Tamoxifen as an Adjuvant Agent for Ductal Carcinoma In Situ (DCIS)
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Tamoxifen has been considered a standard adjuvant agent, for local control in DCIS patients undergoing breast conservation with or without irradiation. This viewpoint derived from the initial results of NSABP-B24, which claimed a significant benefit for ipsilateral local control and contralateral chemoprevention.

Both trials, which had employed tamoxifen as an adjuvant agent in DCIS patients (NSABP-B24 and UK/ANZ) have been updated in 2011 (Wapnier et al 2011 and Cuzick et al 2011), and have initiated some pointed commentary (Cadiz and Kuerer 2012; Warrick and Allred 2012).

Allred et al 2012 presented a subset of 732 B24 DCIS cases (Figure 1), all of which had been tested as positive for estrogen receptor. This represented 40% of the entire 1804 patients in the trial. At a median followup of 14.5 years, P-values for the differences between tamoxifen versus placebo treated patients for ipsilateral in situ and invasive recurrences and for contralateral events all fell short of statistical significance, and the numerical differences were quite small: A six patient numerical superiority of TAM for local control of ipsilateral invasive events, and a two patient numerical superiority of TAM for ipsilateral in situ events.

Wapnir et al 2011 presented the update of the entire trial with a median 163 month followup (Figure 2). There was no statistically significant benefit of TAM for preventing an ipsilateral in situ event (eight fewer events with TAM), but there was a small benefit in preventing an invasive event (22 fewer invasive events).

Cuzick et al 2012 provided an update of the UK/ANZ trial. There was no significant difference between patients with or without tamoxifen therapy either for ipsilateral or contralateral events, in situ or invasive, in those patients who had been treated with radiation therapy (Figure 3). In the non-irradiated group (Figure 4), tamoxifen made no impact on ipsilateral invasive recurrences (51 versus 46), but made a significant but small difference in noninvasive events. These findings are exactly opposite those seen in B24. Additionally, the non-irradiated group showed significant differences in contralateral events related to tamoxifen. Since only the ipsilateral breast undergoes radiation therapy, it is opaque why contralateral events are suppressed by tamoxifen.
in the non-irradiated group, but are not in the irradiated group. The numerical differences and benefits are very small in those cases where a benefit is claimed.

Warrick and Allred in their editorial piece conclude that tamoxifen is probably overused, and advocate more selective use. They particularly note that the major benefit would be seen in patients who are younger (premenopausal) with extensive high-grade disease and/or narrow margins, and clearly only those that are ER positive.

In conclusion, the clinical benefit of tamoxifen intervention based on the randomized trials is meager at best. There appears to be no benefit, at least in the UK/ANZ trial for tamoxifen amongst irradiated patients, and the benefits when claimed are very small.

References:


