A1. QUALITY OF LIFE ISSUES IN PREVENTION TRIALS

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Many novel endocrine therapies are licensed for use in advanced breast cancer. Their efficacy in this setting has led to trials of adjuvant therapy, many of which have shown a reduction in contralateral breast cancers, hence, the real hope that hormonal therapy has an important role to play in chemoprevention. Bilateral prophylactic mastectomy and/or regular surveillance are the only other options available to women who are at high genetic risk of breast cancer but these are not acceptable to all and can impact on certain aspects of quality of life (QoL). Several clinical trials have compared the efficacy of selective oestrogen receptor modulators (SERMs) and aromatase inhibitors in preventing breast cancer in high-risk women. The putative benefits of this approach have to be weighed against potentially serious side-effects, especially on bones and the endometrium. The rigorous assessment of QoL issues such as: – menopausal symptoms, the impact that treatment has on sexual activity, mood state and cognitive function, is also vital in this essentially 'well' population of women. In this talk, some of the QoL results from the tamoxifen chemoprevention trials will be reviewed and the current IBIS-II (International Breast Cancer Intervention Study) trial of anastrozole *vs*. placebo will also be discussed. In the IBIS-II trial, 700 post-menopausal women will complete measures of memory, mood and cognition at baseline, 6 months, 2 and 5 years. The assessment comprises four tests of verbal memory and attention, intelligence quotient (IQ) measurements, self-report evaluations on mood state, cognitive failures and endocrine symptoms.

The aim of interventions in breast cancer has always been to improve the quality of women's lives, either by curing them of their disease or ameliorating its worst effects. Now that we have a realistic prospect of preventing the disease, we must ensure that this does not result in the introduction of other deleterious effects on QoL.

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A2. GENE EXPRESSION SIGNATURES PREDICT BOTH THE STATUS AND ABSOLUTE PROTEIN LEVELS OF STEROID RECEPTORS

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We and others have previously shown that microarrays can be used to identify gene expression profiles that discriminate between oestrogen receptor (ER)-positive and -negative breast tumours. However, these studies focused only on ER status as a binary variable and did not address the relationship of gene expression data to the continuous range of ER protein values. Here, we present a novel approach using expression data and artificial neural networks to accurately predict the ER protein values on a continuous scale in 48 primary breast cancers. Furthermore, this method may be used to determine a more biologically and therapeutically relevant threshold for the ER protein level to redefine ER-positive and ER-negative classes. In the same way, we studied the prediction of other prognostic parameters, such as the progesterone receptor and S phase fraction. Interestingly, there was a consistent reciprocal relationship in the expression levels of the genes that are important for prediction of both ER protein and the fraction of cells in S phase. However, it is clear that the ER status has the strongest impact on the gene expression profile of a tumour suggesting that these two groups are biologically very distinct and should perhaps be treated separately in breast cancer management.

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