cancer Institute

Buffalo, New York
877.275.7724
www.roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

St. Louis, Missouri
800.600.3606
www.siteman.wustl.edu

St. Jude Children's Research Hospital/ University of Tennessee Cancer Institute

Memphis, Tennessee
901.595.4055 • www.stjude.org
877.988.3627 • www.utcancer.org

Stanford Comprehensive Cancer Center

Stanford, California
877.668.7535
www.cancer.stanfordhospital.com

University of Alabama at Birmingham Comprehensive Cancer Center

Birmingham, Alabama
800.822.0933
www.ccc.uab.edu

UCSF Helen Diller Family Comprehensive Cancer Center

San Francisco, California
800.888.8664
<http://cancer.ucsf.edu>

University of Michigan Comprehensive Cancer Center

Ann Arbor, Michigan
800.865.1125
www.mcancer.org

UNMC Eppley Cancer Center at The Nebraska Medical Center

Omaha, Nebraska
800.999.5465
www.unmc.edu/cancercenter

The University of Texas MD Anderson Cancer Center

Houston, Texas
877.632.6789
www.mdanderson.org

Vanderbilt-Ingram Cancer Center

Nashville, Tennessee
800.811.8480
www.vicc.org

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