Surgical Treatment of Breast Cancer

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

Screening and Diagnosis

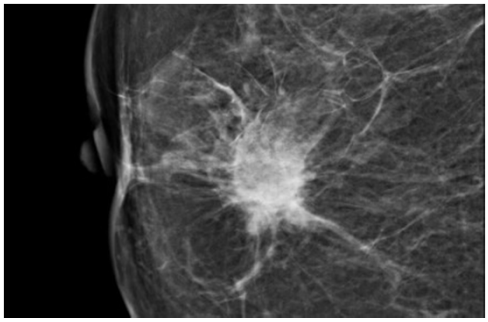
Patient presentations

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

Screening Guidelines, general population

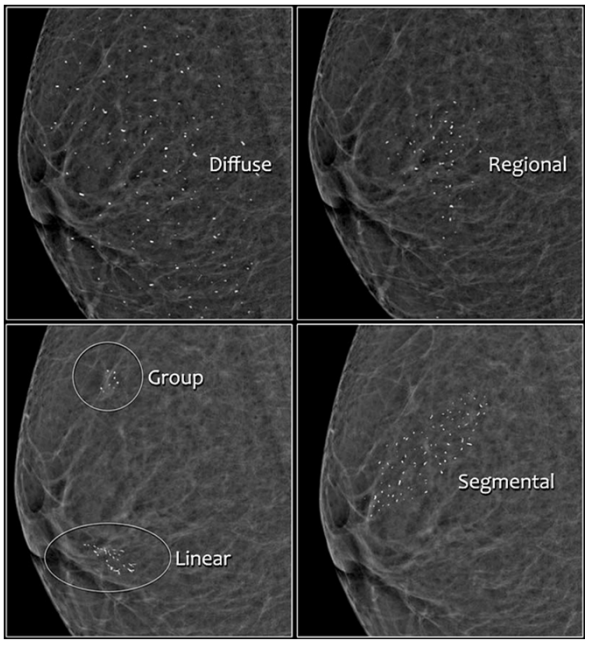
- Clinical encounter about every three years for women in their 20s-30s, and annually for women ≥ 40
- Annual screening mammogram beginning at age 40 (tomosynthesis)
- Breast awareness

NCCN Guidelines, version 2.2016



Source: The Radiology Assistant

Spiculated mass

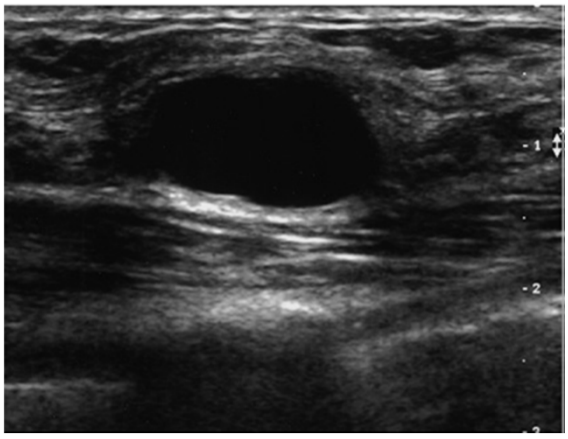


Source: The Radiology Assistant

Suspicious microcalcifications

Symptomatic patients

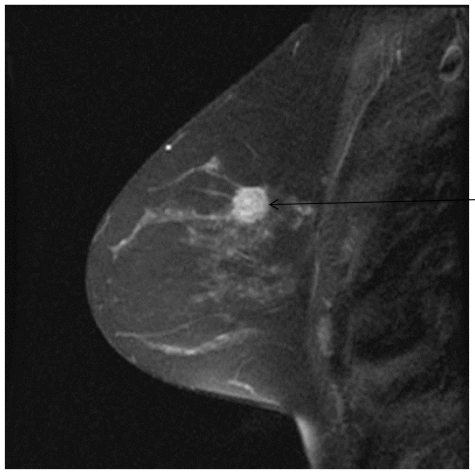
- Evaluate with complete history and physical examination
- Diagnostic imaging
  - Bilateral mammogram, even if unilateral symptoms
  - May use other imaging modalities
    - Ultrasound
    - MRI



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

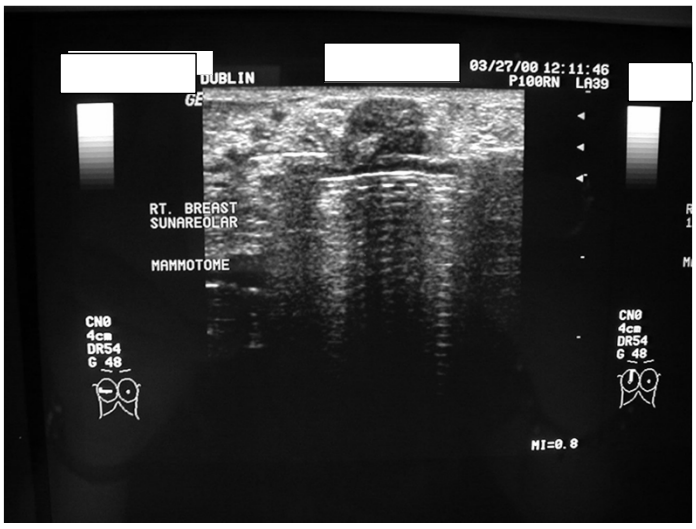
Methods of Diagnosis

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

Stereotactic Breast Biopsy

- Prone position with breast through opening in table
- Mammographic views in different positions
- Target lesion in 3 coordinates
- Post biopsy image to confirm sampling

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 ½ of recurrences are invasive

Management

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

Invasive cancers

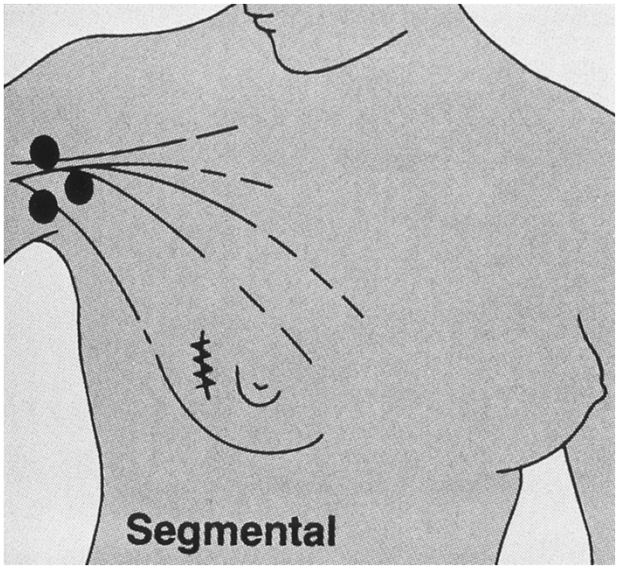
Invasive breast cancer

- 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
  - Signficiant 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

Partial mastectomy/ lumpectomy

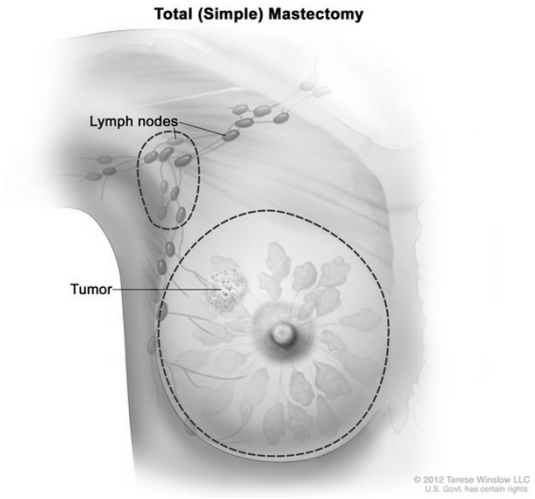


Author: National Cancer Institute/Linda Bartlett (Photographer)

Contraindications to Breast Conservation

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

Total (simple) mastectomy



Author: National Cancer Institute

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
- Role for therapy and prophylaxis unclear
  - Historic rates of nipple involvement in the setting of cancer range from 0-58%
  - 316 conscutive mastectomy specimens (232 therapeutic, 84 prophylactic) evaluated
    - 71% of therapeutic had no path abnormality, 21 % had DCIS and 8% had LCIS
    - None of the prophylactic mastectomies had nipple involvement by DCIS or invasive carcinoma

Brachtel, *JCO* 2009; 27(30): 4948

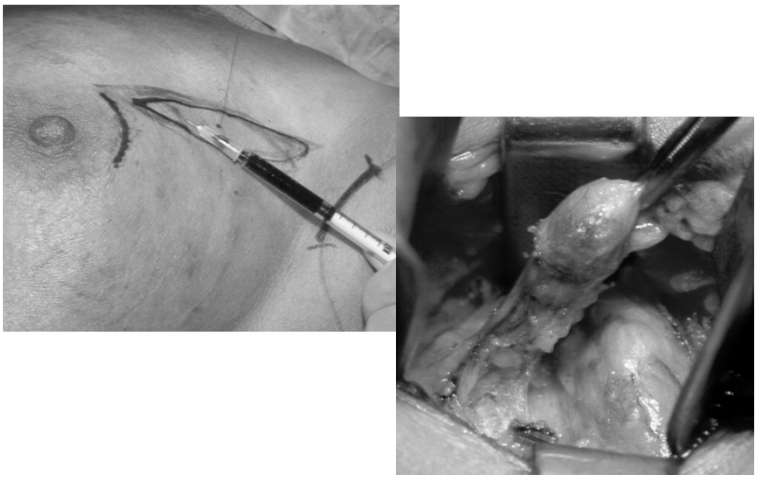
NSABP B-06

- There is no difference in disease-free, distant disease-free or overall survival between mastectomy and lumpectomy.
- The addition of radiation to lumpectomy is important in decreasing the risk of local recurrence.

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

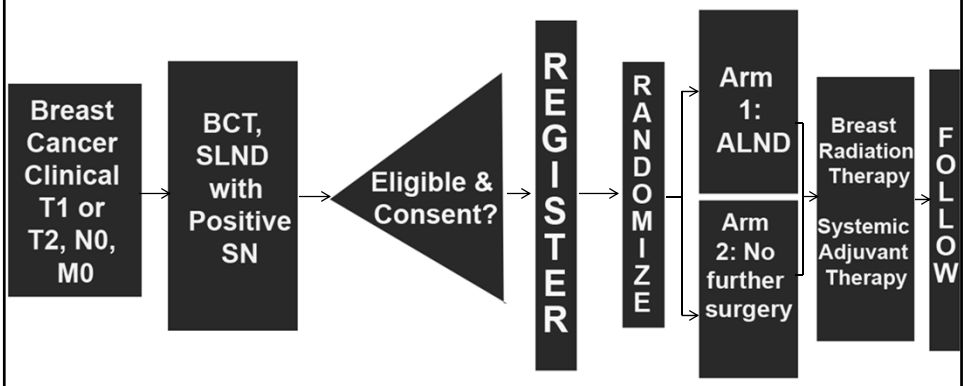
Sentinel Lymph Node Biopsy



Management of Positive SLN

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

ACOSOG Z11



Source: American Society of Clinical Oncology (https://www.asco.org/)

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 peformed
- 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

The Systemic Approach to Breast Cancer

Raquel E. Reinbolt, MD
Division of Medical Oncology
The Stefanie Spielman Comprehensive Breast Center
The Ohio State University Comprehensive Breast Center

Learning Objectives:

- **To review breast cancer systemic therapy approaches for early stage, locally advanced, and (briefly) metastatic breast cancer**

Learning Objectives:

- To review breast cancer systemic therapy approaches for early stage, locally advanced, and (briefly) metastatic breast cancer
- To review principles of survivorship

Stages of Breast Cancer

Localized Disease:

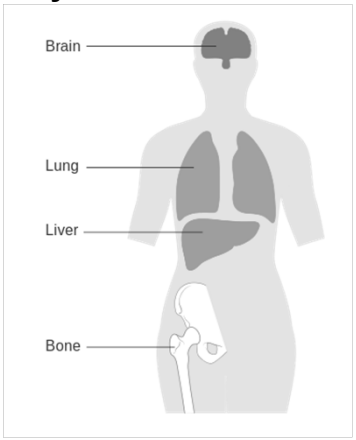
- Distribution - 60%
- 5-Year Survival – 99%

Locally Advanced

- Distribution 32%
- 5-year Survival 85%

Metastatic Disease

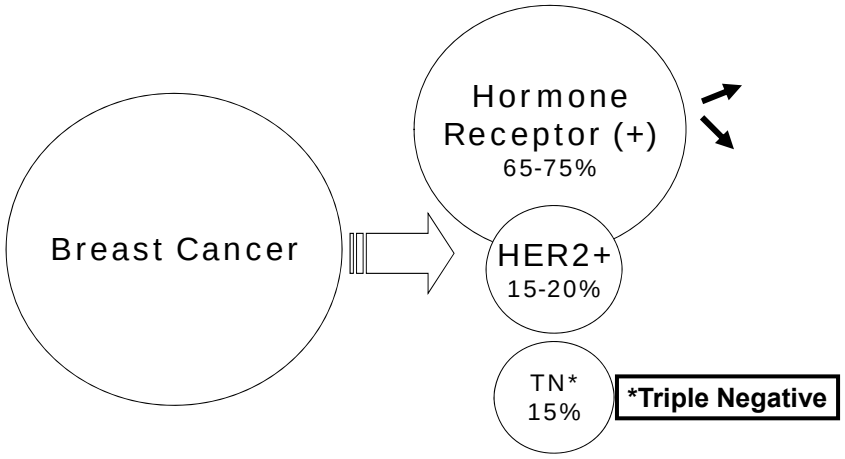
- Distribution 5-7%
- 5-year survival 26%



Based on Surveillance Epidemiology and End Result Database

Cancer Research UK / Wikimedia Commons

Not All Breast Cancer Is The Same



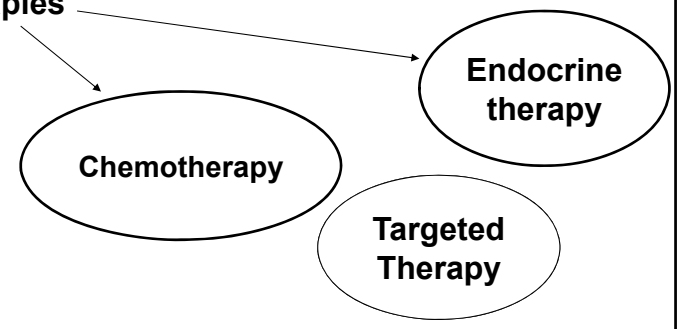
Early Stage Breast Cancer

Excellent Prognosis!

Most individuals diagnosed with breast cancer today have early stage disease, and after the institution of proper treatment, have a low chance of recurrence

Primary Therapies: Early Stage Disease

- Surgery
- Radiation
- Systemic therapies



Systemic Therapy Selection Factors

- Lymph node involvement
- Tumor size
- Tumor grade
- Lymphovascular invasion
- Ki-67 (proliferation)
- Patient age and co-morbidities
- ER, PR, Her-2 → Targeted therapy

Treating & Targeting ER+ Breast Cancer

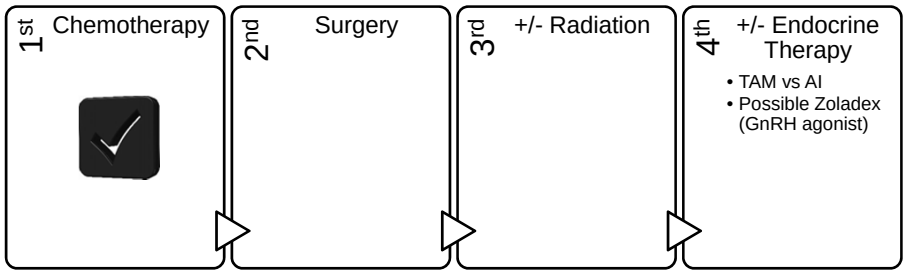
Hormone Positive Disease

Question:

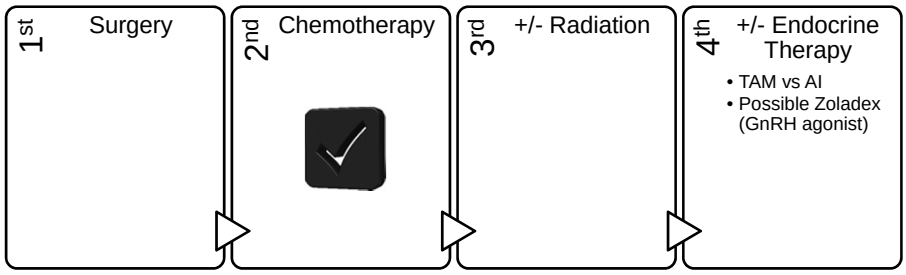
Is chemotherapy required prior to surgery in hormone positive disease?

Answer: It depends!

Answer: Yes!
Plan: Neoadjuvant Chemotherapy



Answer: No!
Plan: Adjuvant Chemotherapy, <u>If Needed</u>



How to Determine Benefit of Chemotherapy In Node Negative Patients After Surgery: Gene Expression Assays

- Predict benefit of chemotherapy
- Predict likelihood of distant breast cancer recurrence by placing patient into a risk category

Risk Category

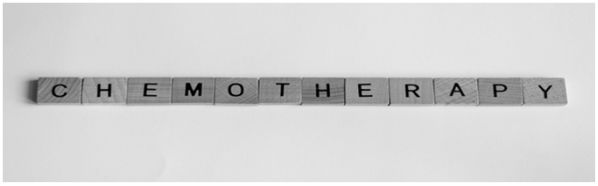
=

Chemotherapy Benefit

Chemo or No Chemo?

- 56yo F with a 2cm invasive ductal carcinoma, node negative
- ER 70% PR 0% HER2 negative
- Oncotype reveals a recurrence score of 36

>30 = HIGH RISK!



Benefit!

- **Regimens for consideration:**
  - **Adriamycin/Cytoxan + Taxol**
  - **Taxotere/Cytoxan**

Treatment Plan: AC & T (Dose Dense)

Adriamycin & Cytoxan (AC)

- Every 2 weeks, 4 times (cycles)
- Total of 8 weeks of therapy
- TTE
- Growth Factor

Taxol (T)

- Every 2 weeks, 4 times (cycles)
- Total of 8 weeks of therapy
- Growth Factor

16 weeks total of therapy

Treatment Plan: AC & T (Weekly)

Adriamycin & Cytoxan (AC)

- Every 2 weeks, 4 times (cycles)
- Total of 8 weeks of therapy
- TTE
- Growth Factor

Taxol (T)

- Every week, 12 times (cycles)
- Total of 12 weeks of therapy

20 weeks total of therapy

Treatment Plan: TC

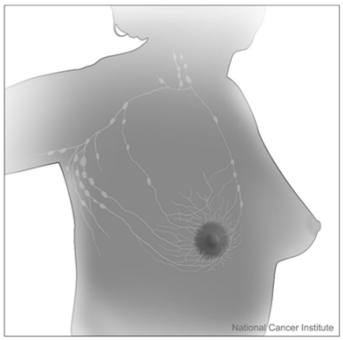
Taxotere & Cytoxan (TC)

- Every 3 weeks, 4 times (cycles)
- Total of 12 weeks of therapy
- +/- Growth Factor

Total 12 weeks of therapy

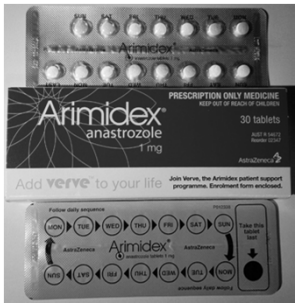
What About Hormone Positive, Lymph Node Positive Patients?

- Discussion of chemotherapy
  - Consideration of age, other comorbidities
  - Number of nodes positive
- 1-3 lymph nodes positive:
  - Potential role for gene expression testing



The Addition of GnRH Agonist Therapy

Can we maximize anti-estrogen therapy?



Endocrine Therapy

- **Have to assess menopausal status prior to therapy (chemotherapy or endocrine therapy)!**

- **Pre-menopausal: Tamoxifen (TAM) x 10yrs; TAM/AI + ovarian suppression**
  - **Side effects:**
    - **Thromboembolic events**
    - **Endometrial cancer**
    - **Hot flashes, vaginal symptoms**
    - **Important to discuss birth control use while on this med!**

Endocrine Therapy

- **Post-menopausal: Aromatase inhibitor (AI)**
  - **5yrs vs 10 yrs**
  - **Letrozole (Femara), Anastrozole (Arimidex), Exemestane (Aromasin)**
  - **Superior to Tamoxifen in this population; none superior to another**
  - **Can use after 2-5yrs of Tamoxifen**
  - **Side effects:**
    - **Mylagias/arthralgias is the major reason for discontinuation**
    - **Osteoporosis- everyone gets calcium/vit D; should get bone density prior to treatment and every 2yrs**

Treating & Targeting Triple Negative Breast Cancer

Triple Negative Disease

=

CHEMOTHERAPY

TNBC: Neoadjuvant vs Adjuvant: Timing

- **Neoadjuvant**
  - **Optimization of surgical margins**
  - **Real time monitoring of disease response**
  - **pCR and prognostication**
    - **Associated with improvement in Disease Free Survival (DFS)**

- **Adjuvant**
  - **Complete staging**

- Cortazar P, Zhang L, Untch M, et al. Pathological complete response and longterm clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet 2014;384(9938): 164-72.
- Liedtke C, Mazouni C, Hess KR, et al. Response to neoadjuvant therapy and long-term survival in patients with TNBC. J Clin Oncol 2008; 26:1275.
- von Minckwitz G, Untch M, Blohmer JU, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes J Clin Oncol 2012;30:1796.

TNBC: Neoadjuvant vs Adjuvant: Regimen Selection

- **Standard Regimens:**
  - **anthracycline + alkylating agent + taxane**
- **How about Platinum agents?**
  - **Must balance additional toxicity added from therapy with potential benefit, particularly in patients with locally advanced disease**

TNBC: Other Therapy Thoughts

- What about residual disease after neoadjuvant chemotherapy?
  - No proven role for continuing systemic therapy
  - Possible time to consider trials
  - Additional data to come
  - Surveillance is key!

How can we target TNBC?

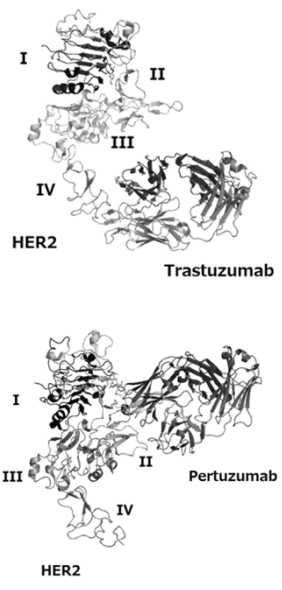
- Platinum chemotherapy
- PARP Inhibitors
- Immunotherapy
- Androgen receptor blockers
- Genomic profiling of tumors

Treating & Targeting HER2+ Breast Cancer

HER2+ Breast Cancer

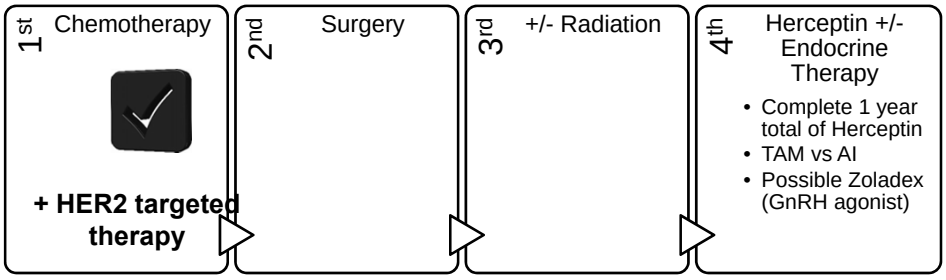
HER2 (human epidermal growth factor receptor 2):

- Gene that may play a role in breast cancer development
- Breast cancers with *HER2* gene amplification or HER2 protein overexpression benefit from HER2-targeted therapy
- HER2 Antibodies = Trastuzumab & Pertuzumab
  - Bind to different domains of the HER2 receptor



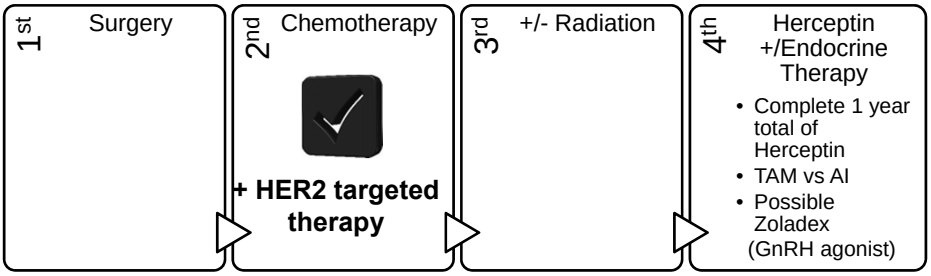
HER2+ Neoadjuvant Chemotherapy

***Consider if a Stage II or > (2cm and above or node positive)**
***Use dual-HER2 targeted therapy with Trastuzumab & Pertuzumab combined with chemotherapy**



HER2+ Adjuvant Chemotherapy

***Consider if a Stage I**
***Ongoing studies to minimize amount of concurrent chemotherapy given in this population**



Early Stage Disease: Survivorship

- **H&P: more frequent after initial diagnosis**
- **Patient education on recurrence signs/symptoms**
- **Genetic counseling**
- **Breast self-exam**
- **Mammography**
- **Pelvic examinations- especially while on TAM**
- **Awareness of therapy-specific sequelae**
- **Not recommended:** routine bloods tests, tumor markers, imaging (outside of breast imaging)

Metastatic Breast Cancer… A Few Thoughts

Metastatic Breast Cancer

- **Approximately 40,000 new cases per year in the United States**
- **Pattern of metastases:**
  - **Bone**
  - **Axillary/Mediastinal lymph nodes**
  - **Lungs**
  - **Liver**
  - **Brain (Triple Negative; HER2+)**
  - **Mucous membranes (Invasive Lobular Carcinoma)**
- **Survival:**
  - **Average 3 years**

INITIAL CONSIDERATIONS FOR NEWLY DIAGNOSED METASTATIC BREAST CANCER

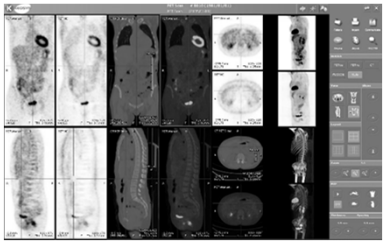
- **Confirmation of Diagnosis**
  - **Biopsy metastatic lesion if possible; consider genomic profiling!**
  - **Re-test hormone receptor and HER2 over expression**
- **Complete Staging**
  - **CT scans of chest, abdomen and pelvis**
  - **Bone scan**
  - **PET/CT (alternative to CT and bone scans)**
  - **Use of tumor markers (CA 15-3, CA 27.29, CEA)- ???**

INITIAL CONSIDERATIONS FOR NEWLY DIAGNOSED METASTATIC BREAST CANCER

- **Therapeutic Goals: <u>INCURABLE DISEASE:</u>**
  - **Palliation of cancer related symptoms.**
  - **<u>Quality of life is the key!</u>**
  - **Prolongation of survival; however, increased response rates do not necessarily correlate with improvement in survival**

Metastatic Breast Cancer

- **A Word On Therapy Selection**
  - **"Pace" of disease**
  - **Location**
  - **Targeted approach still applies**
  - **Performance status**
  - **Clinical trials!**



Conclusions

- **There are about 230,000 new cases of breast cancer in the United States each years (about 40,000 new cases of metastatic breast cancer)**
- **Treatment of breast cancer is complex and depends on multiple factors and patient preference**
- **New approaches to breast cancer treatment that take advantage of breast cancer biology ("targeted" approaches) are being developed with increased frequency**
- **Survivorship programming is essential**