

CALGB Breast Cancer Neoadjuvant Trials:

What are they, why are they important and what can RNs/CRAs and patient advocates do to help to ensure their success?

William M. Sikov, MD

**Alpert Medical School of Brown University
Providence, Rhode Island**

Neoadjuvant Therapy in Breast Cancer

- Standard of care for locally advanced cancers
- In resectable (stage I-III A) patients
 - Increases % of breast-conserving surgery
 - Reduces volume of breast tissue removed
 - Does not diminish recurrence-free survival or overall survival
- Able to assess clinical and pathologic response to treatment (in contrast to adjuvant therapy)

Neoadjuvant Therapy in Breast Cancer

- High grade (HER2+, 'triple-negative') cancers more likely to achieve pathologic CR (T0)
- Pathologic response (and not just path CR) is predictive of risk of distant recurrence, especially in pts with ER- cancers
- Access to tissue and blood pre-, during, and post-treatment and ability to correlate biologic markers with response

Neoadjuvant Therapy in Breast Cancer

Active and pending cooperative group studies

- ACOSOG-Z1031
- CALGB 40601
- CALGB 40603
- SWOG 0800
- NSABP B-40
- ACOSOG-Z1041

ACOSOG Z1031

- PI – M. Ellis
- Target population: postmenopausal, ER+, Stage II-III (T2-4c (T4d excluded), Nany, M0)
- Treatment Plan: Anastrozole 1 mg vs. Letrozole 2.5 mg vs. Exemestane 25 mg PO qD X 16-18 wks, then surgery
- Comparing clinical, radiographic, & pathologic response, surgical & biologic (Ki67<1%) endpoints
- Accrual goal: 375
- Status: Open – accrual to date: 278
- Correlative science: Pretreatment core biopsies in OCT and FFPE + blood required, biopsies after one month on treatment optional, biopsies/blood at surgery required

CALGB 40601

- PIs – L. Carey, L Harris (correlative science)
- Target population: HER+, Stage II-III (T1 N1-2, T2-T4 Nany M0)
- Treatment Plan: Weekly paclitaxel x 16 weeks with trastuzumab or lapatinib or trastuzumab + lapatinib, then surgery
- Primary endpoint is achievement of path CR, but will also compare Residual Cancer Burden (RCB)
- Accrual goal: 400
- Status: Awaiting final CIRB approval, then activation
- Correlative science: Pretreatment core biopsies in RNA later and/or OCT and FFPE + blood samples required; optional core biopsies at time of surgery

CALGB 40603

- PIs – W. Sikov, C. Perou (correlative science)
- Target population: Triple-negative (ER/PR<10%,HER2-), Stage II-IIIa (T1 N1-2, T2-T3 N0-2 M0)
- Treatment Plan: all pts - weekly paclitaxel x 12 followed by dose-dense (q2wk) AC x 4, then surgery
 - Randomized to carboplatin AUC 6 q3wks during paclitaxel and/or bevacizumab q2wks during chemo
- Primary endpoint is achievement of path CR, but will also compare Residual Cancer Burden (RCB)
- Accrual goal: 362
- Status: Pending final CTEP/CIRB approval
- Correlative science: Pretreatment core biopsies in RNA later and/or OCT and FFPE + blood samples required; optional core biopsies at time of surgery

SWOG 0800

- PIs – Z. Nahleh/R. Livingston, D. Hayes (corr science)
- Target population: Locally Advanced (unresectable IIB-IIIa, IIIB - including inflammatory)
- (Tentative) Treatment Plan: Weekly Nab-paclitaxel x 12 ± sunitinib followed by dose-dense AC x 4 vs. dose-dense AC x 4 followed by weekly Nab-paclitaxel x 12
- Primary endpoint is achievement of pathCR
- Accrual goal: 200
- Status: Submitted to CTEP for initial review
- Correlative science: Pretreatment core biopsies, blood samples and q3week blood samples encouraged, week 9 re-biopsies optional

Importance of Research Biopsies, Blood Tests and Tissue/Blood Banking

- Two cancers may look alike but have very different biologic behavior and response to treatment
- Measurement of biologic markers – gene mutations, mRNA, protein levels – often requires fresh tissue
- In neoadjuvant studies, ability to assess correlation between biologic markers and clinical and pathologic response or non-response
- Effectiveness and toxicity of treatment can also be influenced by pt's genetic makeup (pharmacogenomics), obtained from normal tissue, blood samples
- Banking allows new technologies to be tested in previously treated pts for whom outcome is known

CALGB Neoadjuvant Trials: Role of RNs/CRAs

- Assess interest in neoadjuvant therapy at your institution
- Increase awareness of trials (breast surgeons, medical oncologists, pathologists)
- Identify potentially eligible patients (breast tumor boards)
- Assess eligibility
- Assist in obtaining informed consent

CALGB Neoadjuvant Trials: Role of RNs/CRAs

- Encourage MDs and patients to participate in collection of research biopsies and blood samples and tissue/blood banking (if optional)
- Coordinate collection and submission of tissue and blood samples
- Monitor treatment, toxicity, prompt submission of data, AEs, etc.

CALGB Neoadjuvant Trials: Role of Patient Advocates

- Assist MDs, RNs/CRAs in raising awareness of value/safety of neoadjuvant therapy and available studies at your institution
- Provide info sheets to potentially eligible pts
- Encourage pts to agree to research biopsies, blood tests, tissue/blood banking
- Help access underserved communities (African-American, Hispanic, lower SES) – more likely to present with larger/locally advanced, more aggressive (especially triple-negative in African-American) cancers

**CALGB Breast Cancer
Neoadjuvant Trials:**

What are they, why are they important and what can RNs/CRAs and patient advocates do to help to ensure their success?

William M. Sikov, MD

**Alpert Medical School of Brown University
Providence, Rhode Island**