Neoadjuvant Chemotherapy in the Treatment of Breast Cancer
Overview

- Define
- Why?
- What?
- Where are we going?
Treatment of Early Stage Breast Cancer

- Surgery +/- reconstruction
- Evaluation of axillary lymph nodes
- +/- Chemotherapy
- +/- Anti-hormone therapy
- +/- HER2 targeted therapy
- +/- Radiation
Definitions

❖ Adjuvant:
   » Any treatment that is given AFTER surgery

❖ Neoadjuvant
   » Any treatment that is given BEFORE surgery
     • Chemotherapy
     • HER2 directed therapy
Neoadjuvant Therapy

- SAFE: No difference in recurrence
- ER/PR/HER2 status important
- Not appropriate for all
  - Most aggressive chemotherapy combinations used
    - May be more treatment than what some may need
Goal of (neo)Adjuvant Therapy

- Kill seed cells
- Prevent development of metastatic disease
- Risk of seed cells vs side effect/benefit of therapy
Neoadjuvant Therapy: Goal

- **SHRINK THE CANCER**
  - Enable surgery
    - Inflammatory Breast Cancer
  - Enable a lumpectomy
  - Enable fewer lymph node to be removed

- **Goal is pathologic complete response (pCR)**
  - No cancer at the time of surgery
Why pCR?

- Those with pCR have lower rate of cancer recurrence
- Determine after surgery
- pCR is the endpoint of some clinical trials
Study Plan

- **T0**: ENG BREAST CYCLE
- **T1**: (optional)
- **T1a**: Paclitaxel (control gp.)
  - 12 weekly cycles
- **T2**: Anthracycline (AC)
  - 4 cycles
- **T2a**: Only patients with 4FV < 90%
- **T3**: Surgery
- **TS**: RCB

- **Invest. Agent** A ± Paclitaxel
  - 12 weekly cycles
- **Invest. Agent** B ± Paclitaxel
  - 12 weekly cycles

* Patients who are HER2+ may also receive tustuzumab (Herceptin)
† An investigational combination of one or more agents may be used to replace all or some of the standard therapy

I-SPY | The right drug. The right patient. The right time. Now.

Penn University of Pennsylvania
ISPY-2 Arms

**HER2+**
- Paclitaxel + Trastuzumab + Pertruzumab - THP > AC (Control) - 50%
- Tucatinib + THP > AC - 50%

**HER2-**
- Paclitaxel (Control) > AC - 20%
- Durva/Olaparib + THP > AC
- SGN-LIV1A > AC
- Pembro 8-cycle + Taxol
- SD-101 + Pembro – Taxol > AC - 80%

I-SPY | The right drug. The right patient. The right time. Now.
Inflammatory Breast Cancer
ER/PR/HER2 Negative
What About Those with Non-pCR?

- Depends on the ER/PR/HER2 status
- Recent clinical trials have given us additional options
- CREATE X - ER/PR/HER2 negative
- Katherine - HER2 positive
- Penelope - ER/PR+ HER2 negative
CREATE-X

- Residual cancer after neoadjuvant therapy
- ER/PR+ HER2 negative
- ER/PR/HER2 negative
- 6 months of oral chemotherapy or observation

**** Benefit seen with capecitabine for those with ER/PR/HER2- breast cancer*****
KATHERINE: HER2+

- Residual disease
- Trastuzumab (Herceptin) vs TDM-1 (Kadcyla)

****TDM-1 was better than trastuzumab at preventing recurrent HER2+ breast cancer****
ER/PR+ HER2-

- Lower rates of pCR
- Anti-hormone therapy
- PENELOPE Trial
  - Can we decrease recurrence by adding another medication?
  - Completed
  - Awaiting results
ER/PR+ HER2 Negative

- PENEOPE
  - Anti-hormone therapy OR
  - Anti-hormone therapy with palbociclib for 2 years
Important Note

- Adding these additional therapies can add to side effects
- These other therapies are NOT for everyone
- They add options for consideration
- Risks/benefits should be discussed on a patient by patient basis
Conclusions

- Neoadjuvant therapy is not for everyone
- Help some minimize surgery
- Provides important information about response to therapy
- If response not what we hope, there are different therapies to recommend
  - ER/PR/HER2 status
Future Directions

- Use Neoadjuvant therapy
  - Add more therapy upfront
  - Give more effective therapy after surgery
  - Remove therapy that may not be necessary