Mass General Brigham Mass General Cancer Center

OCN Review Course: Breast Cancer

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Agenda

- Statistics/Incidence
- Risk Factor Assessment
- Screening
- Pathophysiology
- Clinical Presentation
- Management of early and late-stage disease
- Survivorship
- Resources

Whether you are a mother or a father, or a husband or a son, or a niece or a nephew or uncle, breast cancer doesn't discriminate. ??

-Stephanie McMahon

Breast Cancer accounts for 12.5 % of all new annual cancers worldwide!



Breast Cancer Statistics

- Most common female cancer in the U.S.
- Average lifetime risk in women: 1 in 8
- Incidence has increased by 0.5% per year
- Second most common cause of cancer death
- There are more than 3.8 million breast cancer survivors living in the U.S.!

- Male breast cancers: 2710 new cases invasive
- White women more likely to be diagnosed than Black, Asian or Hispanic women
- Black women more likely to present at advanced stage and have aggressive type breast cancer
- Black women more likely to die from breast cancer

Risk Factors

Non-modifiable

- •Middle age and female
- •Personal and family history
- •Gail Model (>1.7% in >35 yoa)
- •ADH
- •LCIS/ALH
- •Dense breasts
- •Genetic mutation carriers
- •Ashkenazi Jewish heritage (1/40 have BRCA+)
- Thoracic radiation
- •Early menarche (<12)
- •Late menopause (>55)
- •DES exposure

https://www.cdc.gov/cancer/breast/basic_info/risk_factors.htm

Modifiable

- Socioeconomics
- •Nulliparous
- Not breastfeeding
- •Alcohol intake
- •Overweight/Obesity
- •Endogenous hormones in postmenopause if taken > 5 years

Screening for breast cancer

Mammogram is a low dose xray of the breast.

Breast cancer found on screening mammograms tend to be smaller and less likely to have spread outside the breast.

Size and spread are some of the most important factors that predict prognosis.

Breast MRI uses radio waves and strong magnets to make pictures of the breast.

- Used in addition to annual screening mammogram in certain cases
 - $\,\circ\,$ High risk for breast cancer
 - Diagnostics
 - $\,\circ\,$ Check for breast implant leak

https://www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/american-cancer-society-recommendations-for-the-early-detection-of-breast-cancer.html

Average Risk Screening

Breast Cancer Screening Guidelines For Women with Average Risk

Population Test or Procedure		Frequency	
40-44 years	Mammogram	Should have the opportunity to begin annual screening.	
45-54 years	Mammogram	Annually	
55 years and older	Mammogram	Should switch to mammograms every 2 years, or can continue yearly screening. Screening should continue as long as a woman is in good health and is expected to live at least 10 more years.	

Visit www.cancer.org for more information about the American Cancer Society Guidelines for the Early Detection of Cancer

American Cancer Society www.cancer.org

High Risk Screening

Residual risk >or=20% (largely family hx based models)

- •Mammogram and Breast MRI annually
- •Depends on genetic mutation or youngest age of breast cancer in the family history (or start at 40)
- •Mammogram not prior to age 30
- •Breast MRI not prior to age 25
- •Clinical breast exam every 6-12 months starting when risk identified but not before age 21
- •Consider referral to genetics counselor

Source:V1.2022 NCCN Guidelines Breast Cancer Screening and Diagnosis https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf

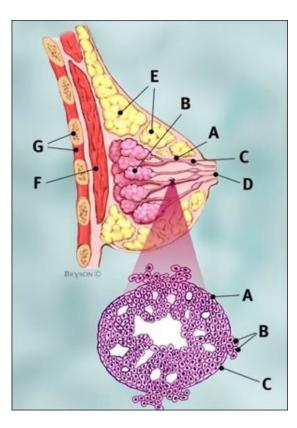
High Risk Screening

H/o thoracic radiation therapy between ages of 10 and 30

- Increased risk of breast cancer
- •Age <25: annual exams starting 8 years after RT
- •Age >25: every 6-12 month breast exams
- •Mammogram starting at 30
- •Breast MRI starting at 25
- •Breast awareness counseling
- •Consider further risk reduction strategies

Source:V1.2022 NCCN Guidelines Breast Cancer Screening and Diagnosis https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf

Anatomy and Physiology



Breast Anatomy

Breast profile:

A Ducts
B Lobules
C Dilated section of duct to hold milk
D Nipple
E Fat
F Pectoralis major muscle
G Chest wall/rib cage

Enlargement:

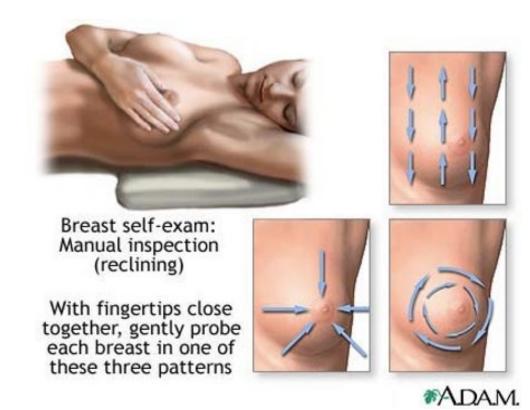
- A Normal duct cellB Ductal cancer cells breaking through the basement membrane.
- C Basement membrane

Clinical Presentation

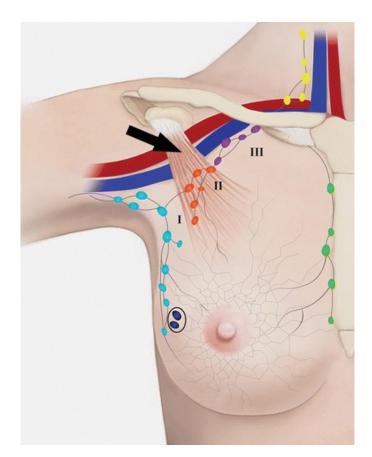
Early-Stage Breast Cancer

Asymptomatic with abnormal screening mammogram or MRI

Breast mass or thickening Skin changes Breast pain Nipple inversion Nipple discharge Lymphadenopathy



Lymphadenopathy of the regional nodes



Level I (Blue): low axillary

Level II (Red): mid-axillary

Level III (Purple): high axillary

Drainage routes: Axillary Interpectoral Internal mammary

 $https://pubs.rsna.org/doi/full/10.1148/radiol.2020192534\#: \sim: text=Axillary \% 20 LNs\% 20 are \% 20 divided \% 20 into, \% 2C\% 20 interpectoral \% 2C\% 20 and \% 20 internal \% 20 mammary for the standard for the sta$

Abnormal Imaging

Abnormal Mammogram

- Mass
- Calcifications
- Irregular shape
- Spiculated margins

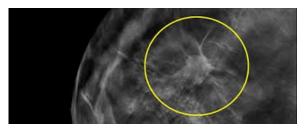
Ultrasound

• Solid vs fluid filled

Breast MRI with gadolinium contrast

- Can locate small breast lesions missed by mammogram
- Do not do well identifying calcifications

https://www.ncbi.nlm.nih.gov/books/NBK12642/



Knowledge Check

Which are considered nonmodifiable risk factors for breast cancer?

- A. Dense breast tissue
- **B. Smoking**
- C. Italian descent
- D. Personal and family history
- E. Late onset menses

Management

Management for Early-Stage Breast Cancer

Surgery

- Breast-conserving treatment
- Mastectomy +/-Reconstruction
- Sentinel lymph node biopsy vs. full axillary dissection

Breast Radiation

- External radiation
- Brachytherapy
- Whole or partial breast radiation
- Include axillary +/supraclavicular lymph node fields

Medical Therapy

- Endocrine therapy
- Targeted therapy
- Chemotherapy
- Immunotherapy
- Clinical Trials

Genetic counseling/testing

Social/Mental Health services

Nutrition and Lifestyle medicine

Integrative therapies

Case Study – B.C.

45 year-old premenopausal woman without personal history, but with family history of breast cancer, presented to breast clinic with an abnormal screening mammogram. Diagnostic mammogram with spot views and ultrasound showed a 2cm irregular and spiculated mass in the lower outer right breast. Biopsy was recommended. A core needle biopsy was done that was positive for malignant cells, invasive ductal cancer. Genetic testing for BRCA 1,2 was negative for mutation. Breast conserving surgery was recommended. The patient underwent a lumpectomy and sentinel lymph node dissection (SLND), two nodes were removed.

Pathology:

- 2.1 cm, grade 2 infiltrating ductal carcinoma, with 0/2 sentinel lymph nodes
- Estrogen and progesterone receptors +
- Her-2/neu protein negative
- Clear margins

Staging: TNM Classification

- 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 N0-2 M0
- Stage IIIC Any T N3 M0
- Stage IV Any T Any N M1

Stage	5-year Relative Survival Rate
0	100%
I	100%
II	93%
III	72%
IV	22%

Case Study – B.C.

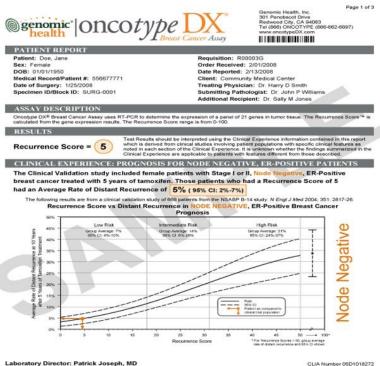
What factors determine this patient's risk of breast cancer recurrence?

- Stage (TNM)
- Grade 0-3
- Presence or absence of hormone receptors
- Her2neu oncogene overexpression
- Age or menopausal status

What type of adjuvant therapy should she receive?

- Radiation
- Hormone therapy
- ?Chemotherapy what is the relative benefit?

Prognostic tool for node negative, ER+ breast cancer



Laboratory Director: Patrick Joseph, MD CLA Number 60D10182 This feel was developed and its performance characteristics determined by Genomic Health, Inc. The laboratory is regulated under the Chical Laboratory improvem Amendments of 1989 (CLM) as guarded to perform high-complexity circus feeting. This test is used for circical purposes. If should not be regarded as investigational or elseanch. These enable are adjunction to the ordering projection's works.

301 Penobscot Drive Redwood City, CA 94063 (866) ONCOTYPE (866-662-6897) www.oncotypeDX.com © 2006 Genomic Health, Inc. All rights reserved. Oncotype DX and Recurrence Score are trademarks of Genomic Health, Inc. RT-PCR to determine expression of 21 genes in tumor tissue

Predicts the value of chemotherapy in addition to hormone therapy

Assumes treatment with 5 years hormone therapy (tamoxifen)

Recurrence score ranges from 0-100

For B.C. - low recurrence score of 5 means NO chemotherapy recommended

Adjuvant endocrine therapy

Tamoxifen: blocks the effect of estrogen on target organs (SERM)

- 40% reduction in breast cancer recurrence
- 30% reduction in breast cancer mortality

Ovarian suppression (GnRH analogs): reduces ovarian estrogen production, causes medically induced menopause

Given with tamoxifen or AI

Aromatase inhibitors: inhibits systemic estrogen production

- Only effective if postmenopase (naturally, medically or surgically induced)
- Reduce recurrence risk by 50% if taken for 5 years (5-10 years extended therapy for higher risk)

Nursing Considerations for Patients on Tamoxifen

Treatment adherence and tolerance monitoring

Patient education of side effects (vasomotor, sexual, arthrlagia/myalgia) and adverse events (DVT, benign gynecologic disorders, uterine cancer)

Side effect management

Annual GYN exam and contraception counseling

Annual Ophthalmologic exam

Smoking cessation and avoidance

CVD screening and prevention

Concurrent medication list (especially antidepressants and herbals)

Exercise counseling, weight management

Is more treatment better?

ATLAS Study: Randomized study 5 versus 10 years of adjuvant tamoxifen

Pros

- Lower cumulative risk of breast cancer recurrence during years 5-14: 21.4% for extended tam; 25.1% for controls
- Lower breast cancer mortality during years 5-14: 12.2% for extended tam; 15% for controls
- Reduction in overall mortality: RR 0.93 (p=0.04)
- Fewer contralateral breast cancers and bone fractures with extended tamoxifen

Cons

 Higher rates of PE (RR 1.87, +20 events), endometrial cancer (RR 1.74, +53 events) with extended tamoxifen

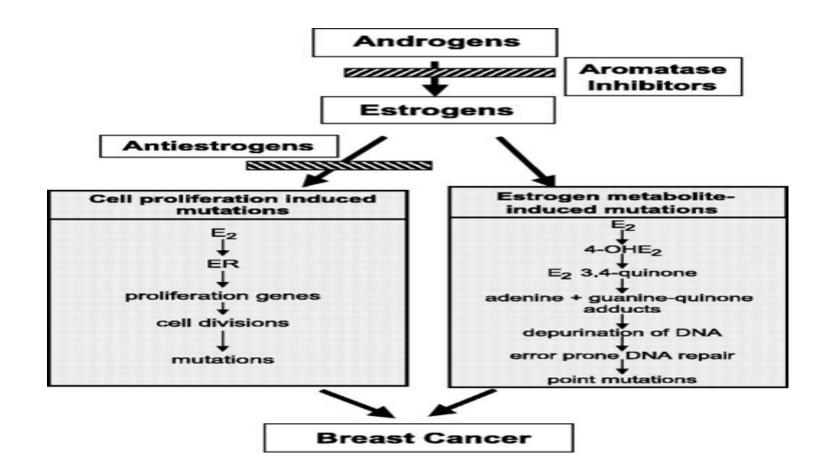
Lancet, 2012



What if B.C. was 65 years old?

What treatment recommendation would be different?

Hormone therapy anti-estrogen versus aromatase inhibitor

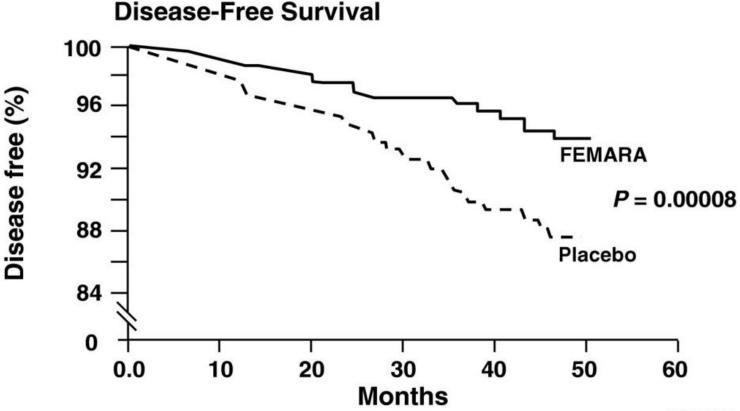


Both stop tumor growth

Tamoxifen blocks estrogen from reaching a cancer cell - by blocking the estrogen receptor signal the cells die.

Aromatase inhibitors inhibit the change from androgens to estrogen, lowering total body estrogen, causing an "estrogen deprivation" state.

MA 17: Letrozole versus placebo following 5 years of Tamoxifen



Breast Cancer Research

Adapted from Goss et al. Pritchard and Whelan Breast Cancer Res 2005

ATAC Trial Results

The Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial compared the efficacy and safety of anastrozole (1mg) with tamoxifen (20mg) daily for 5 years as adjuvant treatment for postmenopausal women with early-stage hormone receptor positive breast cancer.

Significant improvements in the anastrozole group compared to tamoxifen group

- Disease free survival
- Time to recurrence
- And time to distant recurrence
- Lower recurrence rates on anastrozole

ATAC Trial: side effects AI versus tamoxifen

	% of patients		
	Anastrozole	Tam	P value
Hot flashes	35.7	40.9	<0.0001
Vaginal bleeding	5.4	10.2	<0.0001
Vaginal discharge	3.5	13.2	<0.0001
Endometrial cancer	0.2	0.8	0.02
Ischemic cerebrovascular	2.0	2.8	0.03
Venous thromboembolic	2.8	4.5	0.0004
Joint symptoms	35.6	29.4	<0.0001
Fractures	11.0	7.7	<0.0001
Hysterectomy	1.3	5.1	<0.0001

Zarwan, 2013

Nursing Considerations for Patients on Aromatase Inhibitors

Treatment adherence and tolerance monitoring

Patient education of side effects (vasomotor, sexual, arthralagia/myalgia, bone loss, elevated CVD risk - lipids)

Side effect management

Sexual side effect management, use of non-hormonal vaginal moisturizers or topical estrogens

Bone density study (DXA) at baseline and every 2 years, anti-fracture medication if indicated, lifestyle counseling for bone health

Smoking cessation and avoidance

CVD screening and prevention (BP, Lipids)

Concurrent medication list (herbals, estrogen bioequivalents)

Exercise counseling, weight management



- 45 year-old premenopausal woman with an abnormal screening mammogram. Biopsy positive for malignancy.
- Pathology: 2.1 cm, grade 2 infiltrating ductal carcinoma, with negative lymph nodes
 - Estrogen and progesterone receptors +
 - Her-2/neu gene overexpression aka "POSITIVE"

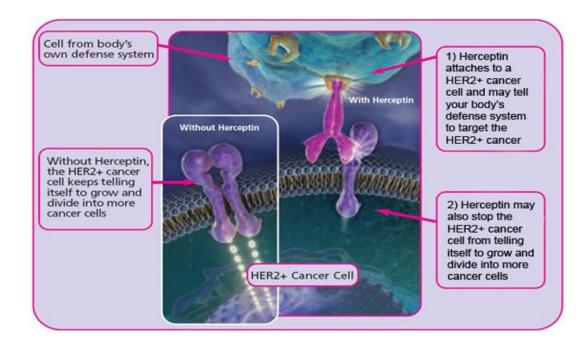
QUESTION: What does this mean?

- A. More aggressive & higher risk of recurrence
- **B. Less aggressive and lower risk of recurrence**
- **C. Eligible for targeted treatment**
- D. Both A & C

Her2neu Oncogene Overexpression

- 20-30% of breast cancers
- More aggressive
- More likely to recur
- Immunohistochemistry (0-3+)
- FISH (amplified/not amplified)

Monoclonal antibody therapy



Who gets chemotherapy?



Risk versus benefit

- Positive regional lymph nodes
- Tumor > 2cm
- High Oncotype Dx Score
- Her 2 neu oncogene overexpression
- Triple negative invasive disease
- Advanced stage disease

Chemotherapy for Breast Cancer

- How does it work?
 - Kills rapidly dividing cancer cells
- Goal is to stop or slow the spread of cancer
 - Treatment: curative
 - Palliative: ease cancer symptoms
- Used with other treatments
 - Neo-adjuvant "pre-operative"
 - Adjuvant "post-operative"
 - Combined with immunotherapies
- Management
 - Toxicities and quality of life "balance"
 - Long term side effects



Monoclonal antibody therapy in Combination with Chemotherapy

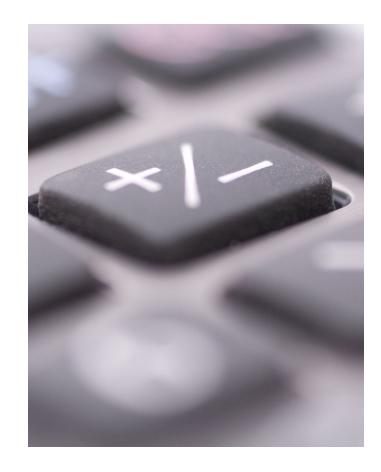
- Taxol (paclitaxel) + Herceptin (trastuzumab) (for small Her2+ early-stage node neg breast cancers)
- TCHP -> with chemo + Herceptin (trastuzumab) + Perjeta (pertuzumab)
- AC->Taxol and Herceptin
- Hylecta (SC version of Herceptin)
- PHESGO (SC version of Herceptin + Perjeta
- Adjuvant therapy duration 1 year
- Cardiac monitoring every 3 months with ECHO or MUGA to assess for drop in LVEF (risk for CHF)

Case –B.C.

- 45 year-old premenopausal woman with an abnormal screening mammogram. Biopsy positive for malignancy. Pathology: 2.1 cm, grade 3 infiltrating ductal carcinoma, with negative lymph nodes
 - Estrogen and progesterone receptors <u>NEGATIVE</u>
 - Her-2/neu NEGATIVE
 - QUESTION: Does B.C. get chemotherapy?
 - A. Yes
 - B. No

Triple Negative Breast Cancer

- 10-15% of all breast cancers
- No overexpression of Her2neu oncogene
- No ER, PR receptors
- Faster growing
- Worse prognosis
- More common
 - younger women
 - BRCA1 mutation carriers
 - African American or Hispanic



Common Regimens for Neo or Adjuvant Therapy

Adjuvant Regimens

- Dose Dense Adriamycin+Cytoxan -> Taxol
- Taxotere+Cytoxan
- Herceptin+Taxol
- TCHP Taxotere+Carboplatin+Herceptin+Perjeta
- Keytruda (pembrolizumab) immune checkpoint inhibitor + chemotherapy (Carboplatin+paclitaxel -> doxorubicin + cyclophosphamide) pre-operatively for high-risk early-stage triple negative breast cancer followed by surgery followed by Keytruda alone (2022)

Nursing Considerations for the Patient on Chemotherapy

- Fatigue
- Nausea, vomiting
- Constipation, diarrhea
- Heartburn, GERD
- Skin changes, rashes
- Alopecia
- Mucositis
- Immune suppression
- Anemia
- Thrombocytopenia
- Kidney dysfunction
- LFT changes
- Fertility concerns

- Heart problems
- Lung problems, pneumonitis
- Taste changes
- Anorexia
- Dehydration, Electrolyte changes
- Myalgia/arthralgia
- Bone pain
- Sleep disorders
- Body image concerns
- Sexual side effects
- Deconditioning
- Immunotherapy adverse effects
- Death



B.C. completes adjuvant chemotherapy followed by 6 weeks of radiation therapy for triple negative breast cancer.

She goes in to see her PCP for routine visit 4 years later complaining of 3 months of persistent lower back pain "dull ache" unrelieved by rest/heat/stretching and over the past month increased fatigue.

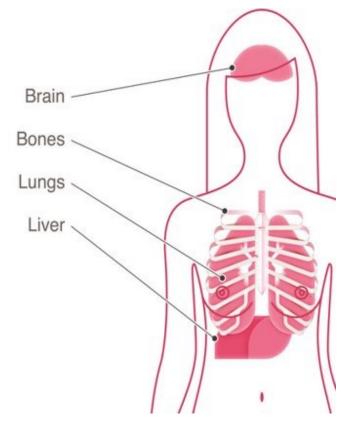
What are your concerns?

Sites of Breast Cancer Metastases

• Bone

- Pain
- Swelling
- Fractures
- Lung
 - Cough, chest pain, abnormal CXR, constitutional s/s
- Liver
 - Jaundice, itching, rash, abdominal pain
 - Elevated transaminases
 - Poor appetite, nausea, vomiting, weight loss
- Brain
 - HA, vision changes, seizure
 - Nausea & vomiting
 - Mood and personality changes

(National Breast Cancer Foundation, (2012)



Regimens for Metastatic Breast Cancer

- CDK 4/6 Inhibitors + Hormone therapy AI or Faslodex (fulvestrant) IM
- Truqap (capivasertib) + Faslodex, for those with PIK3CA/AKT1/PTEN-alterations*
- Trodelvy (sacituzumab govitecan-hziy)
- Keytruda (pembrolizumab) + chemotherapy
- Taxane based docetaxel, paclitaxel, nabpaclitaxel

*Liquid biopsy assays (blood tests) being used to help guide treatment decisions

- Anthracyclines doxorubicin, epirubicin, doxorubicin
- Xeloda (capecitabine)
- Halaven (eribulin mesylate)
- vinorelbine
- Gemcitabine
- And more

Her2+ Management in Advanced Stage Disease

Herceptin (trastuzumab) + Perjeta (pertuzumab)

- HER-2 receptor/ EGFR inhibitor
- Can be given IV or in SC form
- Can be combined with chemotherapy
- Requires cardiac monitoring
- Low side effect profile

Ado-trastuzumab emtansine (Kadcyla)

- Used in early and latestage breast cancer
- Chemotherapy + anti-Her2 drug conjugate
- IV every 3 weeks
- Cardiac monitoring, risk of pneumonitis, LFTs, low PLT, CIPN

Enhertu (ado-trastuzumab emtansine)

- Can be used in patients with "low Her2+" pathology
- IV every 3 weeks
- Cardiac monitoring with ECHO or MUGA
- Risk of pneumonitis
- Nausea requires aggressive management

Oral Her2+ Targeted Therapies

- Nerlynx (neratinib) oral tyrosine kinase inhibitor
 - Indications
 - Extended adjuvant therapy for early stage Her2+ breast cancer
 - Advanced stage breast cancer (with chemotherapy)
- Tuksya (tucatinib) oral tyrosine kinase inhibitor
 - Indication
 - Advanced stage breast cancer
 - Given with Xeloda (capecitabine) and Herceptin (trastuzumab)



Oral targeted therapy in hormone + metastatic breast cancer

CDK 4/6 Inhibitors + aromatase inhibitors or fulvestrant

- palbociclib (Ibrance)
- ribociclib (Kisqali)
- abemaciclib (Verzenio)

MTOR-inhibitor + aromatase inhibitor

everolimus (Afinitor)

Piqray (alpelisib)

- PIK3CA Mutation
- With Faslodex (fulvestrant)
- Hyperglycemiauq

Truqap (capivasertib) + Fulvestrant *

Lynparza (olaparib): for BRCA +

Side effects and monitoring

- Unique side effect profiles
- Laboratory monitoring
- Adherence/compliance
- Cost and coverage

Nurse provided patient education is key!

BRCA 1/2 Her2- Metastatic Breast Cancer PARP Inhibitors

	Olaparib (Lynparza)	Talozoparib (Talzenna)
Dose	300mg PO BID	1mg PO daily
AE	Bone marrow suppression, nausea/vomiting, rash, pneumonitis, secondary malignancies (MDS/AML)	Bone marrow suppression, nausea/vomiting, secondary malignancies (MDS/AML)
Monitoring	CBC and renal function prior to 1st dose and monthly thereafter	
Management	Dose reduce for adverse events, discontinue for pneumonitis. Available as tablets and capsules, which are not interchangeable due to bioavailability differences	Dose reduce for decrease hemoglobin, neutropenia, and thrombocytopenia

MOA: Blocks PARP enzymes from repairing double-stranded DNA breaks in BRCA1/2 deficient tumor cells, leading to cell death

Nursing Considerations for patients on targeted therapies

- Infusion reactions
- Cardiotoxicity
- Hepatotoxicity
- Pneumonitis
- Dermatologic rash
- Diarrhea
- Nausea
- Myelosuppression
- Electrolyte abnormalities

Oncologic Emergencies

- Spinal cord compression
- Superior Vena Cava Disease
- Pericardial Tamponade
- DVT/PE
- Hypercalcemia
- Tumor Lysis Syndrome
- Arrhythmia
- Blood disorders (thrombocytopenia, anemia), DIC
- Febrile neutropenia
- Sepsis



(Smith&Toonen, 2007)

Care of the Cancer Survivor

Ongoing survivorship care, coordination with primary care

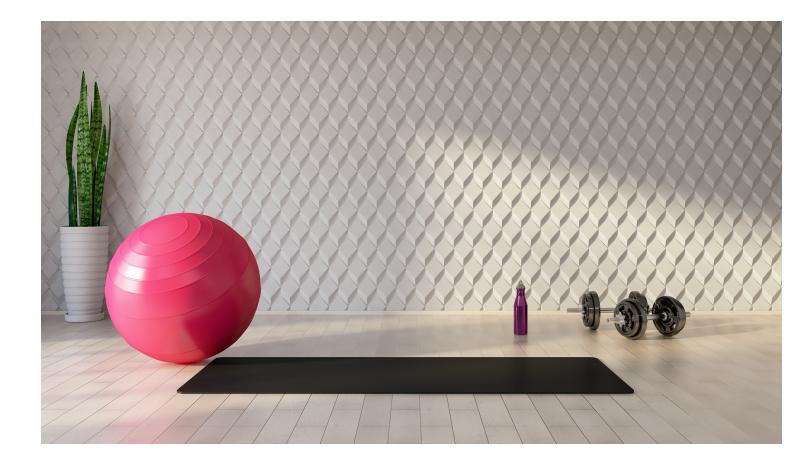
Multidisciplinary care

- Radiation oncology, surgery
- Physical therapy (lymphedema, postsurgical pain, deconditioning, prehab/rehab)
- Endocrine
- Sleep medicine
- Neurology



- Rheumatology
- Gynecology
- Uro-gynecology
- Surgical
- Psych/mental health/SW/Peer support
- Palliative care, pain service
- Cannabis therapeutics
- Integrative therapies
- Healthy lifestyle counseling and Nutrition services

Healthy lifestyle counseling



- Being physically active exercise!
- Maintaining a healthy weight
- Abstaining/limiting alcohol
- Avoiding smoking
- Eating plant predominant diet



National Cancer Institute Breast Cancer: <u>https://www.cancer.gov/types/breast/hp</u>

NCCN Breast Cancer Treatment Guidelines: <u>https://www.nccn.org/guidelines/</u>

American Society of Clinical Oncology Breast Cancer Guidelines: <u>https://old-prod.asco.org/practice-patients/guidelines/breast-cancer</u>

American Cancer Society Breast Cancer Information: <u>https://www.cancer.org/cancer/breast-cancer.html</u>

American Institute of Cancer Research: <u>https://www.aicr.org/</u>

MGH Lifestyle Medicine: https://www.massgeneral.org/cancer-center/patient-and-family-resources/supportive-care/lifestyle-medicine



Care of the patient with breast cancer occurs across the continuum from diagnosis through survivorship and may span over a decade. Treatments are constantly changing and becoming more complex as new targeted therapies emerge.

Care of the nurse is critical:

- Assessment
- Education, providing information and resources
- Compassionate, holistic care to patient and family



Thank you.

