Optimal Neoadjuvant Endocrine Therapy

Chemotherapy is the most frequent form of neoadjuvant systemic therapy utilized in the United States; while in Europe, preoperative endocrine therapy has been used extensively in women with ER-positive cancers. Phase II and III clinical trials have suggested that the antitumor effect of endocrine therapy in these patients is comparable to what has been observed with chemotherapy, although the time to achieve a response is somewhat longer with endocrine therapy. Tamoxifen and ovarian ablation/ suppression were initially utilized as neoadjuvant therapy, and more recently, studies of third-generation aromatase inhibitors and the estrogen receptor downregulator fulvestrant have demonstrated significant antitumor activity. In addition to clinical endpoints, neoadjuvant therapy is also being investigated as an in vivo surrogate of tumor response to adjuvant setting.

A current large EORTC randomized trial is evaluating fulvestrant in the preoperative setting.

**Erbb STATUS AND RESPONSE TO NEOADJUVANT ENDOCRINE THERAPY IN ER+ TUMORS**

<table>
<thead>
<tr>
<th>Marker status</th>
<th>Letrozole</th>
<th>Tamoxifen</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ErbB-1/2 positive</td>
<td>15/17</td>
<td>88</td>
<td>4/19</td>
</tr>
<tr>
<td>ErbB-1/2 negative</td>
<td>50/101</td>
<td>54</td>
<td>42/100</td>
</tr>
</tbody>
</table>

**DERIVED FROM:** Ellis MJ et al. Letrozole is more effective neoadjuvant endocrine therapy than tamoxifen for ErbB-1- and/or ErbB-2-positive, estrogen receptor-positive primary breast cancer. Evidence from a phase III randomized trial. *J Clin Oncol* 2001;19(18):3808-16.

**SELECT PUBLICATIONS**


**CLINICAL AND PATHOLOGICAL RESPONSE RATES WITH NEOADJUVANT ANASTROZOLE IN LOCALLY ADVANCED BREAST CANCER**

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B-27**</td>
<td>718</td>
<td>718</td>
</tr>
<tr>
<td>AC x 4</td>
<td>24 x 4</td>
<td>2414</td>
</tr>
<tr>
<td>Abdomen Trial**</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td>Milla-Santos et al.***</td>
<td>74</td>
<td>74</td>
</tr>
<tr>
<td>Ellis MJ et al.****</td>
<td>126</td>
<td>126</td>
</tr>
</tbody>
</table>

**Abbreviations:** AC=doxorubicin/cyclophosphamide; T=docetaxel; CVP=cyclophosphamide/vincristine/doxorubicin/prednisolone; pCR=pathologic complete response; CR=partial and complete clinical responses.

**NSABP Breast Cancer Res 2001** Abstract 5.

**Smith IC et al. J Clin Oncol 2002;20:1456-66.**

**Milla-Santos A et al. Breast Cancer Res Treat 2001;Abstract 302.**


**EFFECTIVENESS OF ICI 182,780 IN WOMEN WITH STAGE I OR II PRIMARY BREAST CANCER**

**Eligibility**

ER-positive or unknown, pre- or postmenopausal, stage I or II primary operable breast cancer.

**Study**

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARM 1</td>
<td>Fulvestrant IM on day 1</td>
<td>surgery between days 8 and 29</td>
</tr>
<tr>
<td>ARM 2</td>
<td>Placebo IM on day 1</td>
<td></td>
</tr>
</tbody>
</table>

**Patients followed q 3 months x 2 years, q 6 months x 3 years, then annually thereafter.**

**Objectives**

1. Determine the inhibitory effect of fulvestrant on the development of metastases, as measured by disease-free survival and overall survival, in women with operable stage I or II primary breast cancer.
2. Determine toxicity of this regimen in these patients.

**Study Contacts:**

Anthony Howell, Chair. Ph: 0161-446-8037 Breast International Group

Cornellis van de Velde, Chair. Ph: 0161-446-8037 EORTC Breast Cancer Group

**SOURCE:** Physician Data Query, January 2003.


**NSABP B-27**

**Elbow**

**B-27**

**EORTC STUDY 10963: FULVESTRANT VERSUS PLACEBO**

The preoperative EORTC trial evaluates one injection of fulvestrant after the diagnosis of breast cancer but before surgery. The aim is to test the hypothesis of Bernie Fisher and others that adverse events related to metastases occur during the perioperative period. Hopefully, we can alter that with fulvestrant. The aim is to enroll more than 3,000 women into this study.

**Phase III Randomized Study**

**Elbow**

**B-27**

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Fulvestrant is in a completely new class of antiestrogens. It differs from tamoxifen and other SERMs in that it increases degradation of the estrogen receptor, resulting in dramatic reductions in this protein. It also shuts down both AF1 and AF2 transcription functions, and it appears not to have any estrogenic activity. This agent may be hypothesized to be as effective as chemotherapy, and it is much more tolerable.

**—Melody A Cobleigh, MD**

EORTC STUDY 10803: FULVESTRANT VERSUS PLACEBO

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