

# Breast Cancer Basics

Amy K Krie MD  
Medical Oncologist

1

## Topics

Breast cancer  
screening

Breast cancer  
diagnosis

Understanding  
the pathology  
report

Types of  
breast cancer

2

## Breast cancer screening



3

## Screening 40-49 with average risk

- US Preventative Task Force "The decision to start screening with mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin screening once every two years between the ages of 40 and 49 years"
- American Cancer Society "Women aged 40 to 44 years should have the choice to start breast cancer screening once a year with mammography if they wish to do so. The risks of screening as well as the potential benefits should be considered. Women aged 45 to 49 years should be screened with mammography annually"
- American College Radiology "Screening with mammography is recommended once a year"

4

## Screening Women age 50-74 with average risk

- US Preventative Task Force “Screening with mammography once every two years is recommended”
- American Cancer Society “Women aged 50 to 54 years should be screened with mammography annually. For women aged 55 years and older, screening with mammography is recommended once every two years or once a year”
- American College of Radiology “Screening with mammography is recommended once a year”

5

## Women age 75 years and older

- US Preventative Task Force “Current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older”
- American Cancer Society “Women should continue screening with mammography as long as their overall health is good and they have a life expectancy of 10 years or more”
- American College of Radiology “The age to stop screening with mammography should be based on each woman’s health status rather than an age-based determination”

6

## Dense Breast Tissue

- US Preventative Task Force “Current evidence is insufficient to assess the balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging (MRI), digital breast tomosynthesis (DBT), or other methods in women identified to have dense breasts on an otherwise negative screening mammogram”
- American Cancer Society “The balance of benefits and harms of adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging (MRI), digital breast tomosynthesis (DBT), or other methods in women identified to have dense breasts on an otherwise negative screening mammogram. Evidence is insufficient to recommend for or against yearly MRI screening”
- American College of Radiology “In addition to mammography, contrast-enhanced breast MRI is also recommended. After weighing benefits and risks, ultrasound can be considered for those who cannot undergo MRI”

7

## High Risk Screening

Different screening guidelines may be suggested for women who have risk factors such as:

- BRCA or other genetic mutation
- History of mantle or chest radiation therapy especially before age of 30
- Lifetime breast cancer risk of 20% or greater based on their family history.

8

## References

- 1 Siu AL; U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine* 2016;164(4):279–296. Available at <https://pubmed.ncbi.nlm.nih.gov/26757170/>. 2 U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine* 2009;151(10):716–726. Available at <https://pubmed.ncbi.nlm.nih.gov/19920272/>. 3 Oeffinger KC, Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, Walter LC, Church TR, Flowers CR, LaMonte SJ, Wolf AM, DeSantis C, Lortet-Tieulent J, Andrews K, Manassaram-Baptiste D, Saslow D, Smith RA, Brawley OW, Wender R; American Cancer Society. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA* 2015;314(15):1599–1614. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4831582/>. 4 Committee on Gynecologic Practice. Committee opinion no. 625: Management of women with dense breasts diagnosed by mammography. *Obstetrics and Gynecology* 2015;125(3):750–751. Available at <https://pubmed.ncbi.nlm.nih.gov/25730253/>. 5 Committee on Practice Bulletins–Gynecology. Practice bulletin number 179: Breast cancer risk assessment and screening in average-risk women. *Obstetrics and Gynecology* 2017;130(1):e1–e16. Available at <https://pubmed.ncbi.nlm.nih.gov/28644335/>. 6 Committee on Practice Bulletins–Gynecology, Committee on Genetics, Society of Gynecologic Oncology. Practice bulletin No. 182: Hereditary breast and ovarian cancer syndrome. *Obstetrics and Gynecology* 2017;130(3):e110–e126. Available at <https://pubmed.ncbi.nlm.nih.gov/28832484/>. 7 Lauby-Secretan B, Loomis D, Straif K. Breast-cancer screening—viewpoint of the IARC Working Group. *New England Journal of Medicine* 2015;373(15):1478–1479. Available at <https://pubmed.ncbi.nlm.nih.gov/26444742/>. 8 Monticciolo DL, Newell MS, Hendrick RE, Helvie MA, Moy L, Monsees B, Kopans DB, Eby PR, Sickles EA. Breast cancer screening for average-risk women: Recommendations from the ACR commission on breast imaging. *Journal of the American College of Radiology* 2017;14(9):1137–1143. Available at <https://pubmed.ncbi.nlm.nih.gov/28648873/>. 9 Monticciolo DL, Newell MS, Moy L, Niell B, Monsees B, Sickles EA. Breast cancer screening in women at higher-than-average risk: Recommendations from the ACR. *Journal of the American College of Radiology* 2018;15(3 Pt A):408–414. Available at <https://pubmed.ncbi.nlm.nih.gov/29371086/>. 10 Qaseem A, Lin JS, Reem AM, Horwath CA, Wilt TJ. Screening for breast cancer in average-risk women: Statement from the American College of Physicians. *Annals of Internal Medicine* 2019;170(8):547–560. Available at <https://www.acpjournals.org/doi/10.7326/M18-2147>. 11 American Academy of Family Physicians. Summary of recommendations for clinical preventive services. [PDF-276KB] 2

9

## Breast Cancer Diagnosis

10

## BI-RADS score

Category 0 Inconclusive. Physician needs to obtain prior imaging or additional imaging

Category 1 Normal

Category 2 Abnormality seen but benign. Cyst, implant, changes related to prior surgery

Category 3 Probably benign. Chance of cancer <2%. General recommendation for shorter interval follow-up.

Category 4 Biopsy required.

- 4a) 2-10% risk of cancer
- 4b) 10-50% risk of cancer
- 4c) 50-95% risk of cancer

Category 5 >95% chance of being cancer. Biopsy needed.

Category 6 Known biopsy proven cancer

11

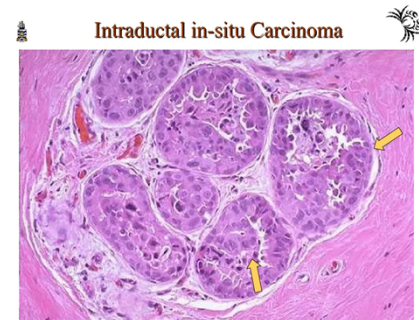
## Call back

- Diagnostic imaging. Diagnostic mammogram and ultrasound.
- Biopsy. Ultrasound guided versus stereotactic guided
- Additional imaging. CESM or breast MRI

12

## Understanding the pathology report

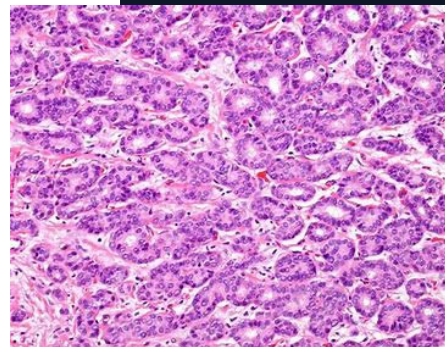
- Benign: Adenosis. Fibrocystic change. Fat necrosis. Usual ductal hyperplasia.
- Benign but need to correlate with mammogram and consider additional excision. Radial scar, papilloma, atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ.
- DCIS (Ductal carcinoma in situ)
- Invasive ductal/lobular/mammary carcinoma



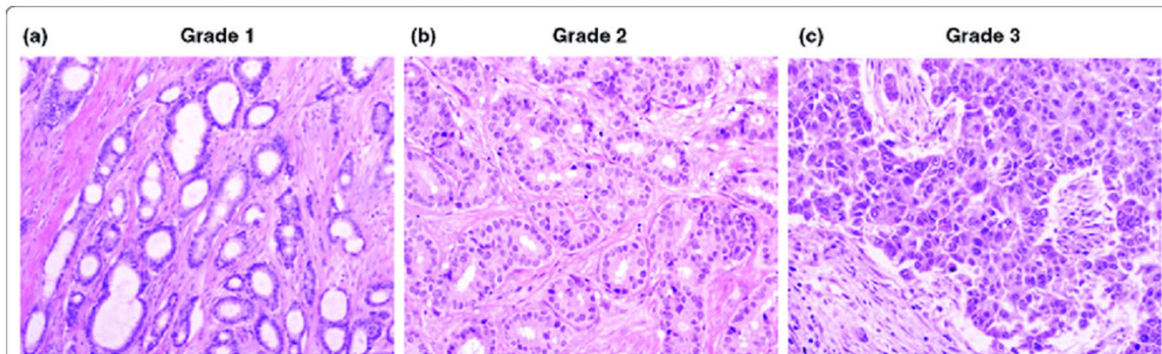
13

## Understanding the path report for invasive cancer

- Ductal or Lobular
- Size
- Nottingham grade
- Dermal or lympho-vascular invasion
- Margin
- Tumor markers ER/PR/Her2
- Nodal status



14



## Nottingham grade

- Grade is not stage.
- Nottingham grade
  - Tubule formation (1-3)
  - Nuclear pleomorphism (1-3)
  - Mitotic activity (1-3)
  - Nottingham grade 1 (3-5 points), grade 2 (6-7 points), grade 3 (8-9 points)

15

## Tumor markers

- Estrogen receptor
  - Percentage of cells staining
  - Intensity of staining
- Progesterone receptor
  - Percentage of cells staining
  - Intensity of staining
- Her2 (Always changing)
  - IHC (0, 1+, 2+, 3+) antibody test to detect protein expression
  - FISH (positive/negative) DNA probe to detect gene amplification

16

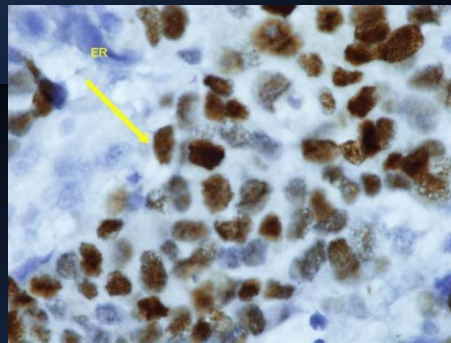
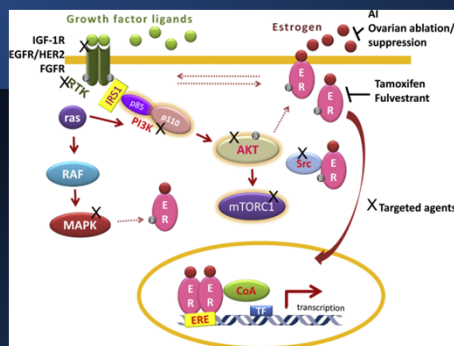


## Types of breast cancer

- Estrogen/Progesterone receptor positive/Her2 negative
- Estrogen/Progesterone receptor positive/Her2 positive (triple positive)
- Estrogen/Progesterone receptor negative/Her2 positive
- Estrogen/Progesterone receptor negative/Her2 negative (triple negative)

17

## ER/PR positive breast cancers



18

## ER positive breast cancers

- Tamoxifen/Fulvestrant- block estrogen by binding to the estrogen receptor
- Aromatase inhibitors- blocks the conversion of other hormones into estrogen by the aromatase enzyme
- CDK 4/6 inhibitors- Palbociclib, Ribociclib, Abemaciclib
- Alpelisib- for PIK3CA mutated breast cancers
- Everolimus- mTOR inhibitor

19

## Her2 positive breast cancer

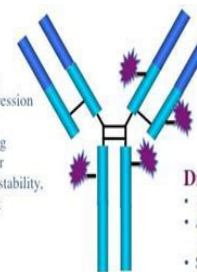


### Target/MAb

- Exploitable Selectivity
  - High Expression on tumor
  - Limited normal tissue expression
- Limited heterogeneity
- Internalizes following binding
- Conjugation sites (cysteine or lysine) should not impact stability, binding, internalization, pk

### Linker

- Stable in circulation
- Selective intracellular release of biologically active drug
  - enzymatic cleavage
  - MAb degradation
- Limited heterogeneity of drug product



### Drug

- Highly Potent
- Amenable to modifications that allow linker attachment
- Stable
  - in circulation
  - in lysosomes
- Defined mechanism of action
- Local bystander effect?

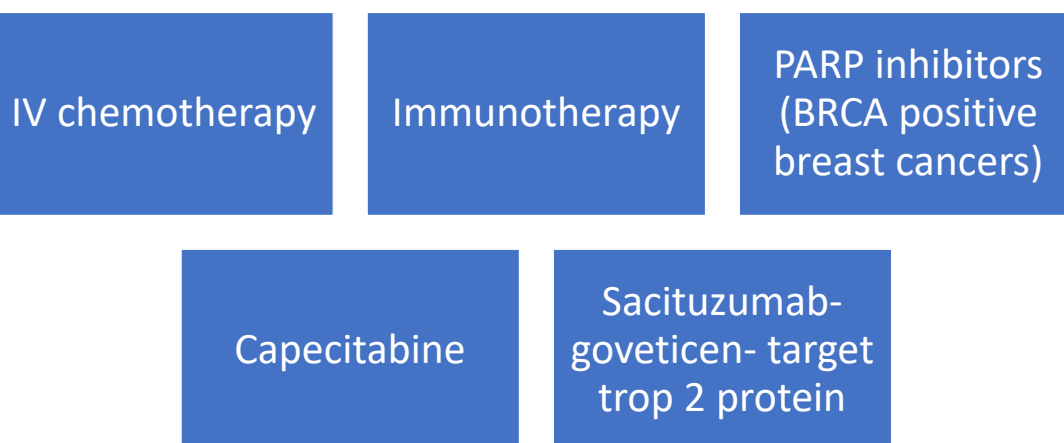
20

## Her2 positive breast cancers

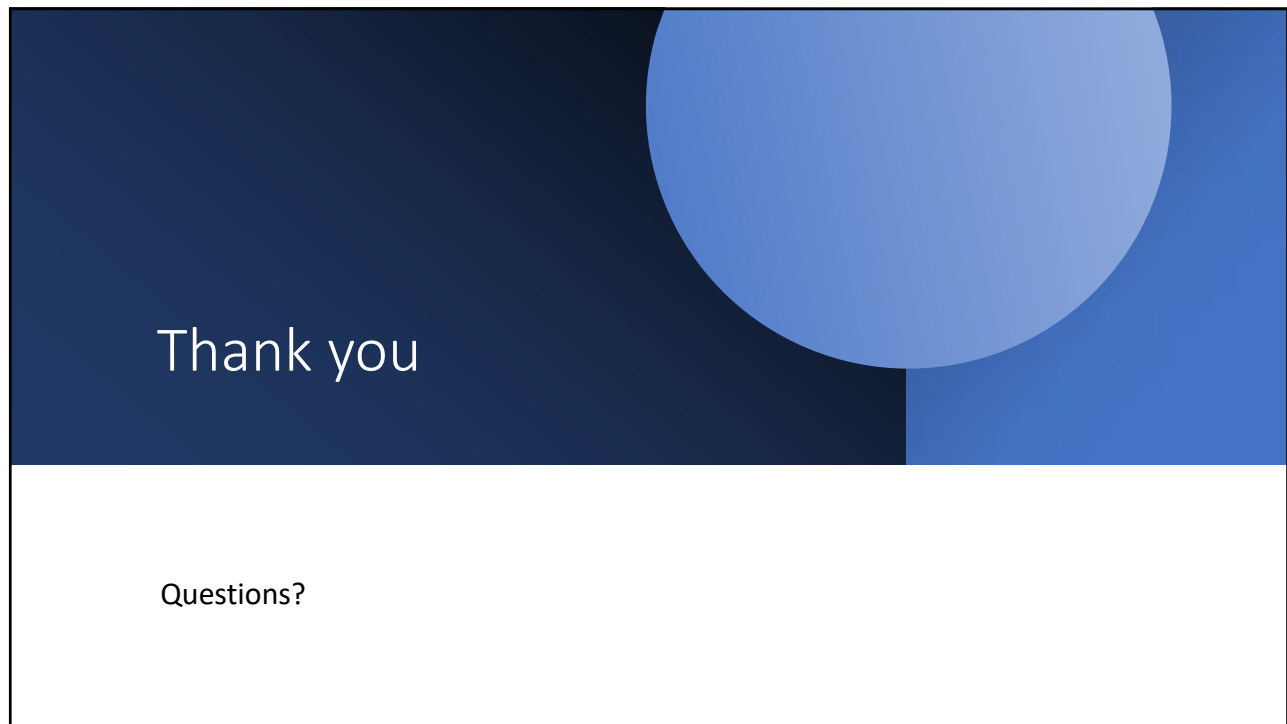
- Trastuzumab
- Pertuzumab
- Herceptin/pertuzumab combined injection
- TDM-1
- Trastuzumab-deruxtecan or T-DXD
- Lapatanib (oral EGFR/Her2 inhibitor)
- Neratinib (oral EGFR/Her2 inhibitor)
- Tucatinib (small molecule inhibitor Her2)- CNS penetration

21

## Triple negative breast cancers



22



23