Neoadjuvant therapy in breast cancer: The how and why

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Objectives

- To understand indications and appropriate patient characteristics for neoadjuvant therapy
- To understand the significance of response to neoadjuvant therapy
- To understand the general framework of the regimens for neoadjuvant chemotherapy and time needed to complete
Neoadjuvant vs adjuvant

- Most chemotherapy regimens for breast cancer can be given either neoadjuvantly or adjuvantly.

- Long term outcomes for pre vs postop chemo

- So how do we decide who gets neo?
Which of these patients is a candidate?

- 50 y/o female with grade 1, 2.4cm invasive ductal carcinoma, node negative, ER/PR+, her2-
- 45 y/o female with grade 2, 0.8cm invasive ductal carcinoma, axillary bx positive, ER/PR+, her2+
- 60 y/o female with inflammatory breast cancer, ER/PR-, her2+
Indications for neoadjuvant therapy

- **Absolute:**
  - 1. Inflammatory breast cancer
  - 2. Locally advanced (non-inflammatory) T3/T4 tumors; particularly if her2+

- **Relative:**
  - 1. Patients with tumors larger than 2 cm regardless of node status
  - 2. Her2+ tumors (T2 or N1) to allow use of pertuzumab
  - 3. Any N2 or N3 disease especially if hormone negative (her2+/-)
Main reasons for neoadjuvant

- Surgically inoperable
- Buy time until surgery $\rightarrow$ Pregnancy
- Initiate systemic therapy quickly on high risk tumors
Non-candidates

- Those with extensive in situ component without clear extent of invasive disease
- Poorly delineated extent of tumor
- Tumors not clinically palpable or assessable
Pretreatment evaluation

- Confirmation of receptors
- Biopsy of suspicious lymph nodes
  - Clinical trial requirements, SLNB
- PET imaging
- MRI breasts
Pathologic response

- Importance of response”
  - Pathologic complete response
    - Extremely favorable disease free and overall survival
    - Triple neg > her2+ > hormone positive
Her2+

- I-SPY trial:
  - 221 patients with tumors>3 cm received NACT
    - AC + T standard
    - 20 of 66 patients with her2+ received herceptin
  - pCR with NACT alone: 39% her2+, 18% her2-
  - pCR with her2+ pts with addition of herceptin: 60%
  - Improvement in DFS and OS for her2+ with herceptin
Her2+ disease

- Trastuzumab (herceptin): at least 9 weeks
- If T2 or N1 → pertuzumab (perjeta)

- Perjeta: developed to overcome herceptin resistance caused by formation of Her2:Her3 heterodimers

- TCPH x6 (18 weeks)
  - Tryphaena trial
- TCH x6 (18 weeks)
- AC +TH (total of 8+12 weeks)

- ***herceptin 52 weeks
Her2+

- Neosphere Trial:
  - 417 women with her2+ disease randomized to one of four arms
    - Docetaxel/herceptin: pCR 29%
    - Docetaxel/herceptin/perjeta: pCR 46%
    - Perjeta/herceptin: pCR 17%
    - Docetaxel/perjeta: pCR 24%
Her2+

- TRYPHAENA Trial:
  - 223 women
  - FEC → D-HP
  - FEC-HP → D-HP
  - TC-HP

- pCR equivalent
Triple negative

- Many regimens acceptable
  - Most common: AC + T (20 weeks)

- ? Platin

- Most response with chemo
  - pCR: 27-45%
  - Residual disease → higher risk early recurrence
Hormone positive disease

- ER/PR+, her2- disease:
  - Can use hormone therapy alone
  - Length of time
  - Postmenopausal vs premenopausal
  - Response to chemotherapy

- Tamoxifen
- Aromatase inhibitors +/- OFS
Assessing response

- Imaging midway
  - US vs MRI
  - Lumpectomy vs mastectomy

- If no response → surgery
Benefits to neoadjuvant

- Inoperable tumors → operable
- Prognostic information from response to therapy
- Allows time for genetic testing
- Allows time to plan for reconstruction if pursuing mastectomy
- Allows early eval for effectiveness of therapy
Downfall of neoadjuvant

- Oncotype testing
- Length of time of to surgery
In summary:

- Consult medical oncology before deciding on plan!
- Many benefit from neo (especially triple negative and her2+)
- Time to surgery with neo will be roughly 18-20 weeks in duration
Any Questions?