S15. Tamoxifen and Familial Breast Cancer

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Case controlled studies have indicated that tamoxifen or oophorectomy may be of benefit in risk reduction of breast cancer for women carrying BRCA1 or 2 mutations.

Results from the largest randomised endocrine chemoprevention trial, the NSABP P-1 trial, clearly showed that tamoxifen reduced the risk of breast cancer in healthy women by nearly 50%. All age groups appeared to gain similar benefit with a trend for younger women and those with a stronger family history having less benefit. Included in these groups are women with lobular carcinoma in situ and atypical ductal hyperplasia, who seemed to gain the most benefit from tamoxifen chemoprevention. Testing for mutations of BRCA 1 and BRCA 2 in 288 women who developed breast cancer in the P-1 trial, detected only 8 BRCA 1 (5 tamoxifen, 3 placebo) and 11 BRCA 2 (3 tamoxifen, 8 placebo) mutations, with no clear evidence that tamoxifen was beneficial for these women (M-C King, ASCO 2001).

The Royal Marsden Trial showed similar results. We detected only one BRCA1 and three BRCA2 mutations likely to be of clinical significance in the 70 patients who developed breast cancer in our trial. Pedigree analysis (Claus model) to estimate the risk of women in our trial having a high penetrance breast cancer predisposing gene mutation, indicated that about 40 of the 70 women who developed breast cancer were likely to be carrying such a gene. Most of these are therefore not BRCA 1 or 2 mutations. With regard to the chemopreventative effect of tamoxifen, there was a trend for more cancers to occur in the high risk women on tamoxifen, whereas the lower risk women appeared to gain a similar benefit to that reported overall from the P-1 trial ($p=0.05$). It is therefore possible that the agonistic effect of tamoxifen on tumour cell proliferation in women carrying high risk gene mutations may, in some women, outweigh the antioestrogenic, antiproliferative effects of the drug.

In conclusion, at this time, there are no randomised clinical trial data to support use of tamoxifen for risk reduction of breast cancer in women who are BRCA1 or BRCA2 or other BRCA mutation carriers.