Breast Cancer Basics

Clinical Oncology for Public Health Professionals

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Breast Cancer

- Approximately 170,000 new cases diagnosed each year in the U.S.
- Approximately 40,000 deaths each year in the U.S.
- Majority of Breast Cancers are curable IF caught early

Biology of Breast Cancer

- Usually ductal or lobular, though other types exist
- Can express ER(alpha)/PR or not (about 50-70%)
- 25-30% overexpress HER2/neu (EGFR family)
- 25-40% have activating PI3 Kinase mutations
- PTEN and p53 tumor suppressor frequently lost in some subtypes
- Spreads via lymphatics to ipsilateral axillary nodes, then beyond

Epidemiology and Screening

- Disease of women; male breast cancer extremely rare and often associated with familial forms
- Risk factors: early menses, late menopause, age at first pregnancy, nulliparity, ie PROLONGED estrogen exposure
- No apparent increased risk with OCP; ?HRT? Never conclusively demonstrated, but studies suggest increased risk

Epidemiology and Screening

- Mammography: does save lives in postmenopausal women (age >50)
- Controversial in premenopausal women; mammography tends to be less effective in younger women due to dense breast tissue, MRI is currently being evaluated
- No uniform screening recommendations; usually yearly after age 50; ?between ages 40-50? ?"baseline" at 35-40?
- The above refer to average risk women

Other screening modalities

- Breast self examination: never proven to affect disease outcomes
- Clinical breast exam does appear to be helpful
- Ultrasound and MRI in selected circumstances

Epidemiology and Screening

- Family hx: first degree relative, (2.5x higher if two first degree relatives c/w general population)
- Twin studies: 6x higher in monozygotic twins, 2x higher in dizygotic twins
- 50-80% in affected BRCA1/2 carriers of developing breast cancer by age 70
- GREATER THAN 10% of all women in US will develop breast cancer!!

Chemoprevention and Breast Cancer

- NSABP P1 trial: tamoxifen for primary prevention in high risk individuals (strong family hx, h/o DCIS/LCIS) demonstrated an overal 49% risk reduction in developing invasive breast cancer. Raloxifene also appears to reduce risk without increased endometrial cancer risk seen with Tamoxifen, though preinvasive lesions may be increased.

When someone is diagnosed with Breast Cancer, what happens?

- Lesion found via mammography or exam
- Biopsied > invasive ductal ca.
- CXR, LFTs (vs. CT scans), bone scan, head CT if symptomatic (yield of finding met. Disease without symptoms is low)
- Rebiopsied for wider/negative margins with XRT vs. mastectomy (are equivalent)
- Axillary lymph node dissection done at time of surgery. Sentinel LN Bx may replace full dissection.
- Radiation to chest wall and axillary nodes in some cases

Staging

- Best and most important predictor is nodal status; whether any are involved and how many
- Tumor size not as important as nodal status
- ER/PR
- HER2/neu

Adjuvant systemic therapy

- About 100,000 women/yr are candidates for adjuvant systemic therapy
- Chemo has minimal benefit; about 2-3% @ 10 years for women over 50
- Translates into large absolute benefit, ie 2000-3000 lives

Adjuvant systemic therapy

- Who gets adjuvant systemic therapy?
- Patient should be in good health
- Positive nodes
- Tumor > 1cm for invasive ductal or lobular
- Tumor>2-3cm in special subtypes like medullary, tubular, papillary and mucinous

Adjuvant systemic therapy

- Types of adjuvant therapy:
- Hormonal, e.g. Tamoxifen for 5 years for women with ER/PR positive disease; biggest benefit in terms of risk reduction, Aromatase inhibitors for *postmenopausal* women is standard of care now
- Combination chemotherapy: CMF (cytoxan, methotrexate, 5FU, old regimen) or AC (adriamycin/cytoxan), TAC newer regimen
- Taxane for node positive disease
- Herceptin for HER2/neu positive disease

Adjuvant systemic therapy

- Tamoxifen: Any premenopausal woman with ER and/or PR positive disease should be on tamoxifen for 5 years. Longer does not confer additional benefit and increases adverse side effects (increased endometrial ca., clots/PE)
- Invasive cancers less than 1cm are debatable, but probably should be treated given P1 data

Adjuvant systemic therapy

- Aromatase inhibitors block peripheral conversion of androgens to estrogens
- Only indicated in postmenopausal women
- Aromatase inhibitors are new standard of care for ER/PR+ disease in postmenopausal women. How long?

Adjuvant systemic therapy

- Chemotherapy
- The absolute benefit of chemotherapy diminishes with increasing age of the patient, ie the biggest benefit of chemotherapy is in younger women. ?medical oophorectomy?
- Can give both chemotherapy and hormonal Rx if appropriate (or just hormonal Rx)
- Addition of Taxol following AC for node positive disease.
- Taxotere with AC (TAC) also for node positive disease.
- Addition of Herceptin for Her2/neu positive disease has become standard of care, with about 50% risk reduction.
- Future drugs: Lapatinib? Avastin?

Metastatic Disease

- Not Curable
- BMT does NOT work (debatable in high risk, 4-10 LN positive, disease)
- Hormonally responsive disease; can use single agent endocrine therapy, eg tamoxifen, aromatase inhibitor (in postmenopausal), megace, withdrawal therapy, etc.

Metastatic Disease

- Hormonally unresponsive disease: single agent vs. combined chemo regimens.
- Better response rates with combined regimens, but does NOT translate into survival benefits
  - e.g. Avastin/Taxol
- Choice must be individualized
- Herceptin (mAB) for HER2/neu positive disease: watch cardiac toxicity with adriamycin!
- Tykerb (lapatinib) with Xeloda for HER2/neu resistant disease is now FDA approved.

Metastatic Disease

- Others:
- Pamidronate for bony mets
- XRT for palliative treatment
- Iressa (EGFR inhibitor): probably not efficacious
- Anti-angiogenic therapy (Avastin): so far effective only when given in combination for disease progression but not overall survival.

Ongoing clinical questions

- Given the minimum benefit of chemotherapy relative to hormonal therapy, and that most breast cancers are being diagnosed at an early stage, how can we stratify women to predict who benefits from chemotherapy and who does not?

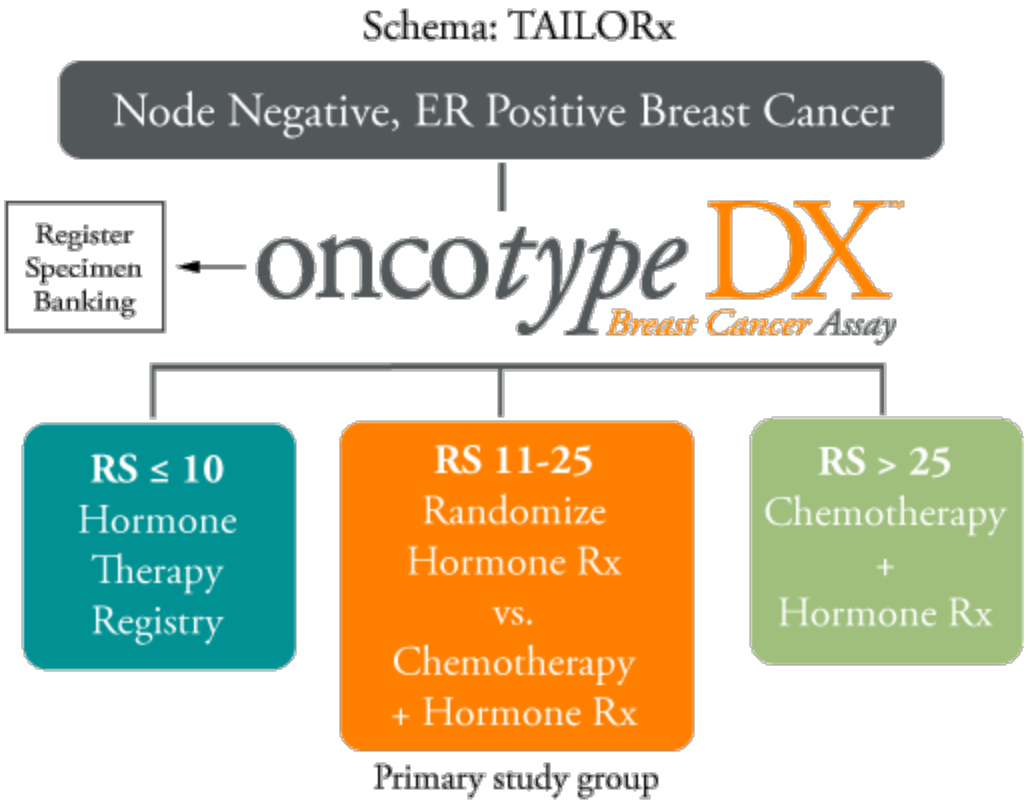
ONCOTYPE DX

- Gene expression assay using quantitative Real Time RT-PCR of 21 genes (16 genes and 5 internal reference genes)
- Has been validated as a prognostic tool, i.e. a high “recurrence” score means a woman is more like to recur vs. intermediate vs. low.
- Only applicable for ER positive disease that is node negative and HER2/neu negative

ONCOTYPE DX

- Prognosis is not the same as predictive
- Retrospective data analysis suggests that Oncotype DX may be predictive.
- Prospective trial, TAILORx is ongoing to address this question.

ONCOTYPE DX


Schema: TAILORx
Node Negative, ER Positive Breast Cancer
Register Specimen Banking
oncotype DX
Breast Cancer Assay
RS ≤ 10
Hormone Therapy Registry
RS 11-25
Randomize Hormone Rx vs. Chemotherapy + Hormone Rx
RS > 25
Chemotherapy + Hormone Rx
Primary study group

Conclusions

- Breast cancer is curable if caught early
- Local regional control is first therapeutic modality for curative intent
- Adjuvant chemo/biologic/hormonal therapy to improve cure rates
- Metastatic disease not curable, but treatable
- Who should get adjuvant therapy and how to predict for response is an ongoing clinical question