Systemic Treatment of Breast Cancer

Hormone Therapy and Chemotherapy, Curative and Palliative
Systemic Therapy

• Invasive breast cancers

• Two forms
  – Curative
  – Palliative
Curative Systemic Therapy

• Adjuvant Therapy
  – Any systemic therapy given AFTER the curative treatment step (surgery)

• Neoadjuvant Therapy
  – Any systemic therapy given BEFORE the curative treatment step
Adjuvant Systemic Therapy--
treatment goal

• Goal
  – To kill “stray” cells, or microscopic metastases
  – Microscopic metastases → divide over time → settle somewhere → recurrence
  – Decrease the chances of recurrence and increase the chances of cure
  – Treatment is CURATIVE
Adjuvant Systemic Therapy -- options

• Adjuvant Hormone Therapy
  – ER+ or PR+ tumors
  – Duration of treatment: 5-10 years

• Adjuvant Chemotherapy
  – Higher risk tumors
    • Large
    • Node positive
    • Triple negative (ER-/PR-/Her2-)
    • Her2 (+)
    • High risk Oncotype Dx recurrence score
  – Duration of treatment: 3-5 months
Adjuvant Systemic Therapy—indications

• Patient selection
  – Stages I, II, and III invasive breast cancers
  – Determined by
    • tumor features
    • tumor biology
    • patient preference
Adjuvant Systemic Therapy--indications

- Medical decision making
  - High risk of recurrence
    - Triple negative (ER-/PR-/Her2-)
    - Her2 (+)
      - Lymph node (+)
  - Treatment can reduce the risk of recurrence
  - Benefit outweighs/balances toxicities
Adjuvant Systemic Therapy--

*risk of recurrence*

- Tumor Risk Factors
  - Size
  - Grade
  - Node status
  - Receptor status
    - ER, PR, Her-2 neu

- Adjuvant Online
  - a computer algorithm that takes information about a specific woman’s cancer and produces survival and recurrence estimates for her based upon whether she receives one set of treatment versus another
Shared Decision Making

Name: __________________________ (Breast Cancer)
Age: 59  General Health: Good

Estrogen Receptor Status: Positive  Histologic Grade: 3
Tumor Size: 2.1 - 3.0 cm  Nodes Involved: 0
Chemotherapy Regimen: CMF-Like (Overview 2000)

Decision: No Additional Therapy
- 70 out of 100 women are alive in 10 years.
- 23 out of 100 women die because of cancer.
- 7 out of 100 women die of other causes.

Decision: Hormonal Therapy
- 7 out of 100 women are alive because of therapy.

Decision: Chemotherapy
- 3 out of 100 women are alive because of therapy.

Decision: Combined Therapy
- 9 out of 100 women are alive because of therapy.
Adjuvant Systemic Therapy--
*risk of recurrence*

- **Oncotype Dx**
  - A multigene diagnostic test that determines the individual risk of cancer recurrence in early-stage invasive breast cancer
  - Identifies patients with minimal, if any, likelihood of benefit of chemotherapy
  - Identifies patients with substantial likelihood of benefit from chemotherapy
  - The Oncotype Dx Recurrence Score reveals the underlying tumor biology to help guide treatment decisions
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<td>Lymph node status</td>
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<td>after 5 years of Tamoxifen</td>
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<td>Prediction of chemotherapy benefit</td>
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Adjuvant Systemic Therapy—options

- Adjuvant Hormone Therapy
  - ER+ or PR+ tumors

- Adjuvant Chemotherapy
  - Higher risk tumors
Adjuvant Hormone Therapy—options

• Menopausal status
  – Pre-menopausal women
    • Tamoxifen
  – Post-menopausal women
    • Tamoxifen
    • Aromatase Inhibitors
      – Arimidex (anastrozole)
      – Femara (letrozole)
      – Aromasin (exemestane)
Adjuvant Hormone Therapy—*tamoxifen*

• A selective estrogen receptor modulator
  – SERMS bind to estrogen receptors throughout the body and act as estrogen agonists or antagonists depending on the target organ
    • Bone → agonist → estrogen binds → strengthens bone
    • ER+ breast cancer cell → antagonist → estrogen does not bind → cuts off crucial fuel supply → kills cell

• Pre- and post-menopausal women
Adjuvant Hormone Therapy—*tamoxifen*

- Side effects
  - Vasomotor hot flashes
  - 2-3% risk of thromboembolism (DVT most common)
  - 1-2% risk of uterine cancer
  - DOES NOT put patients in menopause
Adjuvant Hormone Therapy—*aromatase inhibitors*

• AIs inhibit the enzyme, *aromatase*, which converts pre-estrogens to estrogens → decreases fuel supply for tumor growth
  – Adrenal glands
  – Subcutaneous fat
  – NOT THE OVARIES

• Post-menopausal women only
Adjuvant Hormone Therapy—aromatase inhibitors

• Side effects
  – Vasomotor hot flashes
  – Arthralgias (30% risk)
  – Accelerated osteoporosis
    • Baseline Dexascan and then q2years
    • Calcium and Vit D
Adjuvant Chemotherapy—

options

- Her2 (-)
  - Adriamycin/Cytoxan (AC) followed by Taxol (T)
    - AC q2wks x 4 cycles → T q2wks x 4 cycles
      - 4.5 months
    - AC x 4 cycles → weekly T x 12 weeks
      - 5 months
  - Taxotere/Cytoxan (TC)
    - TC q3wks x 4 cycles
      - 3 months
  - Choice of treatment driven by physician/patient preference
Adjuvant Chemotherapy—options

• Her2 (+)
  – Taxotere/Carboplatin/Herceptin (TCH)
  – Followed by Herceptin maintenance
    • TCH q3wks x 6 cycles → H q3wks to complete a full year
  – AC followed by Taxol (T) /Herceptin (H)
    • AC q2wks x 4 cycles → T q2wks/H q2wks x 4 cycles → H q3wks to complete a full year
  – Taxol (T) + Herceptin (H)
    • Weekly T x12wks + weekly H x 12 weeks → H q3wks to complete a full year
  – Newer agents: pertuzumab (Perjeta)
Adjuvant Systemic Therapy

• Curative intent
• Options
  – Hormone Therapy (duration 5-10 years)
  – Chemotherapy (duration 3-5 months + 1 year of Herceptin when indicated)
  – Both
  – Determined by risk features, tumor biology, patient preference
• Sequence of treatment
  – Surgery → adjuvant chemotherapy → adjuvant radiation → adjuvant hormone therapy
Palliative Systemic Therapy

- 20-30% of patients will develop metastases
  - Liver, lungs, bone, brain
- Less than 10% of newly diagnosed cases will be Stage IV
- Survival has improved
  - MS can exceed 2-3 years
    - Higher in ER+ tumors
    - Lower in triple negative tumors
    - Her2 (+) tumors
      - Significant increase in survival since the advent of Herceptin
      - May do better than Her2 (-) counterparts
Palliative Systemic Therapy—
hormone therapy

• ER+ tumors
  – Indolent
  – Minimal symptoms
  – No visceral involvement

• Options
  – Tamoxifen
  – AIs
  – Faslodex—a selective estrogen receptor downregulator (SERD)
  – AIs or Faslodex + oral targeted agents

• Add Herceptin if also Her2 (+)
Palliative Systemic Therapy—chemotherapy

- Palliative/non-curative
  - live longer and better
- More aggressive tumors
  - Symptomatic
  - Visceral involvement
  - Hormone refractory
- ChemoSENSITIVE
- Many options
  - No specific regimen is superior
  - Choice depends on patient selection, toxicity profile, anticipated tolerance, treatment schedule
  - Her2-directed drugs incorporated when indicated