Tamoxifen added to lumpectomy and radiation therapy reduced breast cancer events in ductal carcinoma in situ


**Question**

In women with noninvasive ductal carcinoma in situ (DCIS), does adding tamoxifen to lumpectomy and radiation therapy (RT) prevent cancer in ipsilateral and contralateral breasts?

**Design**

Randomized [allocation concealed*, †] blinded [clinicians, patients, outcome assessors, and statisticians* †], placebo-controlled trial with median 74-month follow-up.

**Setting**

57 centers in the United States and Canada.

**Patients**

1804 women who had lumpectomy for DCIS, including those with or without lobular carcinoma in situ, and who were expected to live ≥ 10 years. 16% had positive resection margins. Women with previously diagnosed cancer other than in situ carcinoma of the cervix or basal-cell or squamous-cell carcinoma of the skin were excluded. Follow-up was 99.7%.

**Intervention**

Lumpectomy and RT (50 Gy) began within 8 weeks of surgery and were allocated to tamoxifen, 10 mg twice/d for 5 years (n = 902), or placebo (n = 902).

**Main results**

Fewer breast cancer events, both invasive and noninvasive, occurred in women who received tamoxifen than in those who received placebo (P < 0.001) (Table). Use of tamoxifen reduced invasive events in the ipsilateral breast (P = 0.03) and noninvasive events in the contralateral breast (P = 0.02) (Table). For total breast cancer events, 20 women would need to be treated with tamoxifen for 5 years to prevent 1 additional occurrence of breast cancer. At 5 years, survival was 97% in each group (P = 0.74).

**Main outcome measures**

Invasive or noninvasive tumors as first events in the ipsilateral or contralateral breast.

**Conclusion**

In women with ductal carcinoma in situ, the addition of tamoxifen to a treatment regimen of lumpectomy and radiation therapy was effective in preventing cancer in the ipsilateral and contralateral breast at 5 years without affecting survival.

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*See Glossary.
†Information provided by author.

<table>
<thead>
<tr>
<th>Events</th>
<th>Cumulative incidence of events</th>
<th>Relative event reduction (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>All breast cancer</td>
<td>8.2%</td>
<td>13.4%</td>
</tr>
<tr>
<td>Ipsilateral breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td>2.1%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Noninvasive</td>
<td>3.9%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Contralateral breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td>1.8%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Noninvasive</td>
<td>0.2%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

‡Not significant.

Although tamoxifen led to a decrease in noninvasive contralateral DCIS, the absolute reduction was 0.9% (from 1.1% to 0.2%), and no significant effect was seen on the rate of contralateral invasive disease.

Tamoxifen appears appropriate for some women with DCIS, but perhaps not for all. Further well-designed trials should attempt to define the subsets of women who will benefit most from this systemic therapy.

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**Reference**


**Author’s response**

The points raised by Dr. Perez regarding positive margins are similar to those recently published in a letter to the Lancet, to which we gave a detailed response (1).

Bernard Fisher, MD

**Reference**