Neoadjuvant Trastuzumab in HER2-Positive Breast Cancer

In women with HER2-positive early breast cancer, the addition of one year of neoadjuvant trastuzumab to chemotherapy has been shown to significantly improve disease-free and overall survival. Several trials investigating the addition of trastuzumab to neoadjuvant chemotherapy have reported pathologic complete response (pCR) rates ranging from seven to 42 percent. At the 2004 ASCO meeting, Dr Aman Buzdar reported the results from a randomized neoadjuvant trial of paclitaxel + FEC with or without trastuzumab in women with HER2-positive breast cancer. This neoadjuvant trastuzumab/chemotherapy regimen yielded a pCR of 65.2 percent compared to 26.3 percent for chemotherapy alone. NSABP-B-41 has been designed to compare two neoadjuvant regimens: FEC → paclitaxel plus trastuzumab and paclitaxel plus trastuzumab → FEC plus trastuzumab. Another important study, conducted by Dr Jenny Chang, demonstrated impressive clinical responses and interesting intracellular changes after three weeks of neoadjuvant trastuzumab monotherapy.

RESPONSE RATES IN NEOADJUVANT TRIALS OF TRASTUZUMAB PLUS CHEMOTHERAPY

<table>
<thead>
<tr>
<th>Trial</th>
<th>Neoadjuvant regimen</th>
<th>Number of patients</th>
<th>Pathologic complete response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buzdar 2003</td>
<td>Trastuzumab + paclitaxel + docetaxel q2w x 3</td>
<td>57</td>
<td>14%</td>
</tr>
<tr>
<td>Blum 2003</td>
<td>Trastuzumab q4w x 4 + docetaxel q3w x 2 + paclitaxel q3w x 2</td>
<td>33</td>
<td>12%</td>
</tr>
<tr>
<td>Barrett 2003</td>
<td>Trastuzumab q2w x 12 + paclitaxel q3w x 4</td>
<td>40</td>
<td>12%</td>
</tr>
<tr>
<td>Harris 2003</td>
<td>Trastuzumab q2w x 12 + docetaxel q3w x 4</td>
<td>30</td>
<td>21%</td>
</tr>
<tr>
<td>Harris 2003</td>
<td>Paclitaxel q3w x 4 + docetaxel q3w x 4 + trastuzumab q2w x 4</td>
<td>44</td>
<td>20%</td>
</tr>
<tr>
<td>Linenburger 2003</td>
<td>Trastuzumab q2w x 12 + docetaxel q3w x 4 + docetaxel q2w x 4</td>
<td>12</td>
<td>42%</td>
</tr>
<tr>
<td>Miklich 2003</td>
<td>Trastuzumab q2w x 12 + docetaxel q3w x 4</td>
<td>20</td>
<td>20%</td>
</tr>
<tr>
<td>Schiffer 2003</td>
<td>Trastuzumab q2w x 12</td>
<td>20</td>
<td>21%</td>
</tr>
<tr>
<td>Carey 2002</td>
<td>AC x 6 + trastuzumab + paclitaxel q2w x 12</td>
<td>22</td>
<td>22%</td>
</tr>
<tr>
<td>Steger 2002</td>
<td>Trastuzumab q2w x 12 + docetaxel q3w x 4 + paclitaxel q2w x 4</td>
<td>9</td>
<td>22%</td>
</tr>
</tbody>
</table>

G-CSF = granulocyte colony-stimulating factor; EPI = epirubicin

**NEOADJUVANT DOCETAXEL/CARBOPlatin WITH OR WITHOUT TRASTUZUMab**

**Eligibility**

- T1-3, NO-1, MO breast cancer
- ACCRUAL: 42 (Early closure by DSMB)

**Aim 1**

- Paclitaxel q3w x 4
- FEC x 4
- H x 12

**Aim 2**

- Paclitaxel q3w x 4 + H x 12

**Pathologic complete response by hormonal receptor status**

<table>
<thead>
<tr>
<th><strong>Positve</strong></th>
<th><strong>H + (n = 11)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>22%</td>
<td>65.3% (p &lt; 0.001)</td>
</tr>
</tbody>
</table>

**NEGATIVE**

- H + (n = 10)
- 20.0%

**MD ANDERSON PHASE III TRIAL OF NEoadjuvant TRASTUZUMAB/CHEmOTHERAPY**

**Eligibility**

- T1-3, NO-1, MO breast cancer
-HER2-positive by IHC or HER2 3+

**Aim 1**

- Trastuzumab q2w x 12
- Docetaxel q3w x 4
- Cyclophosphamide q4w x 4

**Aim 2**

- Docetaxel q3w x 4 + Carboplatin q4w x 4

**Eligibility**

- 13 or 16, any 9 patients with HER2-positive disease are randomly assigned to neoadjuvant therapy

**PROPOSED NSABP TRIAL B-41: FOLLOW-UP TO THE MD ANDERSON STUDY**

**Eligibility**

- T1-3, NO-1, MO breast cancer
-HER2-positive by IHC or HER2 3+

**Aim 1**

- Paclitaxel q3w x 12 + H x 12
- Trastuzumab q2w x 12

**Aim 2**

- FEC + H x 12

**Pathologic complete response by human epidermal livedo**

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<th><strong>Positive</strong></th>
<th><strong>H + (n = 11)</strong></th>
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**NEGATIVE**

- H + (n = 10)
- 20.0%

**NEGATIVE**

- H + (n = 10)
- 20.0%

**RANDOMIZED TRIAL OF NEoadjuvant CHEMOTHERAPY AND TRASTUZUMab**

**Eligibility**

- T1-3, NO-1, MO breast cancer

**Aim 1**

- Paclitaxel q3w x 12 + H x 12
- Trastuzumab q2w x 12

**Aim 2**

- FEC + H x 12

**Eligibility**

- Paclitaxel, operable HER2-positive breast cancer

**NEGATIVE**

- H + (n = 10)
- 20.0%

**NEGATIVE**

- H + (n = 10)
- 20.0%

**NEGATIVE**

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