

S18. Breast Cancer Chemoprevention: Quo Vadis?

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Epidemiological evidence indicate that most breast cancers depend on oestrogen for development into clinical cancers and that early loss of ovarian function will reduce the incidence of the disease. Four clinical trials have been completed evaluating the anti-oestrogenic selective oestrogen modulator (SERM) tamoxifen in healthy women. A meta-analysis of these trials has shown that tamoxifen given for 5 years will reduce the risk of breast cancer by about 40% with some toxicity including an increased risk of endometrial polyps and cancer, venous thrombo-embolism, vasomotor symptoms and cataract. The Royal Marsden trial has still failed to show a significant reduction in breast cancer incidence in spite of the occurrence of more than 150 cancers. This supports the hypothesis that the high risk women in this trial may be relatively resistant to tamoxifen chemoprevention. Evaluation of the risk factors which predispose to oestrogenic promotion of breast cancer may allow the development of algorithms of risk which identify those women likely to gain benefit from anti-oestrogenic intervention. Raloxifene, another SERM, with impeded oestrogenic activity on the uterus

reduces the risk of breast cancer and osteoporotic fractures in postmenopausal women at risk of osteoporosis, but does not cause endometrial cancer. The NSABP P2 trial is now comparing raloxifene with tamoxifen for risk reduction of breast cancer. Lasofoxifene is also being tested for breast cancer risk reduction. An alternative strategy, is looking at the aromatase inhibitor, anastrozole, which has been shown to reduce the risk of contralateral breast cancer better than tamoxifen in the ATAC adjuvant breast cancer trial. The IBIS II trial has started randomising healthy women with a family history of breast cancer to anastrozole or placebo. No trials at this time are directly comparing an aromatase inhibitor with a SERM. The relative merits of these two types of intervention for chemoprevention of breast cancer need to be addressed. Chemoprevention of breast cancer by using anti-oestrogenic interventions are possible. In my opinion, it will be necessary to use the best agents, and then only in those women likely to gain benefit, in order for healthy women to gain clinical benefit.