

# Breast Cancer Reference Handout

## Breast Cancer Dx

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

#### Abnormal "high-risk" lesions

+/- Surgery (to evaluate up-staging)  
+/- ET (for prevention, not typically stained for HR)

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

#### High-risk lesion (LCIS)

#### Non-invasive cancer, Stage 0, "Pre-Cancer" (DCIS)

Surgery (to evaluate up-staging, treatment for DCIS)  
+/- ET if HR+ (for prevention)

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

#### Invasive cancerous lesions

#### Stage I-IV

Surgical resection +/- RT if stage I-III  
Receptor-based neoadjuvant or adjuvant therapy (I-III)

### Definition of HR+

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

### Definition of HER2+

- HER2 2+ IHC  
AND + FISH  
Ratio >2, CN >4-6
- HER2 3+ IHC

Types of Breast Cancer	Incidence
HR+/HER2-	70%
HR-/HER2+ 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 Regimens

#### HR+ Chemo

ddACT  
TC

#### HER2+ Chemo

TC-HP  
TH

#### TNBC Chemo

ddACT  
TC-AC-Pembro "Keynote 522"

\* 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, Docetaxel → neuropathy, transaminitis  
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

### Simplified Front-Line Approach for tumors >T1a

### HR+ BC:

#### Adjuvant Therapy

**Low Risk Oncotype ( $\leq 25$ ):** ET (+/- OFS if Pre-men)  
**High Risk Oncotype ( $\geq 26$ ):** TC (N-) or ACT (N+) + ET  
\* Pre-men oncotypes more complex  
\* If T3-T4 or N2-N3 = chemo (often ACT)

### HER2+ BC:

**Neoadjuvant Therapy:** TC-HP if T2 or N+

**Adjuvant Therapy RD:** TDM1

**Adjuvant Therapy PCR:** HP (dual antibodies)

\* Adjuvant TH if <2 cm, N0

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

**Neoadjuvant Therapy:** TC-HP if T2 or N+

**Adjuvant Therapy RD:** TDM1 + ET

**Adjuvant Therapy PCR:** HP (dual antibodies) + ET

\* Adjuvant TH if <2 cm, N0

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

**Neoadjuvant Therapy:** ACTC + Pembro if T2 or N+

**Adjuvant Therapy RD:** Capecitabine + Pembro

**Adjuvant Therapy PCR:** Observation + Pembro

\* Neo/Adjuvant ddACT if <2 cm, N0 (no IO)

## HR+ Early Breast Cancer Risk

### Oncotype

21 gene recurrence score sent on tumor to determine risk of recurrence and need for chemotherapy

#### When to send Oncotype:

- T1b-T3, N0-N1

#### When not to send Oncotype:

- Too small (T1a < 5mm)
- Too large (consider in 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 * Consider AI/OFS in place of chemo	
	≥ 26: Chemo + ET	
	≥ 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)** preferred  
anastrozole, letrozole, exemestane
2. **Tamoxifen (SERM)**

#### Important Side Effects:

**AI + SERM** → hot flashes/sweats, vaginal secretion changes, mood/weight changes

**SERM** → 1% DVT, 1% endometrial cancer, teratogenic

**AI** → 10-30% arthritis, osteoporosis

## Chemo

Node Negative or N1 Chemo	N2+ or High Risk N1 Chemo
<b>TC (TC, Q3 week)</b> (T) Docetaxel (C) Cyclophosphamide	<b>ddACT (AC Q2W → T)</b> (A) Doxorubicin (C) Cyclophosphamide (T) Taxol

#### Uncommonly consider neoadjuvant chemotherapy

- Give if unresectable tumor
- Controversial for downstaging tumors as HR+ BCs respond less robustly to chemo (consider if high oncotype)

## Additional Tx

1. **Extended ET**  
7-10Y ET (high risk, ex: stage II-III)
2. **CDK4/6**  
2Y Abemaciclib if N2 or N1 + (T3 or G3)
3. **OFS**  
If premenopausal + high risk (young, N+, high grade, got chemo)
4. **PARP**  
If BRCA+ and high risk

## HR+ Early Breast Cancer Tx

Small  
T1-T2, N0-N1

Surgery →

Low  
Oncotype →

High  
Oncotype →

ET: SERM (Tamoxifen)<sup>PRE-MEN</sup> or AI (Anastrozole)<sup>POST-MEN</sup>  
(5-10Y)

+/- RT: Radiation Therapy

TC [ACT if high risk]

(T) Docetaxel  
(C) Cyclophosphamide

→ ET (5-10Y)  
+/- RT

Large or Unresectable  
T3-T4, N2-N3

ddACT: AC Q2W → T

(A) Anthracycline  
(C) Cyclophosphamide  
(T) Paclitaxel

→ Surgery →

Surgery →

ET (5-10Y)  
RT

## HER2+ Early Breast Cancer Tx

Small  
T1N0

Surgery →

T-H  
(T) Paclitaxel  
(H) Herceptin

→

+/- RT  
H (1Y HER2AB)  
+/- ET (5-10Y)

Large

T2 or N+ (consider neo TCH+/- P in T1cN0)

TC-HP

(T) Docetaxel  
(C) Carboplatin  
(H) Herceptin  
(P) Perjeta

→

Surgery →

→

PCR

+/-RT

HP to complete 1Y HER2 AB  
+/- ET For 5-10Y

→

RD

TDM1 to complete 1Y HER2 AB  
+/- ET for 5-10Y

## TN Early Breast Cancer Tx

Small  
T1N0

Surgery →

ddACT  
(A) Doxorubicin  
(C) Cyclophosphamide  
(T) Taxol

→

+/-RT

Large

T2 or N+ (consider neo ddACT in T1cN0)

TC-AC-Pembrolizumab

(T) Taxol  
(C) Carboplatin  
(A) Doxorubicin  
(C) Cyclophosphamide  
(P) Pembrolizumab

→

Surgery →

→

PCR

+/-RT

Pembrolizumab

→

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 or Paclitaxel

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

**HER2+ Therapy:** Trastuzumab +/- Pertuzumab  
*WITH*  
**Chemotherapy:** Docetaxel or Paclitaxel  
 \* Consider ET in place of chemo in select pts

#### 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 2<sup>nd</sup> line onward therapy. Consider clinical trial

Tx Line	HR+ Breast Cancer
1 <sup>st</sup>	1. AI + CDK4/6 Inhibitor (palbociclib, ribociclib, abemaciclib) <sup>AI Sensitive</sup> 2. Fulvestrant + CDK4/6 <sup>AI Resistant</sup>
2 <sup>nd</sup> + ET Sensitive	1. Elacestrant <sup>ESR1 &gt; WT</sup> 2. Fulvestrant +/- Capiivasertib <sup>PIK3CA/AKT/PTEN</sup> Alpelisib <sup>PIK3CA</sup> Everolimus <sup>WT</sup> CKD4/6 <sup>Alter.</sup>
2 <sup>nd</sup> + ET Resistant	BRCA - = Chemo or ADC: TDXd <sup>HER2 Low</sup> , Sacituzumab <sup>2 prior LOT</sup> BRCA + = PARP inhibitor (olaparib, talazoparib)

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

Tx Line	Triple Negative Breast Cancer
1 <sup>st</sup>	PDL1 >10% = pembrolizumab + chemo PDL1 <10% = single agent chemo (ex: anthracycline, taxane)
2 <sup>nd</sup> - 3 <sup>rd</sup>	BRCA + = PARP inhibitor (consider in other HRD)
2 <sup>nd</sup> - 3 <sup>rd</sup>	ADC: TDXd <sup>HER2 Low</sup> , Sacituzumab <sup>2 prior LOT, 1 for MBC</sup> Single agent chemotherapy