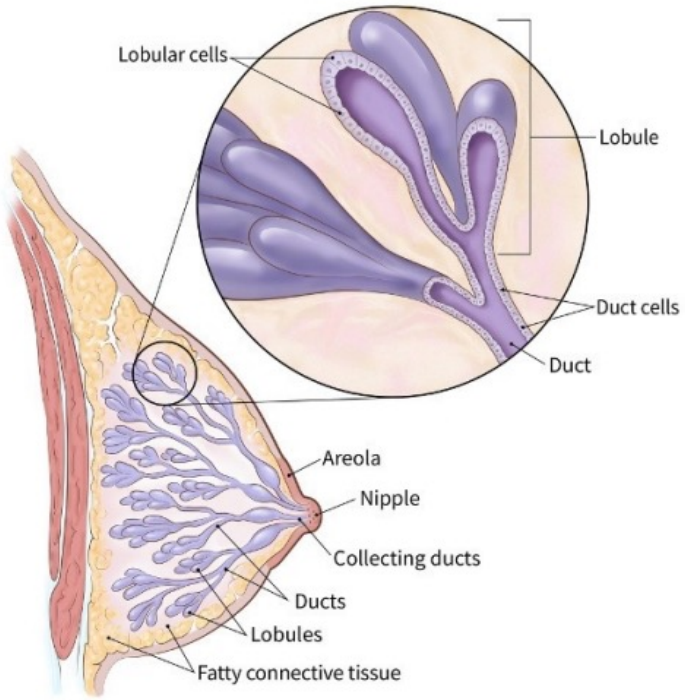
# HR+ Breast Cancer Introductory Lecture

# Breast Cancer Pathology

# Breast Cancer Pathology

**Breast cancer cells develop into malignant cells from normal breast cells**

Cancer cells come from either breast **lobules (10%)** where milk is made or breast **ducts (70%)** where milk is channeled




American Cancer Society

**Lobular Carcinoma**

**Ductal Carcinoma**

# Breast Cancer Pathology

## Breast cancer cells develop into malignant cells along a spectrum

**Atypical Ductal/Lobular Hyperplasia (ADH/ALH)**

Abnormal High-Risk Cells
Portend higher risk of future cancer

**Ductal/Lobular Carcinoma in Situ (DCIS/LCIS)**

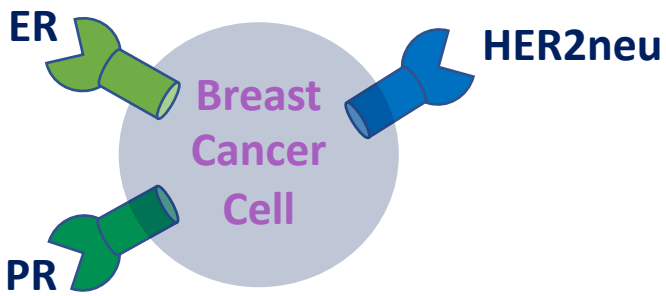
Pre-Cancerous Cells (Stage 0)
"in situ" = stuck "in place"
Does not have the ability to invade outside the breast

**Invasive Ductal/Lobular Carcinoma (IDC/ILC)**

Invasive Cancer (Stage I-III)
Has the potential to invade outside the breast

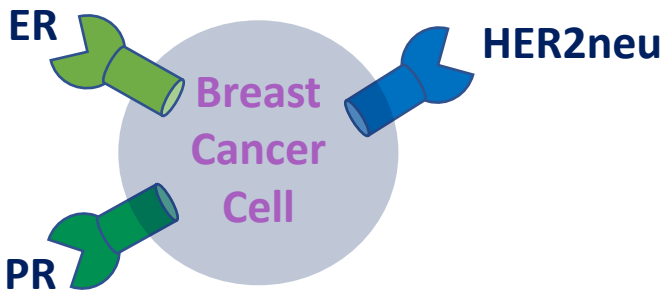
# Breast Cancer Receptors

**Hormone receptors (estrogen and progesterone) & HER2 receptors**
= expressed on <u>some</u> breast cancer cells




| Types of Breast Cancer | |
|---|---|
| HR+/HER2- | HR Positive |
| HR-/HER2+<br>HR+/HER2+ | HER2 Positive<br>Triple Positive |
| HR-/HER2- | Triple Negative |

# Breast Cancer Subtypes




| Types of Breast Cancer | | Incidence |
|---|---|---|
| HR+/HER2- | HR positive | 70% |
| HR-/HER2+<br>HR+/HER2+ | HER2 positive<br>Triple Positive | 20% |
| HR-/HER2- | Triple negative | 10% |

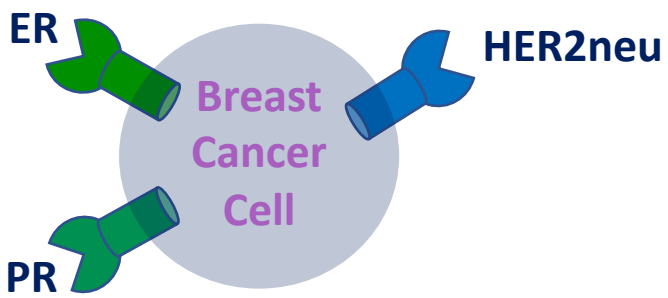
**Positivity determined by tests of biopsy sample:**

**IHC =** immunohistochemistry
**FISH =** fluorescence in situ hybridization

**Receptors always written in order:**

**ER → PR → HER2**
ER+/PR+/HER2- or +/+/-

# Breast Cancer Receptors




## Definition of HR+ (ER+ or PR+)

**Hormone Receptor positive = HR+**

**Estrogen Receptor (ER)**
**Progesterone Receptor (PR)**

**HR "Low"**
1-10% ER or PR = HR "low" but still positive
> 10% ER or PR = positive

**either ER or PR > 1% = HR+**

## Definition of HER2+

HER2+ IHC is graded 1+ to 3+ (1+ = weak; 3+ = strong)

**HER2 IHC 1+ = negative**
**HER2 IHC 2+ = equivocal, requires confirmatory FISH**
**HER2 IHC 3+ = positive**

FISH Tests: HER2/CEP17 and HER2 CN

**HER2/CEP17 > 2 = Positive**
HER2/CEP17 = HER2 gene/chromosome 17 centromere expression

**HER2 CN > 6 = Positive**
HER2 CN = HER2 copy number

# Breast Cancer Staging & Prognosis

## Staging

Receptors:
Staging includes HR and HER2 receptor status, grade, as well as TNM

Notable T Sizes:
T1a: < 0.5 cm
T1b: 0.5 – 1 cm
T1c: 1-2 cm
T2: 2-5 cm
T3: > 5 cm
T4: chest wall or skin

Notable lymph Nodes:
N1 = 1-3 axillary LN
N2 = 4-9 axillary LN or Internal mammary LN
N3 = 10+ axillary LN or supraclavicular LN

M1 = mediastinal or cervical LN

**Prognosis varies significantly based on: staging (early vs late) and receptor status**

## Early Stage Breast Cancer:

Stage I-III BC 5Y OS around 80-95%

| | |
|---|---|
| HR+ | 5Y OS 95% |
| HER2+ | 5Y OS 85% |
| TNBC | 5Y OS 75% |

## Metastatic Breast Cancer:

| | |
|---|---|
| Stage IV HR+ | 5Y OS around 30% |
| Stage IV HER2+ | 5Y OS around 20% |
| Stage IV TNBC | 5Y OS around 10% |

| | |
|---|---|
| Stage IV HR+ | median OS 57 months |
| Stage IV HR- | median OS 31 months |

# HR+ Breast Cancer Early Stage Treatment

# Early HR+ Breast Cancer Treatment Paradigm

## Local Control

Goal = remove cancer locally

Surgery

+/- Radiation Therapy

## Systemic Therapy

Goal = reduce risk of local & distant recurrence

(1) Destroy any microscopic cells not removed in local resection
(2) Modify hormonal environment to reduce risk of recurrence

+/- Chemotherapy

\+ Endocrine Therapy

# HR+ Receptor Based Therapy

Chemotherapy

+

Endocrine Therapy

**Low Risk HR+ early-stage breast cancers do NOT require chemotherapy and can be treated with endocrine therapy ALONE.**

**This is largely determined by a genetic recurrence score test called oncotype.**

# HR+ Early Breast Cancer Treatment Overview

## Small

T1-T2, N0-N1

Surgery →

Low Oncotype →

**ET: SERM (Tamoxifen)$^{PRE-MEN}$ or AI (Anastrozole)$^{POST-MEN}$**
For 5-10Y

**RT: Radiation Therapy**

High Oncotype →

**TC**
(T) Docetaxel
(C) Cyclophosphamide →

**ET** (for 5-10Y)
**RT**

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## Large or Unresectable

T3-T4, N1-N3

**ddACT:** AC → T Q2W
(A) Anthracycline
(C) Cyclophosphamide
(T) Paclitaxel →

Surgery →

**ET** (for 5-10Y)
**RT**

# Adjuvant vs. Neoadjuvant Therapy

## SURGICAL INDICATIONS FOR NEOADJUVANT TX

### (1) Down-Sizing of Surgery

ex: can allow for lumpectomy instead of mastectomy or spare an axillary LN dissection

### (2) Rendering Inoperable Tumors Operable

ex: Inflammatory breast cancer (T4)

# Genetic Recurrence Scores

**Oncotype**

**Oncotype is a <u>Genetic Recurrence Score</u>**
21 gene panel sent on surgical specimen: **T1b-T2N1, (tumors up to 5 cm, up to 3+ LN)** used in HR+ EBC to determine if you can use ET alone in place of Chemo + ET

| Menopausal Status | Node Negative | Node Positive (N1 = 1-3+ LN) |
|---|---|---|
| Post-Menopausal | ≤ 25: ET | ≤ 25: ET |
| | ≥ 26: Chemo + ET | ≥ 26: Chemo + ET |
| Pre-Menopausal | < 16: ET | ≤ 25: Chemo + ET |
| | 16-25: Chemo + ET<br>* Can consider AI/OFS | |
| | ≥ 26: Chemo + ET | ≥ 26: Chemo + ET |

** pre-menopausal women with intermediate oncotypes: some evidence that benefit of chemotherapy is due to chemo induced ovarian suppression rather than direct chemo cytotoxicity, thus chemo can be replaced with AI/OFS*

# Menopause & OFS

## Definition of Menopause

1. **Age > 60**

2. **Age < 60 and amenorrhea x 1 year**
   **in the absence of chemotherapy or tamoxifen**

3. **BSO**

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## Ovarian Functional Suppression (OFS): for pre-menopausal women

**GNRH agonists:** Lupron IM or Goserelin SQ (Q1 or rarely Q3 month)

can be given to strengthen anti-estrogen effect in high-risk HR+ EBC

# Low Risk HR+ EBC Treatment

## Low Risk HR+ Breast Cancer: ET alone

1. T1a
2. Low risk histology: mucinous, tubular
3. Post-menopausal T1b-T2, N0-N1: oncotype ≤ 25
4. Pre-menopausal T1b-T2, N0: oncotype < 16-25

| Post-Menopausal | Pre-Menopausal |
|---|---|
| AI > Tamoxifen | Tamoxifen or AI/OFS |

### Treatment Timeline

1. Surgery

2. +/- Radiation

3. Endocrine Therapy

# High Risk HR+ EBC Treatment

## High Risk HR+ Breast Cancer: Chemo + ET

1. T3+, N2+
2. High risk histology: metaplastic, micropapillary
3. Post-menopausal T1b-T2, N0-N1: oncotype ≥ 26
4. Pre-menopausal T1b-T2, N0: oncotype > 16-25
5. Pre-menopausal N1+: regardless of oncotype

| Node Negative Chemo | Node Positive Chemo |
|---|---|
| **TC (TC, Q3 week)**<br>(T) Docetaxel<br>(C) Cyclophosphamide | **ddACT (AC → T, Q2 week)**<br>(A) Doxorubicin<br>(C) Cyclophosphamide<br>(T) Taxol |

***Neoadjuvant chemotherapy***

- *Give if unresectable tumor*
- *Controversial for downstaging tumors as HR+ BCs respond less robustly to chemo*

**Treatment Timeline**

**1. Surgery**

**2. Chemotherapy**

**3. +/- Radiation**

**4. Endocrine Therapy**

** Consider AI/OFS in pre-menopausal women*

** Consider 2 years adjuvant abemaciclib (CDK4/6 Inhibitor) after chemo if high-risk (N2 or N1 with T3, G3 or Ki67 >20%)*

# Endocrine Therapy (ET)

## Hormone Therapy: 5-10 years adjuvant

**Selective Estrogen Receptor Modulator**
SERM = PRE-MENOPAUSAL drug
*inhibits estrogen receptor*

**tamoxifen**

* SERMs can be used for post-menopausal women

**Aromatase Inhibitors**
AI = POST-MENOPAUSAL drug
*Inhibits peripheral conversion of androgens to estrogen*

**anastrozole (Arimidex)**
**letrozole (Femara)**
**exemestane (Aromasin)**

* AIs can NOT be used for pre-menopausal women unless given with OFS

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**Important Side Effects:**

**SERM → DVT (1-2%), endometrial cancer (1%)**
hot flashes, night sweats, vaginal dryness,
mood/weight changes, cataracts

**AI → arthritis, osteoporosis, cholesterol changes**
hot flashes, night sweats, vaginal dryness,
mood/weight changes, cataracts

# Early Breast Cancer Front Line Therapies Overview

## HR+ Breast Cancer:

**Adjuvant Therapy**
**Low Oncotype (≤ 25):** ET +/- OFS
**High Oncotype (≥ 26):** TC (N-) or ACT (N+) + ET

## HER2+ Breast Cancer:

**Neoadjuvant Therapy:** TC-HP
**Adjuvant Therapy RD:** TDM1
**Adjuvant Therapy PCR:** HP

## HR+/HER2+: Triple Positive Breast Cancer

**Neoadjuvant Therapy:** TC-HP
**Adjuvant Therapy RD:** TDM1 + ET
**Adjuvant Therapy PCR:** HP + ET

## HR-/HER2-: Triple Negative Breast Cancer

**Neoadjuvant Therapy:** ACT or AC-TC + Pembrolizumab
**Adjuvant Therapy RD:** Capecitabine + Pembrolizumab
**Adjuvant Therapy PCR:** Observation + Pembrolizumab

# HR+ Breast Cancer Metastatic Treatment

# MBC: Targetable Mutations

## ADDITIONAL STUDIES:

**NGS: Look for actionable mutations** (targeted agents used 2nd line)

Tumor Testing

Liquid Testing (ctDNA = circulating tumor DNA)

**IHC: Stain for PDL1, androgen receptor**

**ESR1** → Resistance to AIs (use SERDs) in HR+ MBC

**PIK3CA** → Responds to PI3K inhibitors (ex: alpelisib)

**BRCA** → Responds to PARP inhibitors (ex: olaparib, talazoparib)

# HR+ Front Line MBC Treatment

**AI SENSITIVE**
De Novo

**AI INSENSITIVE**
Recurrent


Genetic Testing: ESR1, PIK3CA, BRCA


| | | |
|---|---|---|
| **1st** | **Aromatase Inhibitor +<br>CDK4/6 Inhibitor (abemaciclib, ribociclib, palbociclib)** | **Fulvestrant (or Exemestane) +<br>CDK4/6 Inhibitor (abemaciclib, ribociclib, palbociclib)** |

* Evolving data on whether Palbociclib is as effective as the other CDK4/6 inhibitors

# HR+ Second Line MBC Treatment

**ET SENSITIVE**
Delayed POD on ET

**ET INSENSITIVE**
Rapid POD on ET

 Genetic Testing: ESR1, PIK3CA, BRCA 

| | | |
|---|---|---|
| **2nd** | 1. **Elacestrant** Monotherapy<br>2. **Fulvestrant** Monotherapy<br>3. **Fulvestrant** Combination<br><br>**+ Alpelisib** (PIK3CA inhibitor: if +PIK3CA Δ)<br>**+ CDK4/6** (Abemaciclib, Ribociclib)<br>**+ Everolimus** (mTOR inhibitor)<br>**+ Capivasertib** (AKT inhibitor) *not FDA approved | **BRCA WT: Single Agent Chemotherapy**<br>ex: capecitabine<br><br>**gBRCA: PARP**<br>Olaparib, Talozaparib<br><br>* Consider in sBRCA, PALPB |

# HR+ Third Line MBC Treatment

| | HER2 NEGATIVE | HER2 LOW (1+ or 2+, FISH Negative) |
|---|---|---|
| 3rd | 1. **Sacituzumab**<br>* approved after 2 prior chemotherapy agents | 1. **Sacituzumab**<br>* approved after 2 prior chemotherapy agents |
| | **2. Single Agent Chemotherapy**<br>* rarely double agent, often taxane or anthracycline | **2. TDxd (*Enhertu*)** |
| | | **3. Single Agent Chemotherapy** |

# HR+ MBC Chemotherapy

## Choose based on Efficacy and Toxicity

**Efficacy:**
typically highest RRs
pending prior usage

**Taxanes:**
paclitaxel (Taxol)
docetaxel (Taxotere)
nab-paclitaxel (Abraxane)

**Anthracyclines:**
doxorubicin (Adriamycin)
liposomal doxorubicin (Doxil) slower RR

| Common Agents | Toxicities | Benefits |
|---|---|---|
| **Anthracycline** | Cardiotoxicity, Capped lifetime dose | Q3W<br>Doxil Alopecia sparing |
| **Taxanes** | Neuropathy | Weekly or Q3W |
| **Capecitabine** | Mucositis, GI, PPE | Oral<br>Alopecia sparing |
| **Gemcitabine +/- Carbo** | | Q3W<br>Alopecia sparing<br>Consider doublet for large burden of disease |
| **Eribulin** | Neuropathy | Weekly |

## Toxicity Considerations:

**Alopecia Sparing**
Gemcitabine (Gemzar)
Capecitabine (Xeloda)
Liposomal doxorubicin (Doxil)

**PO**
Capecitabine (Xeloda)

**Q3 Week Dosing**
Docetaxel (Taxotere)
Paclitaxel (Taxol)
Liposomal doxorubicin (Doxil)
Gemcitabine

# HR+ MBC Treatment Overview

| Tx Line | Regimen |  Genetic Testing: ESR1, PIK3CA, BRCA, etc  |
|---|---|---|
| 1st | AI Sensitive: | AI + CDK4/6 Inhibitor (ribociclib, abemaciclib, palbociclib) |
| | AI Insensitive: | Fulvestrant + CDK4/6 Inhibitor |
| 2nd | ET Sensitive: | 1. Elacestrant<br>2. Fulvestrant Monotherapy<br>3. Fulvestrant Combination<br>+ Aleplisib$^{+PIK3CA}$, CDK4/6, Everolimus, Capivasertib$^{not\ FDA}$ |
| | ET Insensitive: | BRCA WT = **Single agent chemo** (ex: capecitabine/*Xeloda*)<br>BRCA Δ = **PARP inhibitor** (olaparib, talazoparib) |
| 3rd | HER2 Low = | 1. **Single agent chemo** (ex: anthracycline, taxane)<br>2. **Sacituzumab** after 2 chemos<br>3. **TDxd (*Enhertu*)** |
| | HER2 Neg = | 1. **Single agent chemo**<br>2. **Sacituzumab** after 2 chemos |

# Metastatic Breast Cancer: Front Line Therapy Overview

## HR+ Breast Cancer:

**Hormone Therapy:** SERM or AI

*with*

**CDK4/6 Inhibitor:** palbociclib, ribociclib, abemaciclib

## HER2+ Breast Cancer:

**HER2+ Therapy:** trastuzumab + pertuzumab

*with*

**Chemotherapy:** docetaxel

## HR+/HER2+: Triple Positive Breast Cancer

**HER2+ Therapy:** trastuzumab + pertuzumab

*with*

**Chemotherapy:** docetaxel
** or with hormone therapy: SERM or AI*

## HR-/HER2-: Triple Negative Breast Cancer

**CPS+ (>10%):** pembrolizumab + chemotherapy

*or*

**Chemotherapy:** single-agent chemotherapy

# Breast Cancer Reference Handout

# Breast Cancer Dx

**Atypical Ductal/Lobular Hyperplasia (ADH/ALH)**

Abnormal "high-risk" lesions
+/- Surgery
+/- ET (not stained for HR)

**Ductal/Lobular Carcinoma in Situ (DCIS/LCIS)**

Non-invasive cancerous lesions
Stage 0, "Pre-Cancer"
Surgery
+- ET if HR+

**Invasive Ductal/Lobular Carcinoma (IDC/ILC)**

Invasive cancerous lesions
Stage I-III
Surgical resection +/- RT
Receptor-based neoadjuvant or adjuvant therapy

**Definition of HR+**

ER or PR > 1%
(1-10% = low)

**Definition of HER2+**

IHC: HER2 2+ AND +FISH
HER2 3+

| Types of Breast Cancer | Incidence |
|---|---|
| HR+/HER2- | 70% |
| HR-/HER2+<br>HR+/HER2+ | 20% |
| HR-/HER2- | 10% |

# Local vs Systemic Tx

**Local Control:**
Lumpectomy + RT or Mastectomy +/- RT

**Receptor-Based Systemic Therapy:**
Chemotherapy, Antibody Therapy, Endocrine Therapy

# Receptor Based Tx

**Chemo/Immunotherapy**

| HR+ Chemo | HER2+ Chemo | TNBC Chemo |
|---|---|---|
| ddACT | ACT-HP | ddACT |
| TC | TC-HP | TC-AC-Pembro "Keynote 522" |
| CMF | TH | |

* All EBC requires chemo EXCEPT low-risk HR+

**HR+** — **Endocrine Therapy [5-10 years]**
Pre-menopausal = SERM (tamoxifen)
Post-menopausal = AI (anastrozole, letrozole, exemestane)

**HER2+** — **HER2+ Antibody Therapy [1 year]**
Trastuzumab (Herceptin) +/- Pertuzumab (Perjeta)

**Important Side Effects:**

**Adriamycin** → cardiotoxicity
**Paclitaxel** → neuropathy
**Trastuzumab** → cardiotoxicity
**A, C, T, M, F** → myelosuppression, hair loss, neuropathy, infertility
**SERM** → DVT, endometrial cancer, hot flashes/sweats, vaginal dryness
**AI** → hot flashes/sweats, vaginal dryness, arthritis, osteoporosis

# Early Stage Breast Cancer Tx

**Common Front Line Approach**
for tumors >T1a

**HR+ BC:**

**Adjuvant Therapy**
**Low Risk Oncotype (≤ 25):** ET +/- OFS
**High Risk Oncotype (≥ 26):** TC (N-) or ACT (N+) + ET

**HER2+ BC:**

**Neoadjuvant Therapy:** TC-HP
**Adjuvant Therapy RD:** TDM1
**Adjuvant Therapy PCR:** HP (dual antibodies)
* Adjuvant TH if <2 cm, N-

**HR+/HER2+ BC: Triple Positive**

**Neoadjuvant Therapy:** TC-HP
**Adjuvant Therapy RD:** TDM1 + ET
**Adjuvant Therapy PCR:** HP (dual antibodies) + ET

**HR-/HER2- BC: Triple Negative**

**Neoadjuvant Therapy:** ACT or ACTC + Pembro
**Adjuvant Therapy RD:** Capecitabine + Pembro
**Adjuvant Therapy PCR:** Observation + Pembro
* Adjuvant ddACT if <2 cm, N-

# HR+ Early Breast Cancer Risk

**Oncotype**
21 gene recurrence score sent on tumor to determine need for chemotherapy

**When to send Oncotype:**
- T1b-T2, N0-N1

**When not to send Oncotype:**
- Too small (T1a < 5mm)
- Too large (T3 > 5 cm, N2 ≥ 4 LN)
- Good prognosis histology (mucinous, tubular)

## Oncotype

| Menopausal Status | Node Negative | Node Positive (N1 = 1-3+ LN) |
|---|---|---|
| POST | ≤ 25: ET | ≤ 25: ET |
| | ≥ 26: Chemo + ET | ≥ 26: Chemo + ET |
| PRE | < 16: ET | ≤ 25: Chemo + ET |
| | 16-25: Chemo + ET<br>* Can consider AI/OFS | |
| | ≥ 26: Chemo + ET | ≥ 26: Chemo + ET |

**Menopause Definition**
1. Age >60
2. Age <60 and no menses >1Y OFF ET
3. BSO

## ET

**For 5-10Y**

**Pre-Menopausal**
1. Tamoxifen (SERM)

**Post-Menopausal**
1. Aromatase Inhibitors (AI)
 --> anastrozole, letrozole, exemestane
2. Tamoxifen (SERM)

**Important Side Effects:**

**AI + SERM** → hot flashes/sweats, vaginal dryness, mood/weight changes
**SERM** → 1% DVT, 1% endometrial cancer
**AI** → 10-30% arthritis, osteoporosis

## Chemo

| Node Negative Chemo | Node Positive or High Risk Chemo |
|---|---|
| **TC (TC, Q3 week)**<br>(T) Docetaxel<br>(C) Cyclophosphamide | **ddACT (AC → T, Q2 week)**<br>(A) Doxorubicin<br>(C) Cyclophosphamide<br>(T) Taxol |

**Rarely consider neoadjuvant chemotherapy**
- Give if unresectable tumor
- Controversial for downstaging tumors as HR+ BCs respond less robustly to chemo

## Additional Tx

**1. Extended ET**
7-10Y ET

**2. CDK4/6**
2Y Abemaciclib if N2 or N1 + (T3, G3 or Ki67 >20%)

**3. OFS**
If premenopausal + high risk (young, N+, required chemo)

**4. PARP**
If BRCA+ and RD

## HR+ Early Breast Cancer Tx

**Small**
T1-T2, N0-N1

Surgery →

**Low Oncotype** →
**ET: SERM (Tamoxifen)$^{PRE-MEN}$ or AI (Anastrozole)$^{POST-MEN}$**
(5-10Y)
**+/- RT: Radiation Therapy**

**High Oncotype** →
**TC**
(T) Docetaxel
(C) Cyclophosphamide
→ **ET** (5-10Y)
**+/- RT**

**Large or Unresectable**
T3-T4, N2-N3

**ddACT:** AC → T Q2W
(A) Anthracycline
(C) Cyclophosphamide
(T) Paclitaxel
→ Surgery →
**ET** (5-10Y)
**RT**

## HER2+ Early Breast Cancer Tx

**Small**
T1N0

Surgery →
**T-H**
(T) Docetaxel
(H) Herceptin
→
**H** (1Y HER2AB)
**+/- ET** (5-10Y)
**+/- RT**

**Large**
T2 or N+, consider T1c

**TC-HP**
(T) Docetaxel
(C) Carboplatin
(H) Herceptin
(P) Perjeta
→ Surgery →

PCR → **HP +/- ET**
To complete 1Y HER2 AB
For 5-10Y
**+/-RT**

RD → **TDM1 +/- ET**
To complete 1Y HER2 AB
For 5-10Y

## TN Early Breast Cancer Tx

**Small**
T1N0

Surgery →
**ddACT**
(A) Doxorubicin
(C) Cyclophosphamide
(T) Taxol
→ **+/-RT**

**Large**
T2 or N+, consider T1c

**TC-AC-Pembrolizumab**
(T) Taxol
(C) Carboplatin
(A) Doxorubicin
(C) Cyclophosphamide
(P) Pembrolizumab
→ Surgery →

PCR → **Pembrolizumab**
**+/-RT**

RD → **Capecitabine + Pembrolizumab**
* if RD and gBRCA+ consider Olaparib in place of cape

# Metastatic Breast Cancer Tx

## Front Line Therapy

### HR+ Breast Cancer:

**Hormone Therapy:** Tamoxifen or AI
*WITH*
**CDK4/6 Inhibitor:** Palbociclib, Ribociclib, Abemaciclib

### HER2+ Breast Cancer:

**HER2+ Therapy:** Trastuzumab +/- Pertuzumab
*WITH*
**Chemotherapy:** Docetaxel

### HR+/HER2+: Triple Positive Breast Cancer

**HER2+ Therapy:** Trastuzumab +/- Pertuzumab
*WITH*
**Chemotherapy:** Docetaxel

### HR-/HER2-: Triple Negative Breast Cancer

**CPS+ (>10%):** Pembrolizumab + chemotherapy
*OR*
**PDL1-:** Chemotherapy: anthracyclines, taxanes, anti-metabolites, anti-tubulins, platins, etc

# Metastatic Breast Cancer Tx

## Additional Lines of Therapy: No SOC 2nd line therapy

| Tx Line | HR+ Breast Cancer |
|---|---|
| 1st | AI + CDK4/6 Inhibitor (palbociclib, ribociclib, abemaciclib) |
| 2nd – 3rd<br>ET Sensitive | PIK3CA - = Elacestrant or Fulvestrant +/- Everolimus or CDK4/6<br>PIK3CA + = Fulvestrant + Alpelisib |
| 2nd – 3rd<br>ET insensitive | BRCA - = single agent chemo or Enhertu (HER2 low)<br>BRCA + = PARP inhibitor (olaparib, talazoparib) |

| Tx Line | HER2+ Breast Cancer |
|---|---|
| 1st | Taxane + Trastuzumab + Pertuzumab |
| 2nd | Trastuzumab Deruxtecan = TDXd (*Enhertu*) |
| 3rd -4th | Trastuzumab Emtansine = TDM1 (*Kadcyla*) |
| 3rd- 4th | Tucatinib + Trastuzumab + Capecitabine<br>* consider 2nd line if brain mets |

| Tx Line | Triple Negative Breast Cancer |
|---|---|
| 1st | PDL1 >10% = pembrolizumab + chemo<br>PDL1 <10% = single agent chemo |
| 2nd – 3rd | BRCA + = PARP inhibitor<br>BRCA - = single agent chemo |
| 2nd – 3rd | Sacituzumab<br>* approved after 2 lines of systemic therapy, at least 1 for MBC |