Preoperative Chemotherapy, 
NSABP Protocols 
B-18 and B-27: 
an update 

Norman Wolmark
Adjuvant Therapy
B-18
Duration: 88-93
ACCRUAL: 1,523

B-27
Duration: 95-00
ACCRUAL: 2,411

B-40
pCR endpoint
Started 11-06
B-18

OPERABLE BREAST CANCER
FNA or Core

Age, T, cN

OPERATION

AC x 4

AC x 4

OPERATION

AC x 4

Tam for women ≥50 yrs. only
NSABP B-18

OPENED: Oct. 1988
CLOSED: Apr. 1993
ACCRUAL: 1,523
MTS: 9.5 years (2001)
       16 years (present)
<table>
<thead>
<tr>
<th>cm</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>&lt; 2.0</td>
<td>28</td>
</tr>
<tr>
<td>2.1 - 4.0</td>
<td>59</td>
</tr>
<tr>
<td>&gt; 4.1</td>
<td>13</td>
</tr>
<tr>
<td>Node neg.</td>
<td>74</td>
</tr>
</tbody>
</table>
Tumor Response
Tumor Response (685pts.)

- CR: 79%
- cCR: 0%
- pCR: 20%
- 100%
Tumor Response (685pts.)

- CR: 79
- cCR: 36
- pCR: -

Percentage distribution: 0% to 100%
Tumor Response (685pts.)

CR: 79

cCR: 36

pCR: 13

*25% pCR w DCIS
Nodal Response

Post | Pre
--- | ---
42% | 60%

P < 0.01
Outcome
B-18 DFS and Survival

\[ \text{Events} = \frac{\text{Pts.}}{\text{Year}} \]

<table>
<thead>
<tr>
<th>Year</th>
<th>Preop Events</th>
<th>Postop Events</th>
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<tbody>
<tr>
<td>2</td>
<td>742</td>
<td>751</td>
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<tr>
<td>4</td>
<td>323</td>
<td>338</td>
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<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
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</table>

\[ P = 0.5 \]

\[ P = 0.8 \]

JNCI Monographs #30 96 2001
Survival

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Ev</th>
<th>HR</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Post</td>
<td>751</td>
<td>311</td>
<td>0.99</td>
<td>0.90</td>
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<tr>
<td>Pre</td>
<td>742</td>
<td>308</td>
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</table>
Treatment by Age Interaction
Qualitative Treatment by Age Interaction

p = 0.01
pCR and Outcome
DFS

pCR (88 pts.)
pINV (159 pts.)
cPR (295 pts.)
cNR (140 pts.)

P = 0.00005

JNCI Monographs #30 96 2001
DFS and pCR

<table>
<thead>
<tr>
<th>No pCR</th>
<th>pCR</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>Ev</td>
</tr>
<tr>
<td>599</td>
<td>344</td>
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<tr>
<td>86</td>
<td>29</td>
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P <0.0001
Survival and pCR

<table>
<thead>
<tr>
<th>No pCR</th>
<th>pCR</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>599</td>
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<tr>
<td>Ev</td>
<td>263</td>
</tr>
<tr>
<td>HR</td>
<td>.28</td>
</tr>
</tbody>
</table>

P < 0.0001
AC chemotherapy

RESPONDERS

NON RESPONDERS
Operable Breast Cancer

Age, T, cN

AC
OPERATION

AC → Txt*
OPERATION

AC
OPERATION

*100mg/m² x 4; Tam for all

Txt
NSABP B-27

OPENED:  Dec. 1995
CLOSED:  Dec. 2000
ACCRUAL: 2,411
MTS: 6.5 years (2006 JCO)
       8.5 years (present)
## B-27/18 Clin.Tumor/Node Status

<table>
<thead>
<tr>
<th>cm</th>
<th>B27</th>
<th>B18</th>
</tr>
</thead>
<tbody>
<tr>
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<td>15</td>
<td>28</td>
</tr>
<tr>
<td>2.1 - 4.0</td>
<td>41</td>
<td>59</td>
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<tr>
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<td>Node neg.</td>
<td>70</td>
<td>74</td>
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Tumor Response
Path Complete Response

AC

AC>T

12.9

JCO Nov ‘03
Path Complete Response

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<tr>
<th></th>
<th>pCR</th>
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</thead>
<tbody>
<tr>
<td>AC</td>
<td>12.9</td>
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<tr>
<td>AC&gt;T</td>
<td>26.1</td>
</tr>
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</table>

P < 0.001

JCO Nov ‘03
Nodal Response

- AC
  - 51

- AC>T
  - 58

P < 0.01

NEG
pCR: AC $\rightarrow$ T

- cN-
- cN+
- 0-2
- 2.4
- 4+
- <50
- >50

Counts:
- cN-: 26
- cN+: 26
- 0-2: 28
- 2.4: 29
- 4+: 23
- <50: 28
- >50: 24
pCR and ER Status

ER v treatment p=0.69

- **Neg**: p=0.002, 13.8% (32%)
- **Pos**: p<0.001, 22.7% (45%)
- **Unk**: p<0.001, 31% (23%)
Nodes and Tumor Response

- pCR: 13%
- cCR: 45%
- cPR: 55%
- cSD: 61%
- cPD: 59%

p < 0.0001
Outcome
RFS

N Ev RR P
AC 784 254
AC→T 783 220 .83 0.04

*X Second Primary; X CBC
Recurrence

Local or IBTR

AC
AC→T  p=0.016

Distant
Survival

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Ev</th>
<th>RR</th>
<th>P</th>
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<tbody>
<tr>
<td>AC</td>
<td>784</td>
<td>192</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC→T</td>
<td>783</td>
<td>182</td>
<td>.93</td>
<td>0.46</td>
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<tr>
<td>ACSx→T</td>
<td>777</td>
<td>189</td>
<td>.97</td>
<td>0.76</td>
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</tbody>
</table>
pCR and Outcome
DFS and pCR

pCR v no pCR
HR 0.45
P <0.0001
Survival and pCR

Survival and pCR

pCR v no pCR
HR 0.33
P <.0001

75%

93
80

No pCR
pCR
B-27 DFS
no pCR and Nodes (1881)

Years after Randomization

% Disease-Free

#N     %
0      47
1-3    32
4-9    16
10+    5

Years after Randomization
N=24
Txt 100mg/m² q3w x 4
92 genes correlated with Txt response (p=0.001)

Jenny Chang
Lancet 362 ’03
NSABP B-40
Her2 Neg ≥2cm

Randomize

T x 4 → AC x 4
TX x 4 → AC x 4
TG x 4 → AC x 4

Tissue for Biomarkers

Endpoints: pCR; 2^0 endpoint: pCR Δ (29→38%)
DFS N=1200 Started: 11-07
NSABP B-41
Her2 Pos

Operable BC

R

Operable BC

AC X 4

Paclitaxel/wk + Trastuzumab

AC X 4

Paclitaxel/wk + Lapatinib

AC X 4

Paclitaxel/wk + Lapatinib + Trastuzumab

Surgery

Tmab

N=522; pCR Δ 22% (42→64%)
Deeper Meanings

Kliban
Mediocrity for a new millennium