S21. Use of aromatase inhibitors in breast cancer prevention

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Eight adjuvant trials have reported on the use of aromatase inhibitors for early breast cancer. In addition to benefits in reducing recurrence rates, all of them show a marked reduction in contralateral tumours compared to tamoxifen of about 50%. This, combined with the approximately 50% reduction in new tumours seen with tamoxifen, both in prevention trials, and for contralateral tumours in adjuvant studies, suggest aromatase inhibitors may be able to reduce the rate of ER positive breast cancer by as much as 75%. These drugs are also better tolerated and have fewer side effects than tamoxifen, suggesting they are very promising agents for breast cancer prevention. In particular they do not lead to the gynecologic side effects (including endometrial cancer) or thromboembolic complications associated with tamoxifen. However they are associated with increased rates if arthralgia and other joint symptoms, and decreased bone mineral density leading to increased fracture rates if not properly managed. These data will be reviewed the implications for ongoing chemoprevention trials will be discussed. In particular these very promising results in the adjuvant setting have provided a strong rationale for using these agents in trying to prevent breast cancer. The IBIS II chemoprevention trial has been set up to compare the aromatase inhibitor anastrozole against a placebo in 6,000 high risk post-menopausal women, and against tamoxifen in 4000 post-menopausal women with completely locally excised oestrogen receptor positive DCIS. Both high efficacy and a low side effect profile are essential for a chemopreventive agent, and this trial is designed to address both of these issues. In particular, a detailed bone substudy in 1000 women is built into the trial, and will evaluate the use of the bisphosphonate risedronate on a randomized basis in osteopenic women. The rationale for, and design of, the trial will be described, and current recruitment status will be reported.