Breast Cancer 101

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Disclosures

Financial

- Advisory board : Gilead, AstraZeneca

Off-label/Investigational use

- None

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OBJECTIVES

- 1. Discuss the epidemiology of breast cancer
- 2. Identify risk factors for development of breast cancer including preventative strategies to help decrease modifiable risks
- 3. Articulate the diagnosis and multidisciplinary approaches to treatment for breast cancer.

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EPIDEMIOLOGY

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Epidemiology

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2019 Estimates

Estimated New Cases

Male			Female		
Prostate	174,650	20%	Breast	268,600	30%
Lung & bronchus	116,440	13%	Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%	Colon & rectum	67,100	7%
Urinary bladder	61,700	7%	Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%	Melanoma of the skin	39,260	5%
Kidney & renal pelvis	44,120	5%	Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%	Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%	Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%	Pancreas	26,830	3%
Pancreas	29,940	3%	Leukemia	25,860	3%
All sites	**870,970**		**All sites**	**891,480**	

Estimated Deaths

Male			Female		
Lung & bronchus	76,650	24%	Lung & bronchus	66,020	23%
Prostate	31,620	10%	Breast	41,760	15%
Colon & rectum	27,640	9%	Colon & rectum	23,380	8%
Pancreas	23,800	7%	Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%	Ovary	13,980	5%
Leukemia	13,150	4%	Uterine corpus	12,160	4%
Esophagus	13,020	4%	Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%	Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%	Brain & other nervous system	7,850	3%
All sites	**321,670**		**All sites**	**285,210**	

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Breast cancer Facts and Figures 2017-18

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Cancer Stat Facts: Female Breast Cancer

Expand All | Collapse All

Reports on Cancer

- Annual Report to the Nation
- Cancer Stat Facts
- Cancer Statistics Review +
- Preliminary Incidence Rates for 2017 +
- SEER Publications +

Statistics at a Glance

At a Glance

Estimated New Cases in 2023	297,790
% of All New Cancer Cases	15.2%
Estimated Deaths in 2023	43,170
% of All Cancer Deaths	7.1%

5-Year Relative Survival

90.8%

2013–2019

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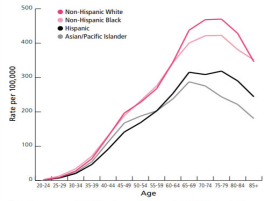
Epidemiology

Figure 1. Age-specific Female Breast Cancer Incidence Rates by Race/Ethnicity, 2010-2014, US



Note: Rates are per 100,000 and age adjusted to the 2000 US standard population.
Sources: Incidence: North American Association of Central Cancer Registries (NAACCR), 2017. Mortality: National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.
American Cancer Society, Inc., Surveillance Research, 2017

Breast cancer Facts and Figures 2017-18

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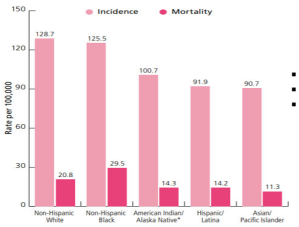
Epidemiology

Figure 2. Female Breast Cancer Incidence (2010-2014) and Mortality (2011-2015) Rates by Race/Ethnicity, US



- Incidence and mortality going down
- Better treatments
- Reduced use of HRT since early 2000s

*Statistics based on data from Contract Health Service Delivery Area (CHSDA) counties. Note: Rates are age adjusted to the 2000 US standard population.
Sources: Incidence – NAACCR, 2017. Mortality – National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.

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SCREENING

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USPSTF recommendation

Women, Age 50-74 Years	The USPSTF recommends biennial screening mammography for women 50-74 years.	B
Women, Before the Age of 50 Years	The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms.	C
Women, 75 Years and Older	The USPSTF concludes that the current evidence is insufficient to assess the benefits and harms of screening mammography in women 75 years and older. Go to the Clinical Considerations section for information on risk assessment and suggestions for practice regarding the I statement.	I
All Women	The USPSTF recommends against *teaching* breast self-examination (BSE).	D

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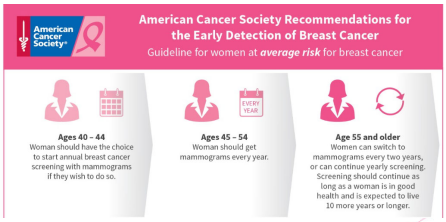
ACS recommendation



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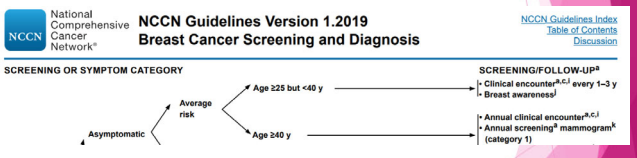
NCCN recommendation



- Similar recommendation by American College of Radiology (ACR) and Society of breast imaging (SBI)

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Why the discrepancy?

- Depends on which trial you look at
- Benefit in age 50-74 is seen across the board
- Magnitude of benefit in age 40-50 is not uniform across trials
- Depends on the type of mammogram (2D vs 3D) and radiologist

Qaseem *et al*. Ann Intern Med.2019 Apr 16;170(8):547-560

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Screening for high risk patients

- BRCA mutation: Start screening at age 25 (Mammogram/MRI)
- Prior h/o thoracic radiation between age 10-30: Start screening 10 years after radiation (Mammogram/MRI)

NCCN, ACR, SBI

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RISK FACTORS

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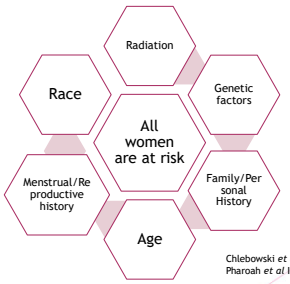
Non-modifiable risk factors



Chlebowski *et al* JNCI 2005; 97:439-448
Pharoah *et al* Int J Cancer 1997; 71: 800-809

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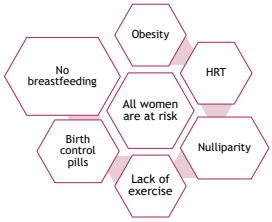
Modifiable risk factors



Chlebowski *et al* JNCI 2005; 97:439-448
Pharoah *et al* Int J Cancer 1997; 71: 800-809

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Benign breast lesions

- **No risk**
  - Fibrocystic change
  - Fibrosis
  - Simple cysts
  - Mild hyperplasia

- **RR 1.5 - 2**
  - Usual ductal hyperplasia (without atypia)
  - Fibroadenoma

- **RR ~ 4**
  - Atypical ductal hyperplasia
  - Atypical lobular hyperplasia (no surgery needed)

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Hereditary risk factors

- 5-10% of all women with breast cancer have a hereditary form of breast cancer
- BRCA 1 and BRCA 2 (Ovarian, pancreatic, prostate, melanoma)
- p53 – Li-Fraumeni syndrome (Leukemia, Sarcoma, GBM)
- PTEN – Cowden syndrome (Thyroid cancers, hamartomas, macrocephaly)

Chlebowski *et al* JNCI 2005; 97:439-448
Pharoah *et al* Int J Cancer 1997; 71: 800-809

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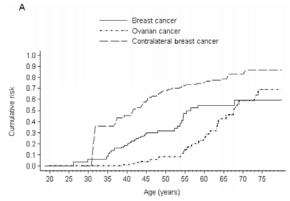
BRCA 1 – cumulative risk



Risk of breast cancer by age 70 – 55-70%
Risk of ovarian cancer by age 70 – 40%
Risk of contralateral breast cancer by age 70 – Up to 60%

J Natl Cancer Inst.2013 Jun 5;105(11):812-22

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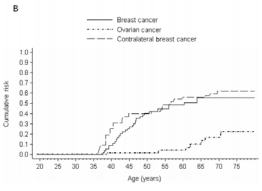
BRCA 2- cumulative risk



Risk of breast cancer by age 70 – 45-70%
Risk of ovarian cancer by age 70 – 15%
Risk of contralateral breast cancer by age 70 – Up to 60%

J Natl Cancer Inst.2013 Jun 5;105(11):812-22

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Who should be tested?

- Any individual with a breast cancer diagnosis meeting any of the following criteria:
  - Breast cancer diagnosed age ≤ 50 yrs
  - Triple negative (ER-, PR-, Her-2-) breast cancer diagnosed age ≤ 60 yrs
  - 2 breast cancer primaries
  - Breast cancer at any age, and:
  - ≥ 1 close blood relative with:
    - Breast cancer ≤ 50 yrs ; or
    - Invasive ovarian cancer; or
    - Male breast cancer; or
    - Pancreatic cancer; or
    - High grade (Gleason score ≥ 7) or metastatic prostate cancer
  - ≥ 2 close blood relatives with breast cancer at any age

NCCN Genetic/familial high risk assessment guidelines 2019

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Who should be tested?

- An individual who does not meet the above criteria but has a 1st or 2nd degree relative with any of the following:
  - Breast cancer ≤ 45 yrs
  - Ovarian cancer
  - Male breast cancer
  - Pancreatic cancer
  - Metastatic prostate cancer
  - ≥ 2 breast primaries in a single individual
  - ≥ 2 individuals with breast cancer primaries on the same side of the family with at least one diagnosed ≤ 50 yrs

NCCN Genetic/familial high risk assessment guidelines 2019

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Risk reduction

- **Prophylactic bilateral mastectomy: Reduces risk by >90%**
- **Prophylactic bilateral salpingo-oophorectomy (by age 35-40)**
  - Reduces risk of ovarian cancer by >95%
  - Reduces risk of breast cancer by 50% in premenopausal women
- **Chemoprevention (Gail model score>1.67, high risk breast lesions)**
  - Tamoxifen – premenopausal women (NSABP-P1, STAR, 49% risk reduction)
  - Raloxifene – Postmenopausal women (less risk of VTE, uterine cancer)
  - Exemestane, Anastrozole

Rockville (MD): Agency for Healthcare Research and Quality (US); 2019 Sep. Report No.: 19-05249-EF-1.
U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.

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DIAGNOSIS

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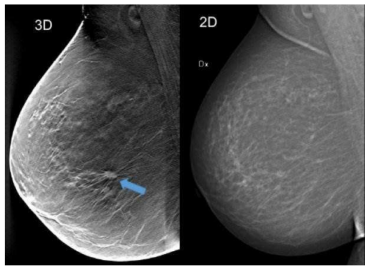
Mammogram



- Microcalcifications, mass

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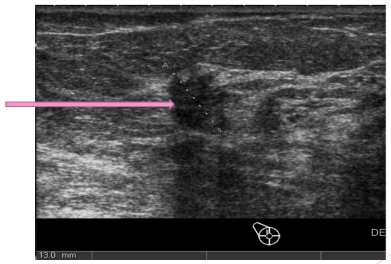
Ultrasound



- Differentiates solid vs cystic lesion

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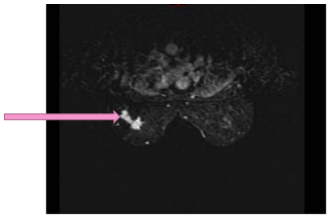
MRI



- More sensitive but less specific
- Dense breasts
- Axillary nodal metastases with occult primary
- Women with high risk for contralateral breast cancer

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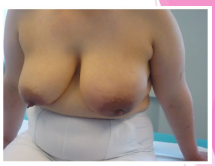
Inflammatory breast cancer



- Often mistaken for an infection
- ≥ 1/3rd of the breast is inflamed
- Clinical diagnosis
- Skin biopsy can confirm diagnosis
- Dermal lymphatic invasion is characteristic but not required for diagnosis
- Staging scans should be done
- Chemotherapy should be administered first, irrespective of biology

Van Uden *et al*. CriticalReviewsinOncology/Hematology93(2015)116-126

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Biopsy

- Image guided core-needle biopsy
- FNA of axillary lymph nodes
- Clip placement at the time of biopsy
- Pathology assessment of malignant lesions (prognostic factors):
  - Histologic type
  - Grade
  - Ki-67 index
  - Receptor status (ER, PR, Her-2)
  - Lymphovascular invasion

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SUBTYPES OF BREAST CANCER

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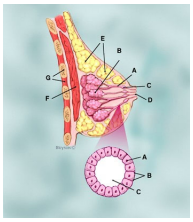
Normal Breast



A. Breast Duct System
B. Lobules
C. Breast Duct System
D. Nipple
E. Fat
F. Chest Muscle
G. Ribs

A. Cells lining duct
B. Basement membrane
C. Open central duct

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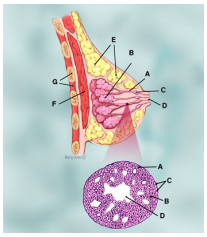
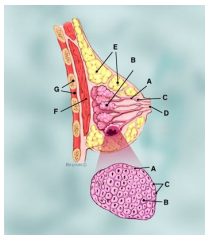
Non-invasive breast cancer



DCIS



LCIS

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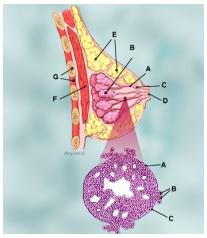
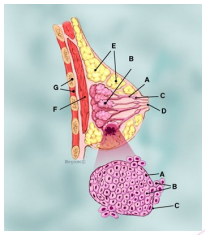
Invasive breast cancer



Invasive ductal carcinoma



Invasive lobular carcinoma

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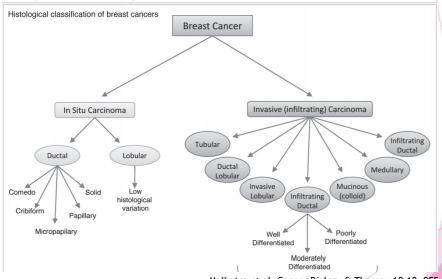
Histologic subtypes



Malhotra et al. Cancer Biology & Therapy 10:10, 955-960; November 15, 2010

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Molecular subtypes

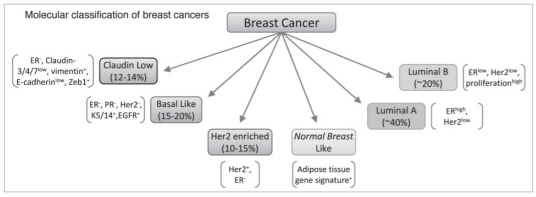

Figure 2. Molecular classification of breast cancer. This classification is based on the intrinsic molecular subtypes of breast cancer identified by micro-array analysis of patient tumor specimens.[14-16]

Malhotra *et al*. Cancer Biology & Therapy 10:10, 955-960; November 15, 2010

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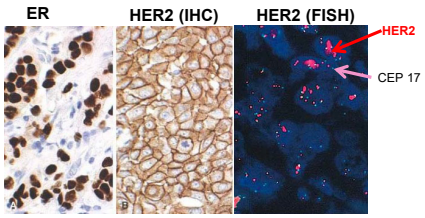
Breast cancer biomarkers



ER: Estrogen Receptor
HER2: Human Epidermal Growth Factor Receptor 2
IHC: Immunohistochemistry
FISH: Fluorescence in situ Hybridization

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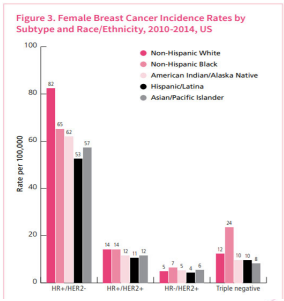
Incidence of subtypes of breast cancer



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STAGING OF BREAST CANCER

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AJCC/TNM Staging

Tumor size **T**	Tumor size < 2 cm **T1**	Tumor size 2-5 cm **T2**	Tumor size > 5 cm **T3**	Tumor extends to skin or chest wall **T4**
Lymph Nodes **N**	**N0** No lymph node metastasis	**N1** Metastasis to ipsilateral, movable, axillary LN's	**N2** Metastasis to ipsilateral fixed axillary, or IM LN's	**N3** Metastasis to infraclavicular/ supraclavicular LN, or to axillary and IM LN's
Metastasis **M**	**M0** No distant metastasis	**M1** Distant metastasis	LN=Lymph Nodes, IM= Internal Mammary	

Breast cancer staging; AJCC 8th edition

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AJCC/TNMC Staging

	N0	N1	N2	N3	M1
T1	I	IIA	IIIA	IIIC	IV
T2	IIA	IIB	IIIA	IIIC	IV
T3	IIB	IIIA	IIIA	IIIC	IV
T4	IIIB	IIIB	IIIB	IIIC	IV

Stage 1 and Stage 2: Routine staging scans not indicated
Stage 3: Consider staging scans

Breast cancer staging; AJCC 8th edition

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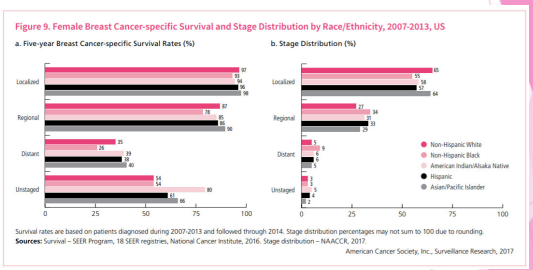
Stage is prognostic



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MANAGEMENT OF BREAST CANCER

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Lobular carcinoma *in situ*

- Risk factor for development of breast cancer
- Not part of breast cancer staging anymore
- 1% annual risk of transformation to breast cancer
- Almost 100% ER+, PR+
- Surgery not needed, if imaging is concordant
- Endocrine therapy for risk reduction
- No chemotherapy
- Can be bilateral

Oppong *et al*. Oncology (Williston Park). 2011 Oct;25(11):1051-6, 1058.

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Ductal carcinoma *in situ*

- Pre-cancerous lesion
- Treated like stage 1 breast cancer – surgery (lumpectomy + Radiation or Mastectomy)
- 99% are ER+, PR+
- No role for checking Her-2
- No chemotherapy
- Endocrine therapy to reduce ipsilateral and contralateral breast recurrence

Badve *et al*. Pathology. 2019 Aug 28

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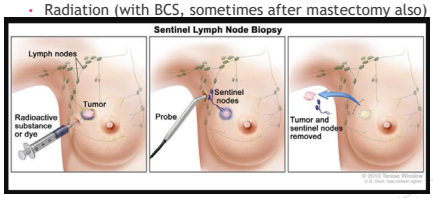
Management - Stage I-III Invasive Breast Cancer

- Loco-regional treatment
  - Breast conservation surgery (BCS)/Mastectomy
  - Axillary lymph node evaluation (Sentinel lymph node)
  - Radiation (with BCS, sometimes after mastectomy also)



NCCN breast cancer guidelines Sept 2019
www.cancer.gov/SLNB

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Systemic treatment

- Chemotherapy (Adjuvant/Neoadjuvant)
- Endocrine therapy (ER+ positive)
- Anti-Her-2 targeted therapy (Her-2 + disease)
- Goal is to eliminate micrometastases
- Reduce the risk of distant metastases
- Downstage disease when used neoadjuvantly

NCCN breast cancer guidelines Sept 2019

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Who needs chemotherapy?

- **Higher risk of recurrence in the next 5 years**
- **Triple negative breast cancer (ER-, PR-, Her-2-)**
- **Her-2 positive breast cancer**
- **ER+ Her-2- breast cancer with:**
  - High risk based on genomic assay (Oncotype Dx, MammaPrint)
  - Multiple lymph nodes positive
  - Large primary tumor
- **Biology is most important**
- **Chemotherapy can be administered before or after surgery depending on the clinical situation**

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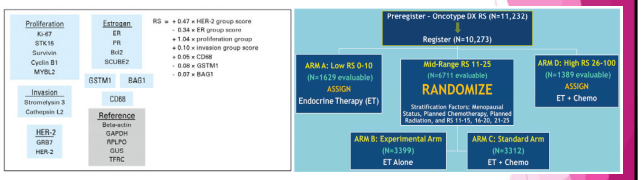
Oncotype Dx



- No chemotherapy benefit for score 0-25
- ER+, Her-2-, LN- disease

JCO, 26: 721-728, 2008
Sparano *et al.* N Engl J Med 2018;379:111-21.

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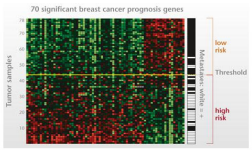
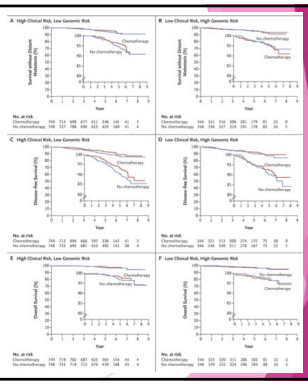
MammaPrint





- Clinically high risk but MammaPrint low risk can skip chemotherapy
- Applicable to ER+, Her-2-, LN+/- disease

Cardoso et al. N Engl J Med 2016;375:717-29.

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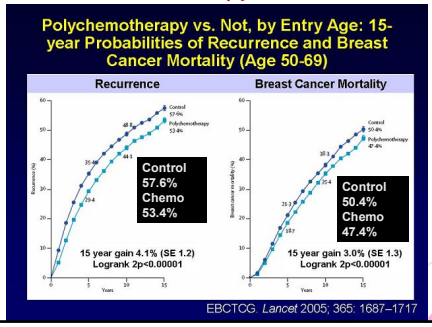
Benefit of chemotherapy



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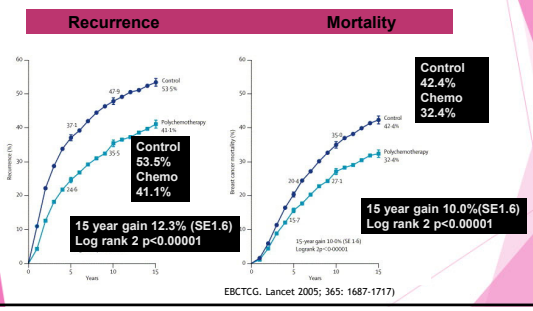
Benefit of chemotherapy – Age < 50



EBCTCG. Lancet 2005; 365: 1687-1717)

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Chemotherapy – common adverse effects

- Nausea, Vomiting
- Mucositis
- Myelosuppression
- Fatigue
- Infection
- Alopecia
- Cognitive dysfunction
- Premature ovarian failure

Chu *et al*. Physicians' Cancer Chemotherapy Drug Manual 2019

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Chemotherapy drugs and adverse effects

- Doxorubicin (Adriamycin) (A)- Cardiotoxicity, secondary leukemia, MDS
- Cyclophosphamide (C)- Renal dysfunction, Secondary leukemia, MDS
- Paclitaxel (T)- Liver dysfunction, Peripheral neuropathy
- AC followed by T is the most commonly used regimen
- Docetaxel (Taxotere) (T)- Mucositis, Liver dysfunction, Peripheral neuropathy
- Eribulin (Metastatic disease)- Neuropathy
- Gemcitabine (Metastatic disease)- TTP
- Carboplatin (Neoadjuvant/Metastatic disease)- Peripheral neuropathy, Myelosuppression
- Capecitabine (Adjuvant/Metastatic disease) - Mucositis, diarrhea, Hand-foot syndrome

Chu *et al*. Physicians' Cancer Chemotherapy Drug Manual 2019

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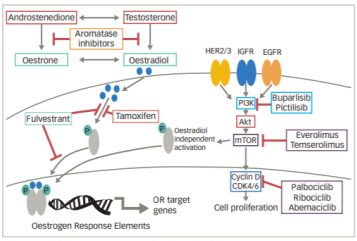
Endocrine therapy – Mechanism of action



Akt = protein kinase B; CDK4/6 = cyclin-dependent kinases 4/6; EGFR = epidermal growth factor receptor; HER 2/3 = human epidermal growth factor receptor 2/3; IGFR = insulin-like growth factor receptor; mTOR = mammalian target of rapamycin; PI3K = phosphatidylinositol-3-kinase; OR = oestrogen receptor.

European Oncology & Haematology, 2017;13(2):127-33

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Tamoxifen

- Significant reduction of breast cancer deaths and recurrence with 5 years of tamoxifen, even after 15 years from study entry
- Benefit of at least 5 years of tamoxifen carries over for at least 10 more years (carry-over effect)
- Improvement in breast cancer mortality was seen across all age groups, irrespective of menopausal status
- Selective estrogen receptor modulator
- Cataracts
- DVTs
- Endometrial cancer
- Hot flashes (can consider duloxetine/venlafaxine), mood changes, vaginal discharge, depression
- Does NOT increase risk for osteoporosis
- Early and advanced stage disease
- Drug interactions - CYP2D6 inhibitors - SSRIs

EBCTCG, Lancet 2005

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Aromatase Inhibitors

- Prescribed for at least 5 years
- Prolonged DFS, TTR
- Reduced risk of distant metastases and contralateral breast recurrence
- Prevent peripheral conversion to estrogen
- Increased risk for osteoporosis
- Myalgias/Arthralgias (can consider duloxetine)
- Hot flashes, mood changes
- Hyperlipidemia
- Anastrozole = Letrozole = Exemestane
- Early and Advanced stage disease

ATAC Trialists' Group Lancet 2005; 365: 60-62

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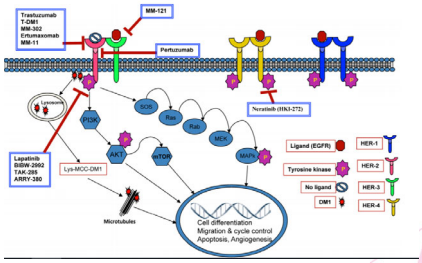
Anti-Her-2 drugs – Mechanism of action



Journal of Cancer 2013; 4(2): 117-132. doi: 10.7150/jca.4925

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Trastuzumab and Pertuzumab

- Adjuvant/Neoadjuvant treatment
- Also in advanced stage
- Overlap with chemotherapy – works better
- Trastuzumab is continued for 1 year when used in localized disease
- Improved overall and disease free survival and changed natural course of Her-2+ breast cancer
- Potentially Cardiotoxic (Echo every 3 months)
- Pertuzumab (used only with Trastuzumab) – can cause diarrhea

Romond et al. N Engl J Med 2005;353:1673-84.
Reviews on Recent Clinical Trials, 2017, 12, 81-92

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Neratinib

- Tyrosine kinase inhibitor
- Blocks Her-4 also
- Approved for extended anti-Her-2 therapy in localized Her-2 positive breast cancer
- After completion of one year of trastuzumab
- Potentially cardiotoxic
- Diarrhea is a common side effect (scheduled loperamide)
- Has shown impressive CNS penetration

Martin *et al*. Lancet Oncol 2017; 18: 1688-700

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Metastatic Disease – ER+

- Prefer endocrine therapy as first line with CDK 4/6 inhibitor
- Can use single agent Fulvestrant also
- Reserve chemotherapy (preferably single agent) for a visceral crisis or endocrine resistant disease
- Role of systemic therapy is palliative only
- Assess performance status
- Skeletal metastases should be treated with Bisphosphonates or Denosumab.
- Palliative care, hospice and advanced directives

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Fulvestrant

- Estrogen receptor antagonist
- Approved only in metastatic disease (first line or subsequent)
- Hot flashes
- Mood changes
- Injection site reactions

Robertson *et al* Lancet 2016; 388: 2997-3005

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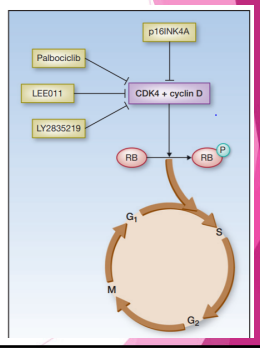
CDK 4/6 inhibitors

- Palbociclib, Ribociclib, Abemaciclib
- Palbocilcib and Ribociclib only in advanced stage ER+, Her-2- breast cancer along with AIs or Fulvestrant
- Halt cell cycle in G1-S phase
- All of them cause cytopenias, especially neutropenia.
- QT prolongation with Ribociclib & diarrhea with Abemaciclib.
- Abemaciclib also approved in high risk adjuvant setting



Clin Cancer Res; 20(13); 3379-83. 2014 AACR
PALOMA 2, MONALEESA 2, MONARCH 3, MonarchE- clinical trials

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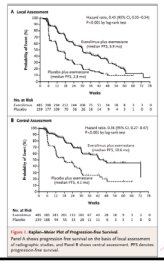
Everolimus

- mTOR inhibitor (common mechanism of resistance to endocrine therapy)
- 2nd line treatment of metastatic ER+, Her-2- breast cancer
- In combination with exemestane
- Stomatitis (prophylactic oral steroid)
- Anemia
- Dyspnea
- Hyperglycemia
- Pneumonitis



Baselga et al. N Engl J Med 2012;366:520-9

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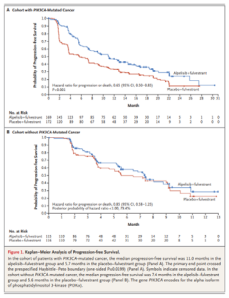
Alpelisib – PIK3CA inhibitor



Adverse effects:
- Hyperglycemia
- Diarrhea
- Nausea
- Rash

Andre et al. N Engl J Med 2019;380:1929-40.

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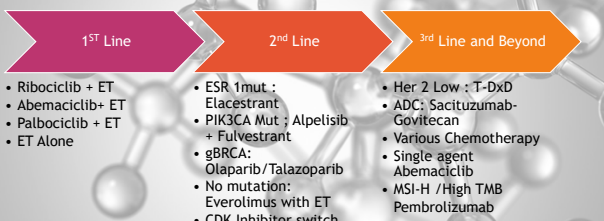
Metastatic HR+/Her-2- Breast Cancer



1ST Line

- Ribociclib + ET
- Abemaciclib+ ET
- Palbociclib + ET
- ET Alone

2nd Line

- ESR 1mut : Elacestrant
- PIK3CA Mut ; Alpelisib + Fulvestrant
- gBRCA: Olaparib/Talazoparib
- No mutation: Everolimus with ET
- CDK Inhibitor switch

3rd Line and Beyond

- Her 2 Low : T-DxD
- ADC: Sacituzumab-Govitecan
- Various Chemotherapy
- Single agent Abemaciclib
- MSI-H /High TMB Pembrolizumab

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Metastatic Disease – Her-2+

- Trastuzumab, Pertuzumab and Docetaxel as first line
- T-DM1 in 2nd line and Lapatinib (with capecitabine) in 3rd line
- Potentially cardiotoxic - periodically check Echo
- Role of systemic therapy is palliative
- Assess performance status
- Skeletal metastases should be treated with Bisphosphonates or Denosumab.
- Palliative care, hospice and advanced directives

Swain *et al*. N Engl J Med 2015;372:724-34

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Trastuzumab Emtansine (T-DM1)

- Antibody drug conjugate
- Adjuvant therapy in some patients
- Advanced stage Her-2+ disease – 2nd line
- Potentially Cardiotoxic
- Hypomagnesemia
- Peripheral neuropathy
- Thrombocytopenia

Verma *et al*. N Engl J Med 2012;367:1783-91

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Trastuzumab deruxtecan

- Approved in second and third line Her-2 positive metastatic disease
- Destiny Breast - 01 was a single arm study with excellent ORR
- Pneumonitis
- Nausea
- Fatigue

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Tucatinib

- Approved in second and third line Her-2 positive metastatic disease
- Her-2 CLIMB was a randomized study comparing it with capecitabine and trastuzumab
- To be used with capecitabine and trastuzumab
- Active for intracranial metastases
- Rash
- Diarrhea

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Lapatinib

- Tyrosine kinase inhibitor
- Able to bind and inhibit p95 Her-2
- Approved only for metastatic Her-2+ breast cancer
- 2nd line and beyond for Her-2+ positive breast cancer
- Diarrhea
- Skin rash
- Potentially cardiotoxic

Opdam *et al*. Oncologist. 2012 Apr; 17(4): 536-542.

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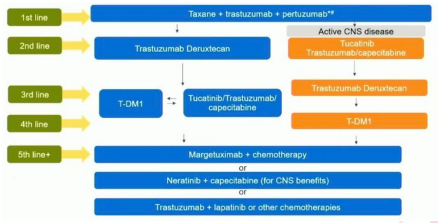
Her-2+ Metastatic Breast Cancer



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Metastatic Disease – Triple negative

- Single agent chemotherapy
- Consider PARP inhibitors (Olaparib, Talazoparib) in patients with BRCA mutations
- Immunotherapy (Pembrolizumab + Chemotherapy) in patients with PD-L1 CPS ≥10%
- Role of systemic therapy is palliative
- Assess performance status
- Skeletal metastases should be treated with Bisphosphonates or Denosumab.
- Palliative care, hospice and advanced directives

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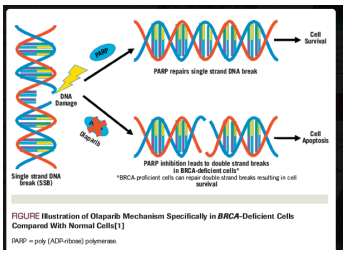
PARP inhibition – Olaparib, Talazoparib



Adverse effects:
- Anemia
- Nausea

Davis *et al* Oncology (Williston Park). 33(2):58-61.

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Sacituzumab govitecan

- Approved in third line for triple negative metastatic disease
- IMMU-132-01 and then ASCENT trials
- Impressive ORR and improvement in PFS and OS
- First ADC approved in this space
- Diarrhea
- Nausea
- Cytopenia

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Metastatic TNBC

- Check for PD-L1 expression by the 22C3 test and if the CPS is at least 10, consider pembrolizumab with either nab-paclitaxel or paclitaxel or carboplatin + gemcitabine (KEYNOTE 355)
- Check for germline BRCA mutation: If positive, can use talazoparib (EMBRACA, Litton *et al*, NEJM 2018) or olaparib (olympiAD, Robson *et al*, Annals of Oncology 2019)
- Check for MSI: If high, Pembrolizumab in 2nd line and beyond
- Check for tumor mutational burden: If high, can consider Pembrolizumab in 2nd line and beyond
- If no target, single agent chemotherapy preferred: Paclitaxel, Docetaxel, Eribulin (2nd line and beyond), Capecitabine, Doxorubicin, Cyclophosphamide, Carboplatin, Gemcitabine, Ixabepilone (microtubule stabilizer, effective in taxane resistant cells, used as monotherapy or in combination with capecitabine)
- Sacituzumab Govitecan: FDA approved for advanced stage triple negative breast cancer, that has progressed on at least 2 prior lines of chemotherapy, with at least one of them in the metastatic setting (IMMU-132-01, ASCENT)

ER-, Her-2 low (1+ by IHC or 2+ by IHC and non-amplified FISH) metastatic breast cancer

- Trastuzumab deruxtecan after progression on at least 1 line of chemotherapy – improved PFS and OS

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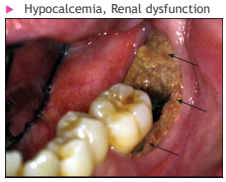
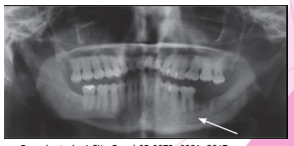
Management of Bone metastases

- Bisphosphonates (IV zoledronic acid, every 3 months)
- Denosumab (subcutaneous, every month)
- Delayed skeletal related events
- Reduced rate of distant recurrence
- Reduced breast cancer mortality
- Hypocalcemia, Renal dysfunction





Poznak *et al*. J Clin Oncol 35:3978- 3986, 2017.
Heng *et al*. Am Fam Physician. 2012 Jun 15;85(12):1134-1141.

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SURVEILLANCE/SURVIVORSHIP

- **Follow up**
  - Every 3-6 months for the first 2 years
  - Every 6-12 months for the next 3 years
- **History and Physical Examination**
  - Symptoms of local recurrence or metastatic disease
  - Update family history and genetic referral if needed
  - Examination of chest wall, breast and axilla
  - Adverse effects from treatments
  - Gynecologic exam – annually for patients in tamoxifen
  - Lymphedema
- **Imaging**
  - Annual mammogram
  - DEXA every 2 years for patient on AI
- **Education**
  - Breast awareness
  - Adherence to medications

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Take Home Points

- Breast cancer is a common but curable disease with multiple treatment options
- It is a heterogeneous group of cancers with varied biology and consequent prognosis
- Multiple risk factors need to be reviewed and strategies to reduce risk need to be incorporated accordingly
- Screening mammogram is an essential tool for early diagnosis
- Pathology and genomic assays provide important prognostic information that helps direct treatment
- Surgery, Chemotherapy, Radiation, endocrine therapy and anti Her-2 drugs have a definite role in localized disease based on biology

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Take Home Points

- Sequence of surgery and chemotherapy does not matter in terms of overall outcome
- Metastatic disease also has numerous treatment options and improved outcomes
- Endocrine therapy, targeted agents (CDK 4/6 inhibitors, PIK3CA inhibitors, PARP inhibitors), anti-Her-2 drugs, Immunotherapy and single agent chemotherapy drugs form the cornerstone of treatment for metastatic disease with the aim of palliation
- Survivorship referrals help improve quality of life

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Thank you!

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