NSABP Pivotal Breast Cancer Clinical Trials:
Historical Perspective, Recent Results and 
Future Directions

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Medical Director
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NSABP Breast Cancer Trials
Six Broad Research Themes

1. Optimizing local-regional management
2. Optimizing adjuvant hormonal therapy in early-stage BC
3. Identifying prognostic and predictive factors for outcome and response to therapy
NSABP Breast Cancer Trials
Six Broad Research Themes

4. Optimizing adjuvant chemotherapy in early-stage BC
5. Evaluating novel targeted therapies alone or in combination with standard adjuvant therapy
6. Evaluating neoadjuvant chemotherapy in order to individualize L-R therapy, outcome, and identify predictive markers of response
Optimizing Loco-Regional Management
Operable Breast Cancer

Clinically Node-Negative

Radical Mast.
Total Mast.
Total Mast. + XRT

Overall Survival

Global p=0.68

Patients
Deaths
RM 362 259
TMR 352 274
TM 365 259

Fisher B: NEJM, 2002
NSABP B-06

Operable Breast Cancer

Clinical Tumor Size ≤ 4 cm

Total Mast. + Ax. Diss.
Lump. + Ax. Diss.
Lump. + Ax. Diss. + XRT

Overall Survival

Patients | Deaths
--|---
MAST 589 | 299
LUMP 634 | 338
LUMP/XRT 628 | 317

Global p=0.57

Fisher B: NEJM, 2002
### NSABP B-06

**Effect of XRT on IBTR (20-Years)**

<table>
<thead>
<tr>
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<th>IBTR (%)</th>
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<tr>
<td></td>
<td>Lump.</td>
</tr>
<tr>
<td>All Patients</td>
<td>39%</td>
</tr>
<tr>
<td>Node-Negative</td>
<td>36%</td>
</tr>
<tr>
<td>Node-Positive*</td>
<td>44%</td>
</tr>
</tbody>
</table>

* Received adjuvant chemotherapy

Fisher B: NEJM, 2002
Effect of Systemic Therapy on IBTR
Ten-Year Cumulative Incidence
NSABP Node-Negative Trials

Mamounas, SSO 2003
Tamoxifen and XRT for Occult Breast Cancer

NSABP B-21
Tumors ≤ 1 cm
Treated with Lumpectomy

Breast XRT Placebo 9.3%
Breast XRT Tamoxifen 2.8%
Tamoxifen 16.5%

8-Yr IBTR

NSABP Trials in Patients with DCIS

B-17: Lumpectomy + XRT

B-24: Lumpectomy + XRT
   Placebo vs. TAM

B-35: Lumpectomy + XRT
   TAM vs. Anastrozole

B-43: Lumpectomy + XRT
   + Trastuzumab
NSABP B-17 and B-24
12-Yr Cumulative Incidence of IBTR

NSABP B-17 and B-24
12-Yr Cumulative Incidence of IBTR

Invasive IBTR

Non-Invasive IBTR

NSABP B-24

Effect of Tamoxifen by ER-Status

ER-Positive

10-year $P < .001$
Overall $P = .003$

Placebo group (n = 274): 84 events
Tamoxifen group (n = 284): 58 events

ER-Negative

10-year $P = .59$
Overall $P = .68$

Placebo group (n = 94): 25 events
Tamoxifen group (n = 80): 20 events

Allred et al: J Clin Oncol, 2012
NSABP B-35
Anastrozole vs. Tamoxifen for DCIS

- Postmenopausal Patients
- ER or PR Positive DCIS
- Lumpectomy with free margins

Randomization

XRT

Tamoxifen  Anastrozole

Activated: 1/03
Completed: 3106 pts

Primary endpoint: BC event
Secondary endpoints: DFS, OS, IBTR, CBC, fractures, QOL
NSABP B-43: Trastuzumab + XRT for HER-2 + DCIS

HER2+ DCIS Lx

Radiation Therapy

Radiation Therapy + Trastuzumab

q3-week Trastuzumab cycles x 2

- Trastuzumab 8 mg/kg loading dose
- Trastuzumab 6 mg/kg final dose

Activated: 11/08
Accrual: 1095/2000 pts
NSABP B-32: Lymphatic Mapping and Sentinel Node Biopsy
NSABP B-32 Schema

Clinically Negative Axillary Nodes

Stratification
- Age
- Clinical Tumor Size
- Type of Surgery

Randomization

GROUP 1
Sentinel Node Biopsy
Axillary Dissection

GROUP 2
Sentinel Node Biopsy*

*Axillary node dissection only if the SN is positive

Accrual: 5611 (5/99-2/04)
NSABP B-32
Technical Results

• Identification Rate: 97%
• False Negative Rate: 9.7%
• Average number of SNs: 2.9

• Factors significantly affecting ID rate:
  – Age, Tumor Size and Tumor Location

• Factors significantly affecting FN rate:
  – Type of Biopsy and Number of Removed SNs
* 300 deaths triggered the definitive analysis
* 309 reported as of 12/31/2009

Krag D et al: ASCO 2010 Abstr. LBA 505
NSABP Protocol B-32

DFS for Sentinel Node Negative Patients

% Disease-Free

Years After Entry

Trt
SNR+AD  N  Deaths
1975  315
SNR  2011  336  HR=1.05  p=0.542

Data as of December 31, 2009

Krag D et al: ASCO 2010 Abstr. LBA 505
NSABP B-32: Local and Regional Recurrences as First Events

- Local: 2.7%
- Axillary: 0.1%
- Extra-axillary: 0.25%

SNR + ALND (n = 1975)

SNR (n = 2011)

Krag D et al; ASCO 2010 Abstr. LBA 505
NSABP B-32: Significantly Lower Morbidity Without vs. With ALND

- Shoulder Abduction Deficit: SNR + ALND (19%) vs. SNR (13%)
P < .001

- Arm Volume Difference > 5%: SNR + ALND (28%) vs. SNR (17%)
P < .001

- Arm Numbness: SNR + ALND (31%) vs. SNR (8%)
P < .001

- Arm Tingling: SNR + ALND (13%) vs. SNR (7%)
P < .001

Krag D et al: ASCO 2010 Abstr. LBA 505
NSABP B-32: Occult Metastases

Clinically Negative Axillary Nodes

Randomization

GROUP 1
Sentinel Node Biopsy
Axillary Dissection

GROUP 2
Sentinel Node Biopsy*

*Axillary node dissection only if the SN is positive

IHC and detailed pathologic examination of the SNs performed centrally and results were not disclosed

NSABP B-32: Effect of Occult Metastases on Survival in Node-Negative Breast Cancer

- 1608 were negative for occult metastases
  - 316 were positive for occult metastases

- 1660 were negative for occult metastases
  - 300 were positive for occult metastases

3268 were negative for occult metastases

- 616 were positive for occult metastases
  - 430 had isolated tumor-cell clusters
  - 172 had micrometastases
  - 14 had macrometastases

15.9%
NSABP B-32: Effect of Occult Metastases on Survival in Node-Negative Breast Cancer

A. Overall Survival

- Occult metastases not detected
- Occult metastases detected

No. at Risk
- Occult metastases not detected: 3197, 3085, 2295, 575
- Occult metastases detected: 598, 581, 416, 108

P = 0.03
HR: 1.4

B. Disease-free Survival

- Occult metastases not detected
- Occult metastases detected

No. at Risk
- Occult metastases not detected: 3092, 2897, 2115, 520
- Occult metastases detected: 574, 539, 375, 92

P = 0.02
HR: 1.3

Isolated tumor-cell clusters vs. no mets: HR 1.27 (1.04-1.54)
Micro- and macrometastases vs. no mets: HR 1.60 (1.32-1.96)

NSABP B-32: Effect of Occult Metastases on the FNR of SNB

• Including the information from the additional pathologic assessment, the FNR of SLNB in B-32 was reduced to 6.4% (49 of 763 cases)
• This 35% reduction in FNR was statistically significant \((p < 0.001)\)
• Among the 23 FN SLNs with occult mets, the number of positive non-SLNs was:

<table>
<thead>
<tr>
<th>Number of + non-SLNs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Pts</td>
<td>16</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>
NSABP B-39/RTOG 0413
Accelerated Partial Breast Irradiation vs. Whole Breast XRT

Operable Breast Cancer Treated with Lumpectomy

External Beam Whole Breast XRT

Partial Breast XRT

Accrual: 4175/4300

Primary endpoint: IBTR rates between whole breast XRT and PBI
Optimizing Adjuvant Hormonal Therapy in Early-Stage BC
NSABP ER-Positive Trials

- B-14: Plac. vs TAM
- B-20: TAM vs MFT/CMFT
- B-33: TAM --> AI vs PLAC
- B-42: AI --> LET vs PLAC
NSABP Node (-), ER (+) Studies

**Results**

**B-14**

- **RFS**: 78%
- **OS**: 71%
- HR: 0.58 (95% CI: 0.50-0.67)

**B-20**

- **RFS**: 89%
- **OS**: 87%
- HR: 0.52 (95% CI: 0.39-0.68)
- HR: 0.78 (95% CI: 0.60-1.01)
More Than Half of Breast Cancer Recurrences and Deaths Occur Post-Tamoxifen

Recurrences

<table>
<thead>
<tr>
<th>Years</th>
<th>Tamoxifen</th>
<th>Control</th>
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<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>85.2</td>
<td>73.7</td>
</tr>
<tr>
<td>10</td>
<td>76.1</td>
<td>62.7</td>
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<tr>
<td>15</td>
<td>68.2</td>
<td>54.9</td>
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Breast Cancer Deaths

<table>
<thead>
<tr>
<th>Years</th>
<th>Tamoxifen</th>
<th>Control</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>91.4</td>
<td>87.8</td>
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<tr>
<td>10</td>
<td>80.9</td>
<td>73.2</td>
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<tr>
<td>15</td>
<td>73.0</td>
<td>64.0</td>
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NSABP B-14
Tamoxifen Duration

Node-Negative ER-Positive

Randomization

Registration

Placebo X 5 yrs

TAM X 5 yrs

Placebo X 5 yrs

TAM X 5 yrs

Disease-Free Survival

Fisher et al: JNCI, 2001

TRT N Events

PLAC 569 106

TAM 583 137 p=0.03

Years

0 1 2 3 4 5 6 7
NSABP B-33 Trial

Stage I-II Breast Cancer
Postmenopausal, ER or PgR-Positive

Randomization

Tamoxifen for 5 Years
Disease-Free

Exemestane
X 5 years

Placebo
X 5 years

Opened: May 1, 2001
Target Accrual: 3000 pts
Accrual in 10/03: 1598 pts

Accrual stopped in 10/03 after disclosure of results from the NCIC MA.17 trial and the study was unblinded

B-33: Disease-Free Survival*

% Event-Free

Years After Randomization

Group         N    Events
Placebo     779  52
Exemestane  783  37

RR=0.68  p=0.07

91%  89%

*Eligible pts with follow-up

Mamounas E. et al. J Clin Oncol 200
B-33: Relapse-Free Survival*

% Event-Free

Years After Randomization

RR = 0.44  
p = 0.004

Group | N | Events
--- | --- | ---
Placebo | 779 | 37
Exemestane | 783 | 17

*Eligible pts with follow-up

NSABP B-42: Trial Evaluating Adjuvant AI Duration

Postmenopausal, Disease-free, Stage I, II, or III invasive BC at diagnosis
ER-positive and/or PgR-positive

- Primary Endpoint
  Disease-free survival
- Secondary Endpoints
  Overall survival
  Time to treatment failure
  Osteoporosis-related fractures

Accrual: 3966 pts
Identifying Prognostic and Predictive Factors for Outcome and Response to Therapy
21-Gene Recurrence Score Validation Study

16 Cancer and 5 Reference Genes

ESTROGEN
ER
PR
Bcl2
SCUBE2

PROLIFERATION
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

INVASION
Stromolysin 3
Cathepsin L2

BAG1

HER2
GRB7
HER2

CD68

5 REFERENCE GENES

NSABP B-14
668 Node (-), ER (+) Pts

P<0.00001

NSABP B-20: Chemotherapy Benefit By Recurrence Score Category

Low Risk (RS < 18)
- Tam + Chemo
- Tam
- p = 0.76

96% vs 95%

Low Risk Patients (RS < 18)

Interm. Risk (RS 18–30)
- Tam + Chemo
- Tam
- p = 0.71

89% vs 90%

Int Risk (RS 18–30)

High Risk (RS ≥ 31)
- Tam + Chemo
- Tam
- p = 0.001

88% vs 60%

High Risk Patients (RS ≥ 31)

RS and Loco-Regional Failure
TAM-Treated Patients (B-14/B-20, n=895)

Optimizing Adjuvant Chemotherapy in Early-Stage BC
NSABP: Node-Negative, ER-Negative Protocols

B-13: Surg. vs MF

B-19: MF vs CMF

B-23: CMF vs AC+/- TAM

B-36*: AC vs FEC+/- CEL

*ER-/ER+
NSABP Node (-), ER (-) Studies

Results

NSABP B-23
Contralateral Breast Cancer

NSABP Node-Positive Trials Evaluating Adjuvant Taxanes

- **B-28:** AC vs. AC $\rightarrow$ T
  - n=3059

- **B-30:** AC $\rightarrow$ T vs. AT vs. TAC
  - n=5351

- **B-38:** TAC vs. dd AC $\rightarrow$ T vs. dd AC $\rightarrow$ TG
  - n=4800
NSABP B-28
AC vs. AC → Paclitaxel

Disease-Free Survival

Overall Survival

RR = 0.83  p = 0.008
AC 1528 pts, 461 events
AC-T 1531 pts, 400 events

RR = 0.94  p = 0.46
AC 1528 pts, 255 deaths
AC-T 1531 pts, 243 deaths

Mamounas E, et al: J Clin Oncol 2005
NSABP B-28: Effect of RS on Outcomes

**DFS**
- RS Low: 75.8%
- RS Intermediate: 57.0%
- RS High: 48.0%

**OS**
- RS Low: 90.0%
- RS Intermediate: 74.7%
- RS High: 63.0%

**DRFI**
- RS Low: 80.9%
- RS Intermediate: 64.9%
- RS High: 55.8%

**BCSS**
- RS Low: 95.0%
- RS Intermediate: 78.9%
- RS High: 68.2%
NSABP-30: Results
AC → T vs. AT vs. TAC

**OS (ITT)**

- **AC**
  - N: 1753
  - HR: 0.86 vs TAC
  - P Value: 0.086

- **T**
  - N: 1753
  - HR: 0.83 vs AT

- **AT**
  - N: 1753
  - HR: 0.80 vs AT
  - P Value: 0.006

- **TAC**
  - N: 1758
  - HR: 0.96 vs AT
  - P Value: 0.58

**DFS (ITT)**

- **AC**
  - N: 1753
  - HR: 0.83 vs TAC
  - P Value: 0.006

- **T**
  - N: 1753
  - HR: 0.80 vs AT

- **AT**
  - N: 1753
  - HR: 0.96 vs AT
  - P Value: 0.01

- **TAC**
  - N: 1758
  - HR: 0.96 vs AT
  - P Value: 0.58

Swain SM et al.; N Engl J Med 2010
NSABP B-30: Effect of Amenorrhea

**Disease-Free Survival**

- RR* = 0.70
- p* = 0.00041

**Status** | N | Events
--- | --- | ---
Amenorrhea | 1868 | 424
No Amenorrhea | 475 | 173

**Overall Survival**

- RR* = 0.76
- p* = 0.038

**Status** | N | Events
--- | --- | ---
Amenorrhea | 1868 | 247
No Amenorrhea | 475 | 103

*HR and p-value were adjusted by Treatment, ER, age, LN, tumor size and hormonal therapy

NSABP B-38 DFS

Disease-Free Survival

<table>
<thead>
<tr>
<th>Treat</th>
<th>N</th>
<th>Events</th>
<th>P-value* (vs AC→PG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAC</td>
<td>1610</td>
<td>327</td>
<td>0.410</td>
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<tr>
<td>AC→P</td>
<td>1618</td>
<td>294</td>
<td>0.388</td>
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<tr>
<td>AC→PG</td>
<td>1613</td>
<td>320</td>
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# at risk

<table>
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<tr>
<th>Years since Randomization</th>
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<td>1348</td>
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<td>1533</td>
<td>1453</td>
<td>1350</td>
<td>1244</td>
<td>730</td>
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* Stratified log-rank test adjusting for randomization factors
NSABP B-38 OS

Overall Survival

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<thead>
<tr>
<th>Treat</th>
<th>N</th>
<th>Deaths</th>
<th>P-value* (vs AC→PG)</th>
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<tbody>
<tr>
<td>TAC</td>
<td>1617</td>
<td>185</td>
<td>0.167</td>
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<tr>
<td>AC→P</td>
<td>1624</td>
<td>188</td>
<td>0.133</td>
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<tr>
<td>AC→PG</td>
<td>1618</td>
<td>167</td>
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# at risk

<table>
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<tr>
<th></th>
<th>0</th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<td>1588</td>
<td>1539</td>
<td>1487</td>
<td>1433</td>
<td>913</td>
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<tr>
<td>1624</td>
<td>1602</td>
<td>1557</td>
<td>1504</td>
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<tr>
<td>1618</td>
<td>1596</td>
<td>1557</td>
<td>1514</td>
<td>1446</td>
<td>928</td>
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</table>

* Stratified log-rank test adjusting for randomization factors
Evaluating Novel Targeted Therapies Alone or in Combination with Standard Adjuvant Therapy
**U.S. Adjuvant Trastuzumab Trials**

**NSABP B-31**
- Operable Breast Cancer
- HER-2 neu Positive
- Path Node-Positive

**Randomization**
- AC x 4
- Paclitaxel x 4
- Paclitaxel x 4 + Trastuzumab X 1 year

TAM X 5 years for ER+ or PgR+, Optional for ≥ 50 yrs. With ER– and PgR–

Opened: 2/00

**NCCTG 9831**
- HER 2/Neu Positive
- NP/High-Risk NN

**Randomization**
- AC x 4
- Paclitaxel weekly X 12
- Trastuzumab weekly X 52

Opened: 5/00
Updated N9831/B-31 Joint Analysis

Disease-Free Survival*

P = 0.00001

N=619 events

HR*adj = 0.48 (95% CI: 0.41-0.57)

*Nodes, receptor status, paclitaxel schedule, protocol

*Intent to Treat Events: Recurrence, Contralateral BC, 2nd Primary, Death

Perez EA et al: J Clin Oncol 2011
Updated N9831/B-31 Joint Analysis
Overall Survival*

258 (36%) of the 710 events needed for final analysis have occurred
unadjusted HR=0.65 (95%CI: 0.51-0.84)
P=0.0007

*Intent to treat
Effect of Trastuzumab According to HER-2 Status by Central IHC and FISH

RR of ACTH/ACT for DFS (NSABP B-31)

- FISH+ (1588)
- FISH- (207)
- IHC 3+ (1488)
- IHC <3 (299)
- FISH- & IHC <3 (174)

NSABP B-47

Node-Positive or High-Risk Node-Negative IBC
HER2-Normal (n=3260)

Stratification
Age, # nodes, ER/PR Status, Adj. Chemo

Randomize

TC(6) or AC(4) → T(4)

TC(6) + H or AC(4) → T(4) + H

+ Hormonal Therapy for ER or PR positive

Accrual: 1195/3260
NSABP B-41: Neoadjuvant Study with Lapatinib vs. Trastuzumab vs. Combo

Operable Breast Cancer HER-2 neu Positive

Endpoints: pCR, cardiac events, DFS, OS

Trastuzumab for a total of 1 year

Accrual: 529 pts
NSABP B-41: pCR Breast and Negative Nodes

Percentage (%)

AC→WP+T N=176
49.4

AC→WP+L N=171
47.4

AC→WP+T+L N=171
60.2

P=0.056
P=0.78
HER2 Upregulates VEGF Expression

Increased # of vessels
* Vessel dilation
* Vessel tortuosity

Epstein, et al., SABCS 2003
NSABP B-44 Trial: TCH +/- Bevacizumab

Stratified by Nodes and Hormonal Receptor Status

HER2+ (Central Testing)
N+ or high risk N-

TCH
6 x Docetaxel and Carboplatin
1 Year Trastuzumab

TCHB
6 x Docetaxel and Carboplatin
1 Year Trastuzumab
1 Year Bevacizumab

Accrual: 3509 pts

Stratified by Nodes and Hormonal Receptor Status
Evaluating Neoadjuvant Chemotherapy in Order to Individualize L-R Therapy, Outcome, and Identify Predictive Markers of Response
NSABP Neoadjuvant Trials

B-18: Adj. vs. Neoadj. AC

B-27: Neoadj. AC vs. AC→T

B-40/B-41: Neoadj. Chemo +/- Biologics
B-18: 16-Year Update

DFS

OS

B-18: Overall Survival by Age

<50yrs

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Ev</th>
<th>HR</th>
<th>P</th>
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<tr>
<td>Post</td>
<td>388</td>
<td>167</td>
<td>1.23</td>
<td>0.07</td>
</tr>
<tr>
<td>Pre</td>
<td>361</td>
<td>171</td>
<td>0.81</td>
<td>0.06</td>
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</table>

≥50yrs

<table>
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<th></th>
<th>N</th>
<th>Ev</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post</td>
<td>363</td>
<td>148</td>
<td>1.23</td>
<td>0.07</td>
</tr>
<tr>
<td>Pre</td>
<td>361</td>
<td>171</td>
<td>0.81</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Qualitative Treatment by Age Interaction

p=0.01

NSABP B-27 Schema

Operable Breast Cancer (2411 pts)

Randomization

AC x 4, Tam X 5 Yrs, Surgery

pCR: 13.7%

AC x 4, Tam X 5 Yrs, Docetaxel x 4, Surgery

pCR: 25.6%

AC x 4, Tam X 5 Yrs, Surgery

AC x 4, Tam X 5 Yrs, Docetaxel x 4

pCR: 25.6%
B-27: 8-Year Update

**DFS**

- **HR** = 0.93, 0.92  \( P = .29, .29 \)

<table>
<thead>
<tr>
<th>Trt</th>
<th>N</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Op AC</td>
<td>784</td>
<td>304</td>
</tr>
<tr>
<td>Pre-Op ACT</td>
<td>783</td>
<td>292</td>
</tr>
<tr>
<td>Pre-Op AC + Post Op T</td>
<td>777</td>
<td>286</td>
</tr>
</tbody>
</table>

**RFS**

- **HR** = 0.83, 0.87  \( P = .04, .14 \)

<table>
<thead>
<tr>
<th>Trt</th>
<th>N</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Op AC</td>
<td>784</td>
<td>254</td>
</tr>
<tr>
<td>Pre-Op ACT</td>
<td>783</td>
<td>220</td>
</tr>
<tr>
<td>Pre-Op AC + Post Op T</td>
<td>777</td>
<td>227</td>
</tr>
</tbody>
</table>

**OS**

- **HR** = 0.93, 0.97  \( P = .46, .76 \)

<table>
<thead>
<tr>
<th>Trt</th>
<th>N</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Op AC</td>
<td>784</td>
<td>192</td>
</tr>
<tr>
<td>Pre-Op ACT</td>
<td>783</td>
<td>182</td>
</tr>
<tr>
<td>Pre-Op AC + Post Op T</td>
<td>777</td>
<td>189</td>
</tr>
</tbody>
</table>

Effect of pCR on Overall Survival

NSABP B-18

NSABP B-27

SNB After NC
Multi-Center Studies: NSABP B-27 (n=428)

- Identification Rate: 85%
  - With blue dye: 78%
  - With isotope ± blue dye: 88-89%
- False Negative Rate: 11%
  - With blue dye: 14%
  - With isotope ± blue dye: 8.4%

Clinically Node (-): 12.4%
Clinically Node (+): 7.0%  

P=0.51

Mamounas EP: J Clin Oncol, 2005
## Combined Analysis of B-18/B-27 Independent Predictors of LRF

<table>
<thead>
<tr>
<th>Lumpectomy + XRT (1890 Pts, 190 Events)</th>
<th>Mastectomy (1070 Pts, 128 Events)</th>
</tr>
</thead>
</table>
| **Age**  
(≥50 years vs. <50 years) | **Clinical Tumor Size**  
(＞5 cm vs. ≤5 cm) |
| **Clinical Nodal Status**  
(+ vs. (-)) | **Clinical Nodal Status**  
(+ vs. (-)) |
| **Breast/Nodal Path Status**  
Node(-)/No pCR vs. Node(-)/pCR  
Node(+ vs. Node(-)/pCR | **Breast/Nodal Path Status**  
Node(-)/No pCR vs. Node(-)/pCR  
Node(+ vs. Node(-)/pCR |

NRG 9353: Schema

Clinical T1-3N1M0 BC

Axillary Node (+) (FNA or Core Needle Biopsy)

Neoadjuvant Chemo (+ Anti-HER-2 Therapy for HER-2 neu + Pts)

Path Negative Axillary Nodes at Surgery (Axillary Dissection or SNB ± Axillary Dissection)

Randomization

No Regional Nodal XRT with Breast XRT if BCS and No Chest Wall XRT if Mastectomy

Regional Nodal XRT with Breast XRT if BCS and Chest Wall XRT if Mastectomy
NSABP
New Directions with Neoadjuvant Chemotherapy

• Use pCR as a correlate of chemotherapy efficacy to test new drugs and regimens

• Utilize micro-array technology to identify genomic profiles associated with pCR to specific drugs or combinations

• Candidates:
  • Sequential anthracycline/taxane combinations
  • New targeted therapies alone or in combination with chemo
Endpoints: pCR, cCR, DFS, OS, gene expression patterns
NSABP B-40: Effect of Chemotherapy Regimen on pCR

Chi-square test: T→AC vs TC→AC (p=0.411)
T→AC vs. TG→AC (p=0.896)

NSABP B-40: Effect of Bevacizumab on pCR

NSABP B-40: Effect of Bevacizumab on pCR by Hormone-Receptor Status

<table>
<thead>
<tr>
<th></th>
<th>W/O BEV</th>
<th>BEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR+</td>
<td>15.2</td>
<td>23.3</td>
</tr>
<tr>
<td>TNBC</td>
<td>47.3</td>
<td>51.3</td>
</tr>
</tbody>
</table>

OR = 1.70, p=0.008 (HR+)
OR = 1.17, p=0.44 (TNBC)

Interaction p value = 0.166

Summary/Conclusions

• Several of the pivotal NSABP breast cancer clinical trials have been instrumental in establishing/changing the standard of care for patients with early stage breast cancer:
  – Loco-regional management
  – Adjuvant hormonal therapy
  – Adjuvant chemotherapy
  – Adjuvant targeted therapy with biologics
  – Neoadjuvant chemotherapy