



Surgical treatment of breast cancer

Doreen M. Agnese, MD
Professor, Division of Surgical Oncology
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

 **THE OHIO STATE UNIVERSITY**
WEXNER MEDICAL CENTER



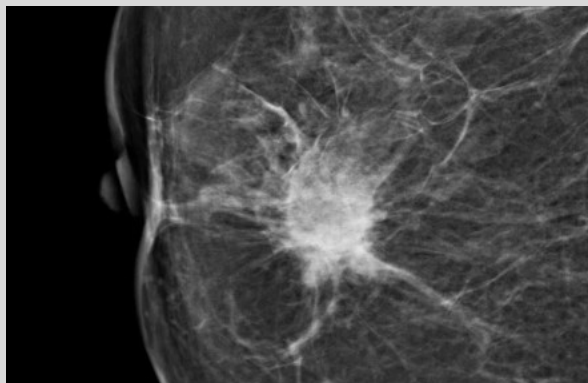
**Screening and
Diagnosis**

Patient presentations

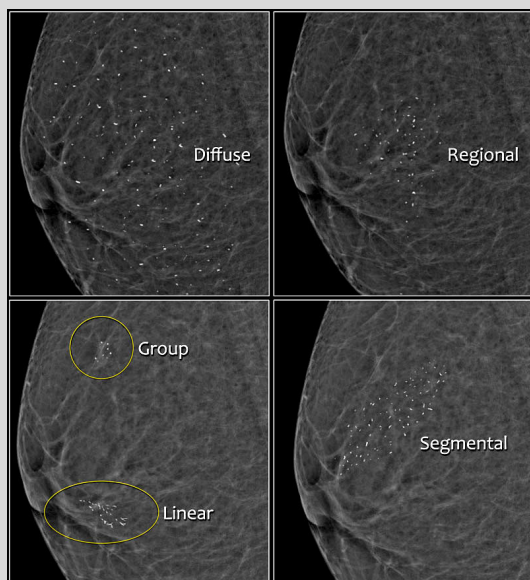
- Asymptomatic
 - Abnormal mammogram
- Symptomatic
 - Palpable mass
 - Changes in the skin of the breast/nipple
 - Nipple discharge
 - Axillary mass

Screening Guidelines, general population

- Clinical encounter about every three years for women in their 20s-30s, and annually for women ≥ 40
- Annual screening mammogram beginning at age 40 (tomosynthesis)
- Breast awareness



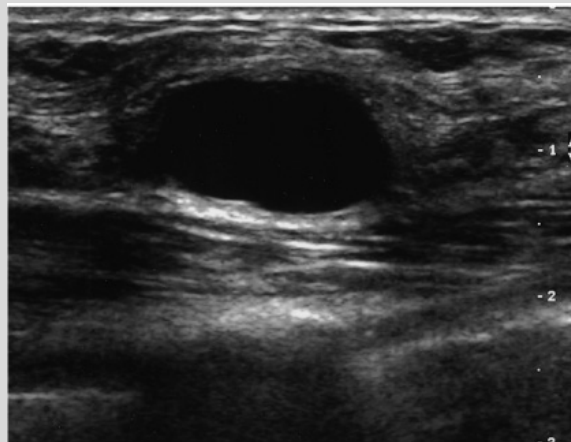
Spiculated mass



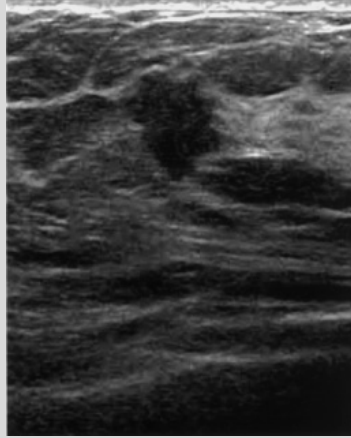
Suspicious microcalcifications

Symptomatic patients

- Evaluate with complete history and physical examination
- Diagnostic imaging
 - Bilateral mammogram, even if unilateral symptoms
 - May use other imaging modalities
 - Ultrasound
 - MRI

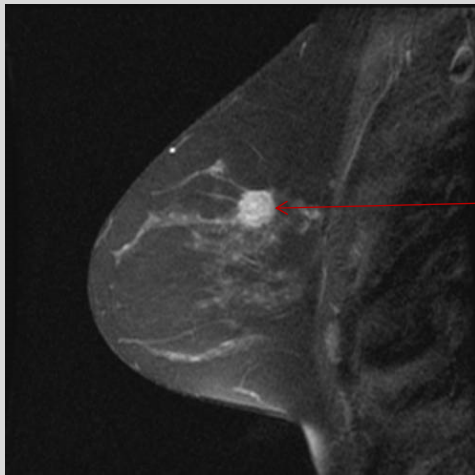


Cystic lesion, requires no further therapy



Solid mass with features suspicious for malignancy

MRI

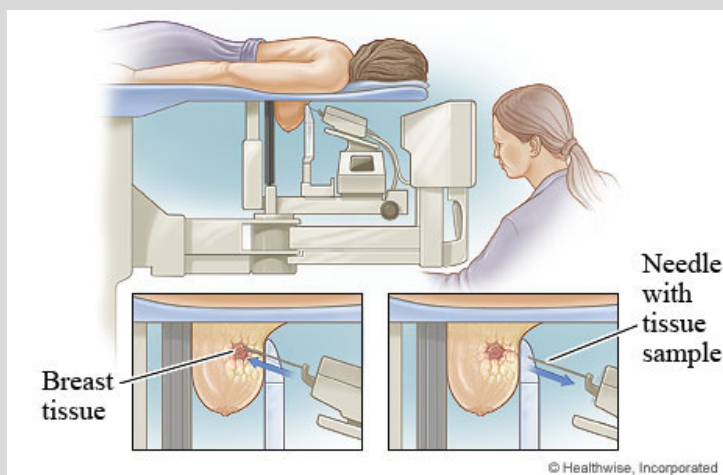


Enhancing mass, suspicious

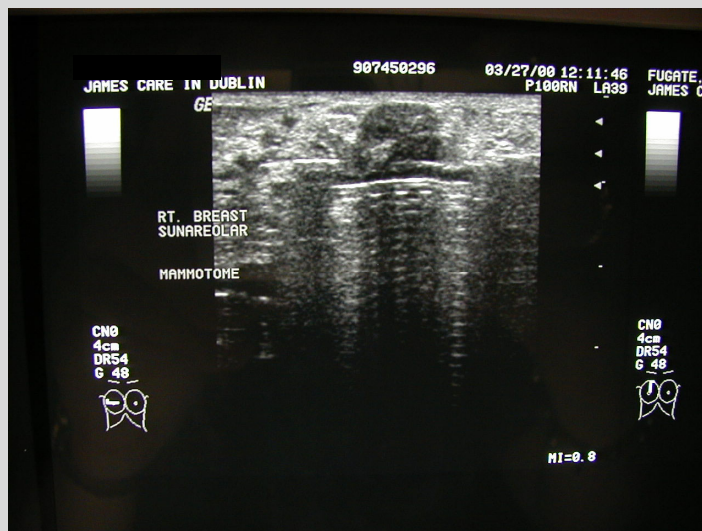
Methods of Diagnosis

- Palpable lesion
 - fine needle aspiration (FNA)
 - Core/Tru-cut biopsy
 - excisional biopsy
- Nonpalpable lesion
 - stereotactic biopsy
 - ultrasound-guided core needle biopsy
 - imaging localized excisional biopsy
- Abnormal skin—punch biopsy

Stereotactic Breast Biopsy



Ultrasound-Guided Core or Mammotome Biopsy



Non-invasive breast cancer

DCIS

- Usually presents as an abnormal mammogram with clustered calcifications
- Nodal metastases are rare (1%), likely associated with unrecognized microinvasion
- Up to 1/2 of recurrences are invasive

Management

- Treatment → lumpectomy with radiation therapy (negative margins) or total mastectomy
- Evaluation of the axillary lymph nodes is generally **not** necessary (unless mastectomy)



Invasive cancers

Invasive breast cancer

- Most common type is infiltrating ductal (75%)
- Less common variants of ductal
 - Medullary (6%)-better prognosis
 - Tubular (2%)-excellent prognosis
 - Colloid (1-2%)-better prognosis
- Invasive lobular (10%)
 - Indistinct margins, extensive infiltration
 - Harder to detect mammographically
 - Significant incidence of multicentricity

Surgical Management of Invasive Breast Cancer

Breast (removal of primary tumor)

total mastectomy

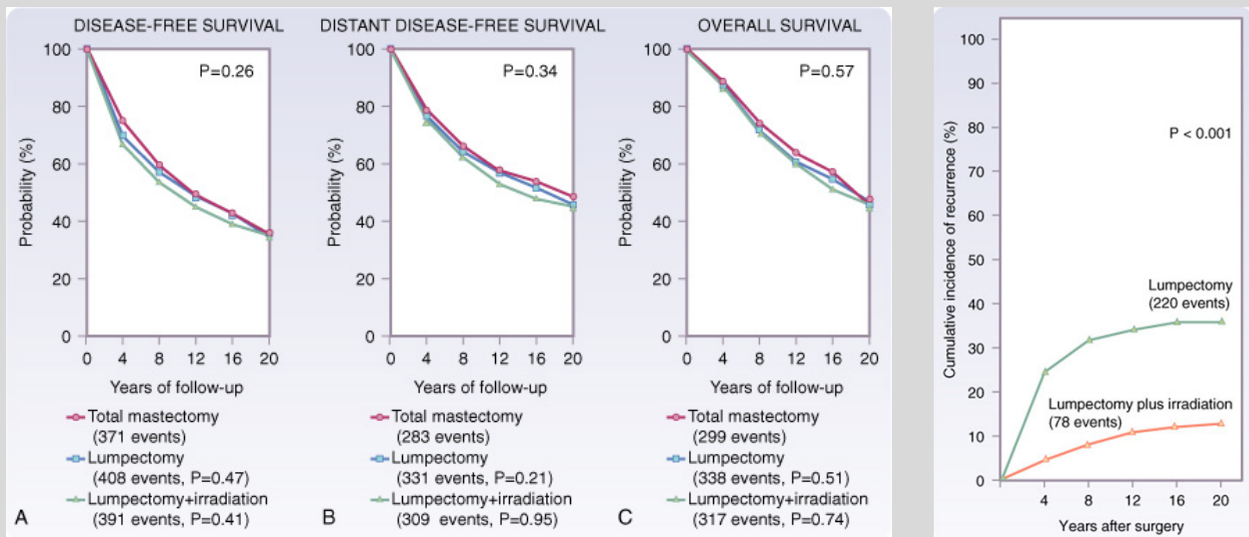
lumpectomy (breast conservation) plus radiation therapy

Axillary lymph nodes (staging evaluation)

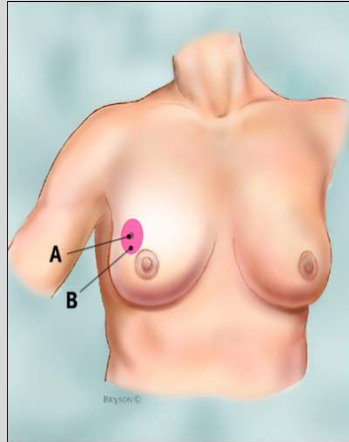
axillary node dissection

sentinel lymph node mapping and biopsy

NSABP B-06



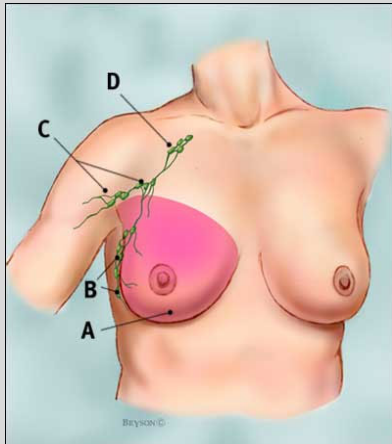
Partial mastectomy/ lumpectomy



Contraindications to Breast Conservation

- Large tumors or large tumor : breast ratio
 - Oncoplastic lumpectomy
- Multicentric disease
- Extensive DCIS
- Indeterminant mammographic findings elsewhere in breast
- Previous breast radiation
- Autoimmune disorders affecting skin: scleroderma (contraindication to RT)

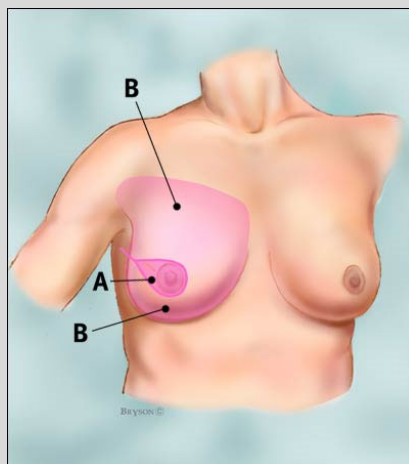
Total (simple) mastectomy



A. Tissue in pink is removed. This represents all breast tissue

- No effort is made to remove axillary lymph nodes
- Can be used for treatment or prophylaxis

Skin-sparing mastectomy



- “Keyhole” incision (skin preserved)
- Tissue removed at mastectomy
- Allows for more natural reconstruction by preserving breast envelope

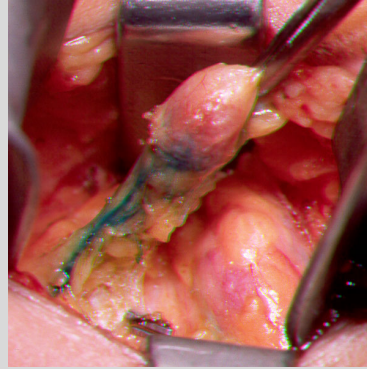
NSM/ASM

- Combines skin sparing mastectomy with preservation of nipple and/or areola
- Appropriate when nipple is not involved with cancer or atypical cells.
- Usually involves incision in inframammary fold with preservation of entire skin envelope.
- Most appropriate in breasts without ptosis as nipple can not be repositioned.

Nodal assessment

- Sentinel lymph node biopsy current standard
- Axillary node dissection if sln pos or can't be identified
 - Higher risk of lymphedema (25% vs 5%)
 - Higher likelihood of nerve injury
 - More mobility issues

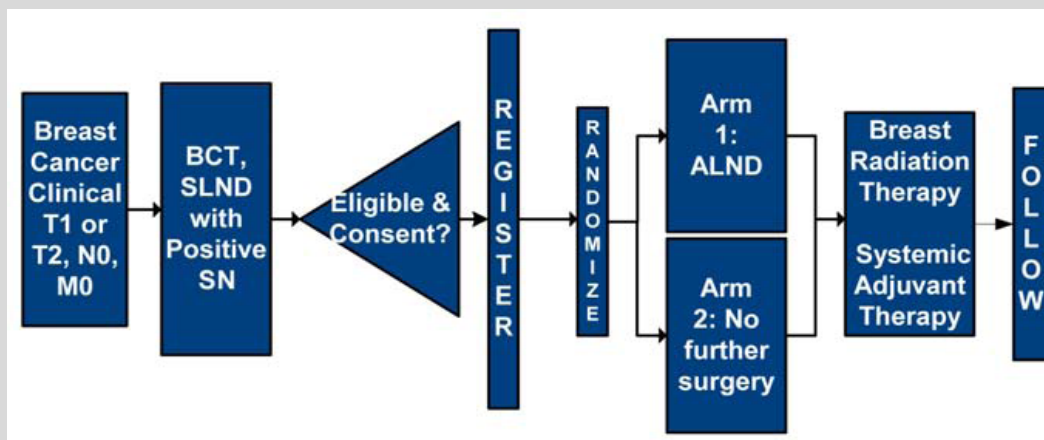
Sentinel Lymph Node Biopsy



Management of Positive SLN

- Previously, completion node dissection in all cases
- Currently, completion node dissection still standard for patients treated with mastectomy (Amaros)
- Certain patients treated with BCT may be able to avoid completion node dissection

ACOSOG Z11



Clinical Implications

In clinically node-negative patients undergoing BCT with macrometastases in the SN:

- Systemic Rx decision made
- ALND not necessary for local control
- ALND does not contribute to survival

Reconstruction Options/Issues Following Mastectomy

- Skin-sparing procedures
- Saline tissue expanders / saline implants
- Tissue transfer procedures
 - DIEP flap
 - TRAM or other rotational flaps
- Immediate versus delayed reconstruction

Locally advanced breast cancers

- Large tumor (>5cm) or skin changes (edema, ulceration, chest wall fixation) or fixed axillary lymph nodes
- Account for 10-15% of breast cancer in US, higher in developing countries
- Best results with neoadj chemo, followed by surgery with adjuvant RT as needed

Inflammatory breast cancers

- Account for <3% of breast cancers
- Characterized by brawny induration, erythema, and edema of the skin (peau d'orange)
- Dermal lymphatic involvement seen on skin biopsy
- May be mistaken for bacterial infection

Inflammatory breast cancer

- Distant metastasis is present in about 25% at presentation
- Neoadjuvant chemo may affect dramatic regression
- After chemo, MRM is performed
- Adjuvant chemo is often given
- RT to chest wall, supraclav, IM and axillary nodal basins is also given
- 5-yr survival rates approach 30%



Complications of
local therapy

Angiosarcoma



Lymphedema



Systemic Therapy for Breast Cancer

Margaret Gatti-Mays, MD, MPH

*Assistant Professor, Division of Medical Oncology
James Cancer Hospital Solove Research Institute
The Ohio State University Wexner Medical Center*

Learning Objectives

- To Review Breast Cancer Basics
- To Review Systemic Therapy of Breast Cancer
- To Review Approved Indications for Immunotherapy in Breast Cancer

Breast Cancer Basics

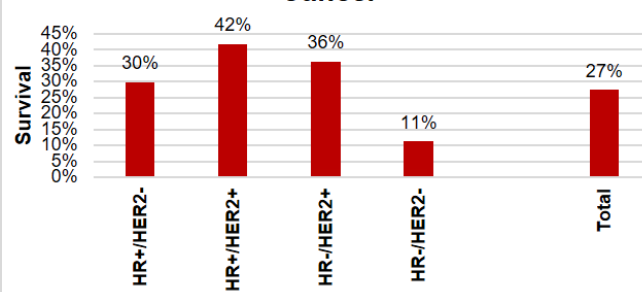
Breast Cancer Basics: Stats

- **Incidence:** In 2022, there will be an estimated 290,560 new cases of breast cancer with 43,780 deaths
 - 2nd most common cause of death in women

- **De novo Metastatic:** 5% of cases are metastatic at diagnosis

	Women	Men
New Cases	287,850	2,710
Deaths	43,250	530
Lifetime Risk	1 in 8 women	1 in 833 men

5 year Survival in Metastatic Breast Cancer



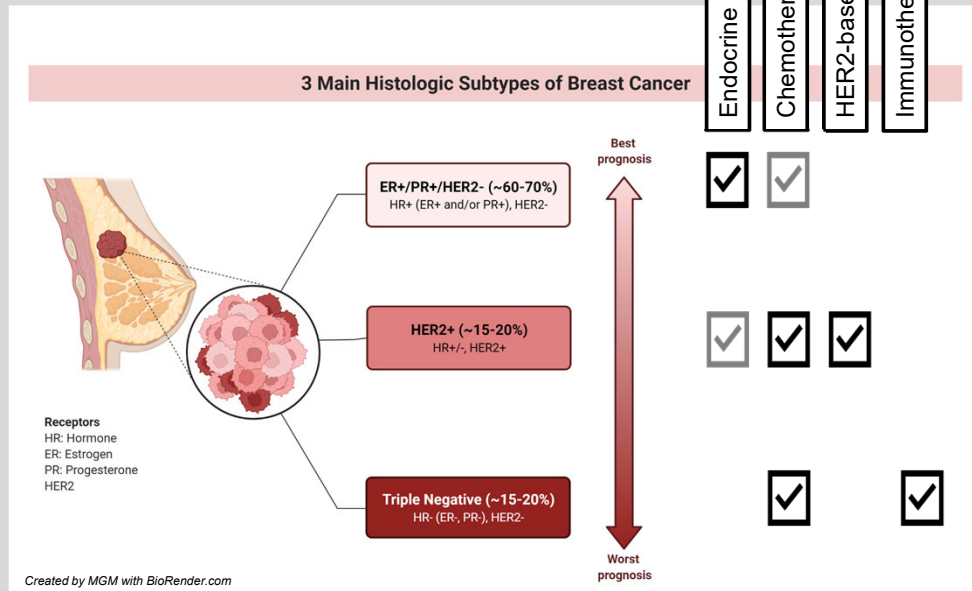
Siegel et al. Ca Cancer j Clin. 2022.
 Malmgren et al. Breast Cancer Res Treat. 2018.
 Howlander et al. CEBP. 2018.

It's All About the Receptors

- Breast Cancers are typically tested for 3 main receptors
 - Estrogen Receptor (ER)
 - Progesterone Receptor (PR)
 - Human Epidermal Growth Factor Receptor 2 (HER2)

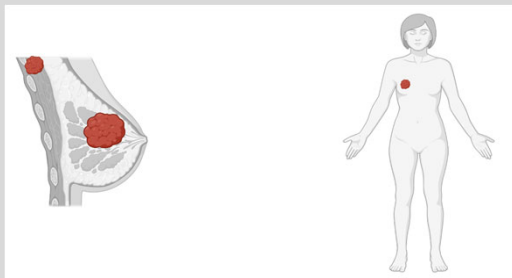
- The presence (or absence) of these receptors determines:
 - Clinical Outcomes
 - Systemic Treatment
 - Timing of treatment
 - Type of treatment
 - Duration of treatment

Breast Cancer Basics: Subtypes



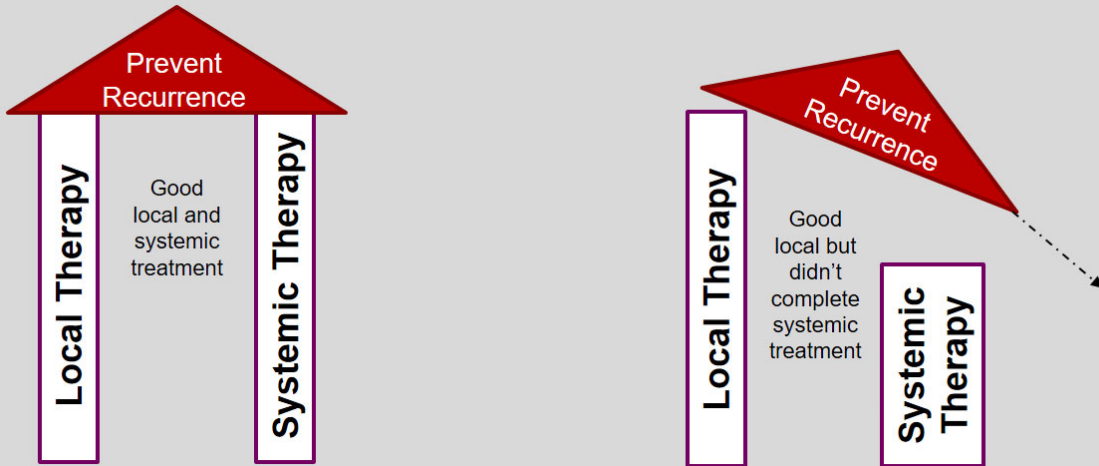
The Pillars of Early Breast Cancer Treatment

- | Local Therapy | Systemic Therapy |
|---|--|
| <ul style="list-style-type: none"> ▪ Breast Surgery and Nodal Evaluation <ul style="list-style-type: none"> ▪ Mastectomy vs lumpectomy ▪ Sentinel node vs axillary node dissection ▪ Radiation | <ul style="list-style-type: none"> ▪ Neoadjuvant or Adjuvant <ul style="list-style-type: none"> ▪ Chemotherapy ▪ HER2-Base Therapy ▪ Immunotherapy ▪ Endocrine therapy |



Created by MGM with BioRender.com

The Pillars of Breast Cancer Treatment



Systemic Therapy

Neoadjuvant (before surgery) Breast Cancer Treatment

Biopsy

Chemo

Surgery

Radiation

Endocrine +/- PARPi,
+/- Abemaciclib or
Capecitabine

Trastuzumab/Pertuzumab (or adjuvant T-DM1) for 1 year

Pembrolizumab for 1 year

- **Who gets neoadjuvant chemotherapy?**
 - Triple Negative Breast Cancer \geq 1cm or + lymph nodes
 - HER2+ Breast Cancer \geq 2cm or + lymph nodes
 - Some ER+ Breast Cancer
- Can be followed by adjuvant therapy after surgery
 - Some agents will span both neoadjuvant and adjuvant settings

Adjuvant (after surgery) Breast Cancer Treatment

Biopsy

Surgery

Chemo

Radiation

Endocrine +/-
PARPi +/-
Abemaciclib

Trastuzumab +/- Pertuzumab for 1 year

- **Who gets adjuvant chemotherapy?**
 - Triple Negative Breast Cancer, < 1cm and no lymph nodes
 - HER2+ Breast Cancer, < 2cm and no lymph nodes
 - Some ER+ breast cancer, Oncotype \geq 26*
- **Who can be spared chemotherapy?**
 - Most ER+ patients
 - Some small (<5mm), node negative triple negative or HER2+ breast cancers

Multigene Assays Help with Risk Recurrence Estimates

	Oncotype (preferred)	MammaPrint
No. Genes	21 genes	70 genes
Predictive	YES	Unknown
Prognostic	YES	YES
Result Range	0 to 100 [0 to 11 = Stage 1A] [0 to 25*, no chemo] [26+, chemo]	Low [no chemo] High [chemo]

**Premenopausal patients with oncotype score 18 to 25, consider ovarian suppression and/or chemotherapy*

ALL patients with ER+ breast cancer will receive 5 to 10 years of endocrine therapy (Tamoxifen or an aromatase inhibitor like anastrozole, letrozole, or exemestane)

Metastatic (advanced) Breast Cancer Treatment

Biopsy

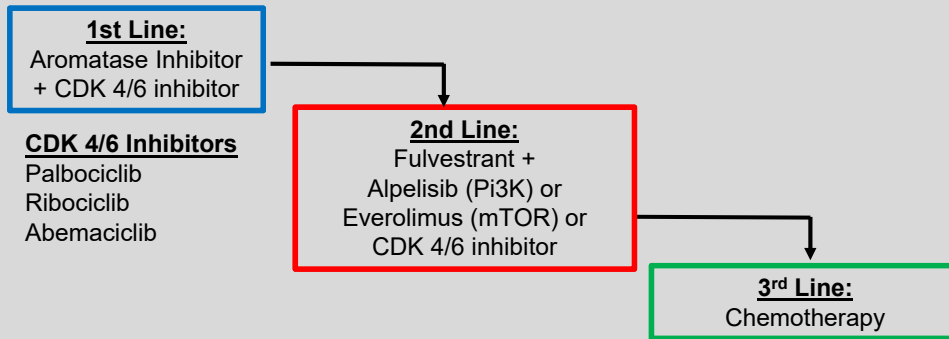
Systemic Therapy Based on Receptors

RT

- Receptors determine if a patient will receive oral or IV chemotherapy for advanced disease
- There is a very limited role for surgery in metastatic breast cancer
- Radiation can help with pain associated with metastatic tumors

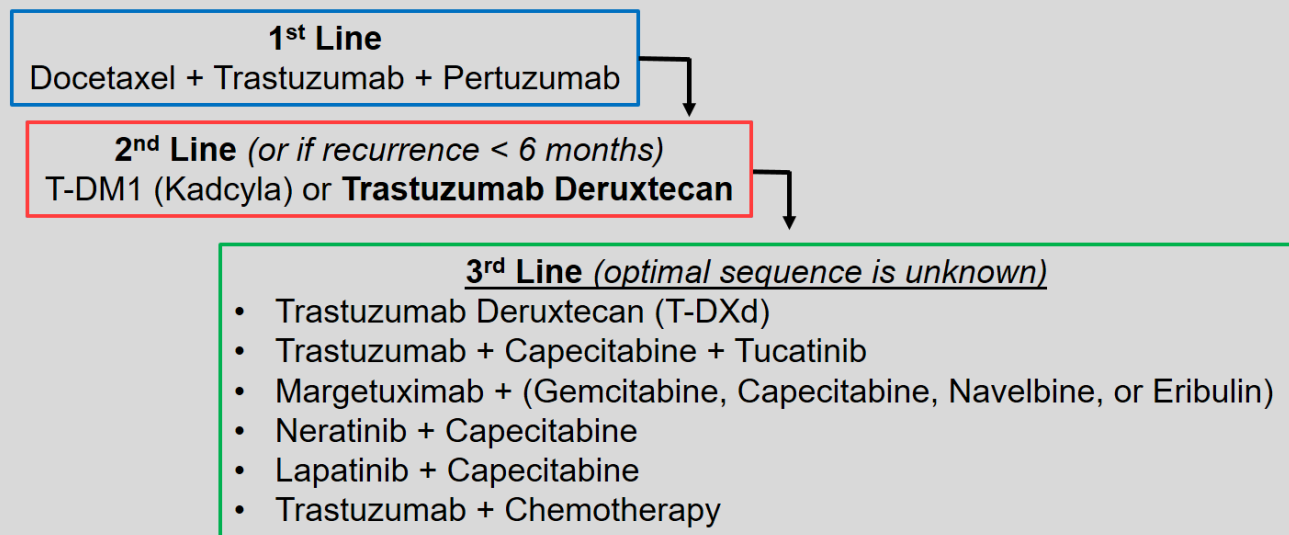
Metastatic ER+/PR+ Breast Cancer

- First and second line treatment is generally oral chemotherapy



Metastatic HER2+ Treatment Algorithm

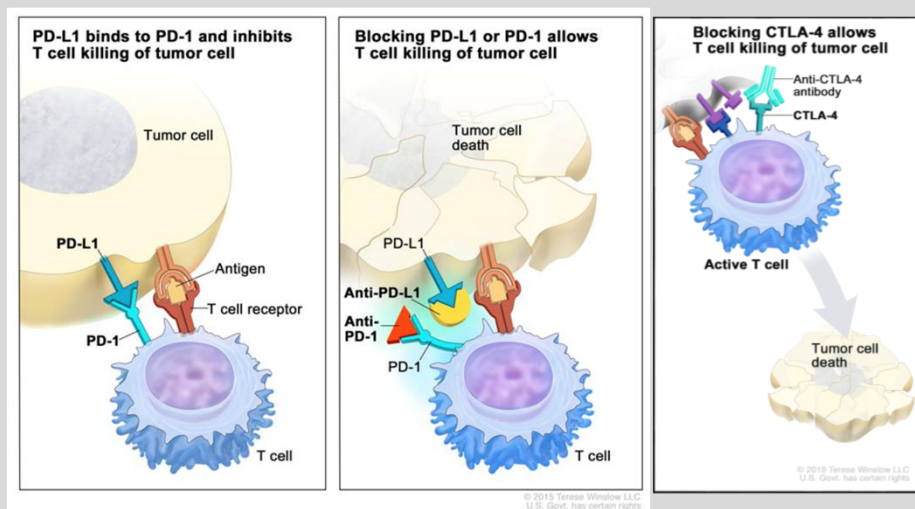
- Chemotherapy + HER2-Directed Antibody



Immunotherapy

53

Immune Checkpoint Inhibitors (ICIs)



Accessed 4/24/18: <https://visualsonline.cancer.gov/details.cfm?imageid=10396>
 Accessed 10/10/21: <https://nci-media.cancer.gov/pdq/media/images/776560.jpg>

Approved Indications for ICIs in Solid Tumors

- Most indications are for advanced/metastatic cancer, but some* are in earlier settings
 - Indications are for ICI +/- other agents (chemotherapy, small molecules, etc)

Lung Cancers

Non-Small Cell*

Small Cell

Pleural Mesothelioma

Genitourinary Cancers

Kidney (Renal Cell) Cancer

Bladder Cancer*

Skin Cancers

Melanoma*

Merkel Cell Carcinoma

Squamous Cell Carcinoma

Basal Cell Carcinoma

Women's Cancers

Cervical Carcinoma

Triple Negative Breast Cancer*

Endometrial Cancer

Gastrointestinal Cancers

Colorectal Cancer, MSI-H

Hepatocellular Carcinoma

Gastric/GE Junction/Esophageal

Head and Neck, Squamous

Not Tumor Specific

MSI-High

TMB-High

	Nivolumab (<i>Opdivo</i>)	PD-1
	Pembrolizumab (<i>Keytruda</i>)	
	Cemiplimab (<i>Libtayo</i>)	PD-L1
	Dostarlimab (<i>Jemperli</i>)	
	Atezolizumab (<i>Tecentriq</i>)	PD-L1
	Durvalumab (<i>Imfinzi</i>)	
	Aveumab (<i>Bavencio</i>)	PD-L1
	Ipilimumab (<i>Yervoy</i>) + nivolumab	

55

<https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm279174.htm>. Accessed Sept 29, 2021

Survival and ICI

- Patient outcomes are improved with ICI when compared to chemotherapy
 - Among responders, we see longer periods of disease control and better overall survival
- Ipilimumab (Nov 2011 FDA approved for metastatic melanoma)
 - Overall Cancer Death Rate significantly decreased in future years
 - Cancer Statistics 2020: ↓ by 29% from 1991 to 2017, with a **2.2% decline from 2016 to 2017**
 - Progress in treatment for melanoma drove the **most rapid death rate decline** seen, as the overall melanoma death rate dropped by 7% per year during 2013-2017.
 - Cancer Statistics 2021: ↓ by 31% from 1991 to 2018, with a **2.4% decline from 2017 to 2018**

Siegel et al. *Ca Cancer J Clin.* 2020. Siegel et al. *Can Cancer J Clin.* 2021.
 Sun et al. *Scientific Reports.* 2020.
 Accessed 10/13/20: <https://www.cancerresearch.org/immunotherapy/timeline-of-progress>

Approved FDA Indications of ICI in Breast Cancer

Not Breast Cancer Specific

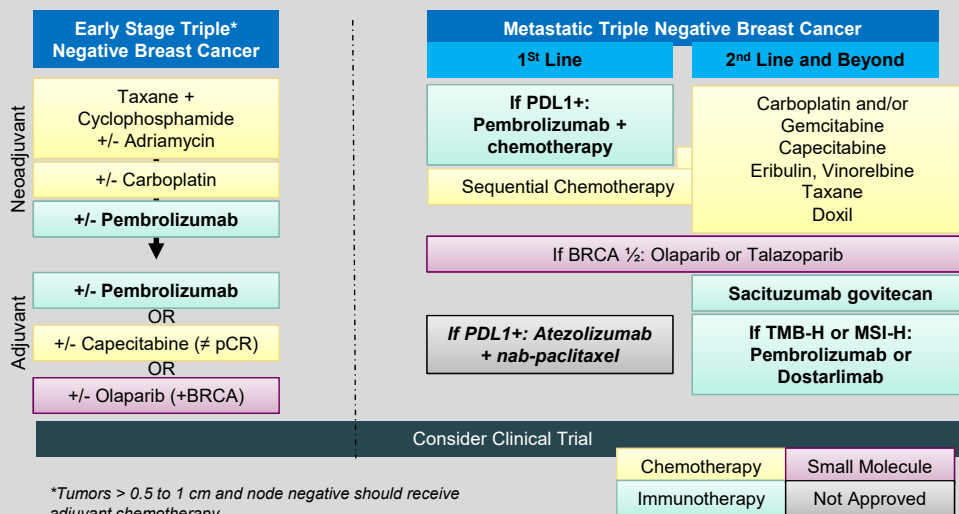
- **Pembrolizumab*** in MSI-High or mismatch repair deficient tumors
- **Pembrolizumab*** in TMB-High (≥ 10 mutations/megabase)
- **Dostarlimab*** in mismatch repair deficient tumors

Breast Cancer Specific

- ~~**Atezolizumab*** + Nab-Paclitaxel in 1st line, metastatic TNBC~~
- **Pembrolizumab** + Chemotherapy (nab-paclitaxel, paclitaxel or gemcitabine/carboplatin) in 1st line, metastatic TNBC
- **Pembrolizumab*** + neoadjuvant chemotherapy in early stage, high risk TNBC

*Accelerated approvals based on PFS, response rate/durability. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Triple Negative Breast Cancer Treatment



Learning Objectives

- ✓ To Review Breast Cancer Basics
 - ✓ Stats and Subtypes
 - ✓ Sequencing of Local and Systemic Therapies

- ✓ To Review Systemic Therapy of Breast Cancer
 - ✓ Neoadjuvant Breast Cancer Treatment
 - ✓ Adjuvant Breast Cancer Treatment
 - ✓ Metastatic Breast Cancer Treatment for ER+ and HER2+

- ✓ To Review Approved Indications for Immunotherapy in Breast Cancer
 - ✓ Early and Adjuvant Triple Negative Breast Cancer