

SYSTEMIC TREATMENT FOR DUCTAL CARCINOMA

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There has been a tremendous rise in recent years in the diagnosis of ductal carcinoma in situ of the breast. This so-called pre-cancer is often first seen by mammography even before a woman or her physician could otherwise detect its' presence. Mammograms have been encouraged to find breast lesions while small or when they are pre-cancerous. This produces the best outcome. So, as more women are obtaining mammograms, more also are being diagnosed with this type of breast cancer.

Ductal carcinoma in situ (DCIS) tumors often has distinctive characteristics under the mammogram. Sequential mammograms can show new developments in the breast and radiologists following these tests encourage biopsies when suspicious lesions arise. Only a biopsy will make the diagnosis for certain. One might rest somewhat comfortably in that 80% of breast biopsies are benign - never enough.

Data over the years has shown the different treatment options that are available for DCIS. While historically mastectomies were performed, many physicians currently recommend lumpectomy - removal of the lump of cancer - followed by breast radiation. These recommendations are based upon data, not hearsay. This approach of lumpectomy/radiation yields a very high success rate and leaves the woman with her breast intact. However, a small sub-set of women with DCIS have recurrences either of the same type of tumor or of truly invasive breast carcinoma. For this reason there has been an incentive to evaluate systemic treatment to further improve treatment results.

Recently, a randomized study was reported by Fisher, et al, and published in the prestigious Lancet Medical Journal. The purpose of the study was to randomly allocate Tamoxifen - hormonal treatment for five years - to half the group to determine whether cancer recurrence rates would be favorably impacted. The other half would have placebo treatment not knowing which group they had been placed in.

Previously performed randomized studies were carried out to evaluate the effectiveness of radiation added to lumpectomy compared to lumpectomy alone. Eight-year data showed that there were lower rates of both invasive as well as DCIS cancer in women having lumpectomy and radiation compared to lumpectomy alone. The authors concluded, "Mastectomy was not warranted in women who had ductal carcinoma in situ." This came as a big relief to many women with this early cancer.

It is for this reason that most women I see have lumpectomy and radiation as preferred treatment for DCIS.

Unfortunately, not every woman with DCIS is eligible for lumpectomy and radiation since, in some cases, the cancer has spread throughout the breast making lumpectomy technically impossible. Who is a candidate for breast-conserving therapy is based upon interaction and discussions between the patient, her surgeon and radiation oncologist.

Patients in this study with DCIS had lumpectomy and after the informed consent process were randomly allocated either to radiation --- placebo in 902 patients or radiation therapy followed by Tamoxifen in the same number of patients. Randomized study means neither the patient nor physicians know which treatment the woman is receiving until the end.

The patients were categorized by age, tumor type and methods of detection. Medication, either placebo or Tamoxifen was given twice a day for five years. There were subsequently 295 breast cancer and non-breast cancer events in the 1,798 women followed. 83.3% of patients who received placebo were event free compared to 87.4% who were on Tamoxifen.

In the placebo group subsequently, 130 women had invasive and non-invasive breast cancer events in either the same breast or opposite breast or metastases. This number was 84 women in the group that received Tamoxifen as systemic treatment. Thus, there were 37% fewer events in the group of women taking Tamoxifen than non-Tamoxifen. Additionally, there were 43% fewer invasive breast cancers and 31% fewer non-invasive breast cancers in the Tamoxifen group of women.

In the treated breast in women getting Tamoxifen there was a 44% reduction in invasive cancers and an 18% reduction in non-invasive cancers. Of women with same-sided recurrences, 64% had mastectomy and the others had a second lumpectomy.

What about breast cancer in the opposite side? For women who received placebo there were 36 contra lateral breast cancers compared to 18 in the Tamoxifen group. Overall, the opposite breast at five years had a 3.4% risk of developing tumors in the placebo group compared to 2% in the Tamoxifen group.

The reduction in opposite breast cancers at 5 years was 37% for invasive breast tumors. In non-invasive contra lateral tumors the reduction was 78% in women using Tamoxifen. As a first event, contra lateral breast cancers occurred first in 39 women of the placebo group and 23 of the Tamoxifen group, representing a 42% reduction in women taking Tamoxifen.

Other than breast or endometrium there was no difference in the rate of development of other cancers. Seven women in the Tamoxifen group developed endometrial cancer compared to two in the placebo group. The authors found that younger women were at higher risk for development of same-sided breast tumor. For those less than 49 years of age, ipsilateral breast tumors occurred at a rate per hundred thousand of 33 in women 49 years or younger and a rate of 13.03 in those 50 years or older.

Tamoxifen decreased the ipsilateral breast tumors in younger women by 38% and in older women by 22%. Furthermore, a woman who's DCIS showed comedo necrosis had twice the rate recurrence in the same breast as those with DCIS and no comedo necrosis. Comedo necrosis is the appearance of the cancer area as viewed through a microscope by a pathologist.

Overall, 28 women in the placebo group and 26 women in the Tamoxifen group died. Survival was 97% for the two groups. There were no strokes seen in any of the patients but there was an increased rate of endometrial cancer of 1.53 per thousand patients per year in the Tamoxifen group compared to 0.45 per thousand in the placebo group. There were no deaths occurring from endometrial cancer in the Tamoxifen group.

The authors concluded that "women with DCIS treated by lumpectomy and radiation showed additional benefit from Tamoxifen. The advantage was due mainly to a decrease in the rate of invasive cancer especially in the ipsilateral breast. That effect was also seen in the rate of invasive and non-invasive tumors in the contra lateral breast and that in regional and distant sites.

When the events of those sites were combined, there was a significantly lower rate and cumulative incidents of all breast cancer related events than in the placebo group. These observations suggest that focusing on the frequency with which ipsilateral breast tumors occur after lumpectomy for DCIS is too limited; the possible effect that treatment strategies for DCIS have on all invasive and non-invasive breast cancer events at any sites seem more important. Therefore, the few metastases that were detected at regional and distant sites in this study cannot be ignored especially since Tamoxifen led to fewer such events."

While Tamoxifen currently is not approved for DCIS patients, it has been reported that the FDA is studying the matter seriously and is about to prove this agent for women with ductal carcinoma in situ. This data suggests that there will be a decrease in breast cancer rates in women treated.