

**Strict embargo: 21:00hrs**

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## **RESEARCH OFFERS HOPE FOR LONG TERM BREAST CANCER PREVENTION**

NEW results of a worldwide breast cancer prevention study<sup>1</sup> confirm that tamoxifen - a well established treatment for breast cancer - also reduces the risk of breast cancer in women at increased risk of the disease.

The research published in the Journal of the National Cancer Institute\* today also shows the protective effect of the drug continues for several years after treatment has stopped, while the risk of side-effects returns to normal levels.

Initial IBIS-I results<sup>2</sup> released in 2002 showed tamoxifen reduced hormone receptor positive breast cancer by about one third in pre and postmenopausal women at an increased risk of the disease. Today's results confirm that these benefits continue for at least another five years after treatment has stopped.

The IBIS-I study, funded by Cancer Research UK, involved 7,154 pre and postmenopausal women in seven countries with an increased risk of breast cancer. Women on the study were given either 20 mg of tamoxifen or a placebo (dummy pill) every day for five years. After an average follow up of 96 months, 142 breast cancers were diagnosed in women in the tamoxifen group and 195 in the placebo group.

Lead researcher Professor Jack Cuzick, from the Cancer Research UK Centre for Epidemiology, Mathematics and Statistics, said: "These latest IBIS-I results\* confirm that tamoxifen continues to help prevent oestrogen

receptor positive breast cancer in women at an increased risk of the disease for at least five years after treatment has stopped. Additionally we found that almost all of the excess side effects reported on tamoxifen do not continue after treatment stops.”

Researchers found that serious side effects like blood clots and endometrial cancer limit the use of tamoxifen in helping to prevent breast cancer. These new IBIS-I data demonstrate that these serious side effects stop after women stop taking tamoxifen.

Tony Howell, IBIS co-chair and Professor of Cancer Prevention at the South Manchester University Hospitals Trust, said: “Previous studies have already shown that tamoxifen lowers the risk of developing breast cancer during active preventive treatment but this is the first time that clear evidence is available on the benefits and side-effects of tamoxifen after treatment with the drug has stopped. These findings together with the effectiveness results suggest that over a longer follow-up time the risk of side-effects decreases while the benefit of prevention continues.”

Kate Law, director of clinical trials at Cancer Research UK, said: “These results are promising for women at increased risk of breast cancer. They are important in furthering our knowledge of the role of tamoxifen in the prevention of the disease and also raising the possibility of making it available on a wider scale. We are now investigating drugs that could be more effective at preventing breast cancer and have fewer side-effects. We hope to provide women with as many options as possible in protecting themselves against the disease.”

Professor Jack Cuzick added: “This is a major step towards the approach now used for preventing heart disease, where the major risk factors - such as high blood pressure and cholesterol - are identified and managed

before disease occurs. We are continuing our search for a preventive option which is safer and more effective than tamoxifen in our current trial.”

The follow on study to IBIS-1 is IBIS-2 which is currently recruiting post-menopausal women to see whether the aromatase inhibitor anastrozole is more effective at preventing breast cancer in post-menopausal women at increased risk. IBIS-2 will also investigate whether anastrozole has fewer side effects than tamoxifen. Results from IBIS-2 are expected in 2010.

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For media enquiries, please contact the press office on 020 7061 8300, or, out of hours, the duty press officer on 07050 264 059.

Notes to Editors

\*Cuzick et al. Long-Term Results of Tamoxifen Prophylaxis for Breast Cancer - 96 month Follow-up of the Randomised IBIS-I Trial. JNCI 2007;**99**: 272-282.

- 1 IBIS-1, **I**nternational **B**reast **C**ancer **I**ntervention **S**tudy I
- 2 IBIS-I investigators, 2002, First results of the International Breast cancer Intervention Study (IBIS-I): a randomised prevention trial. **360**, p: 817-24.

### **Breast cancer**

- Breast cancer is by far the most common cancer for women with more than 44,091 new cases in the UK in 2003.

### **IBIS-I Patient Population**

- A total of 7,154 women were included in this analysis.
- 97 per cent of all women reported some family history and 8 per cent had a benign lesion associated with an increased risk of developing breast cancer.

- The largest risk group was women who had a mother or sister who developed breast cancer before the age of 50 and those with second-degree relatives with breast cancer.
- The mean age of the women at the start of the trial was 51 years and 55 per cent were between the ages of 45 to 54 years. 54 per cent were postmenopausal, 40.2 per cent used HRT at some point during the trial.

### **IBIS-I Efficacy Results**

- After a median follow-up of 96 months, 142 breast cancers were diagnosed in women in the tamoxifen group and 195 in the placebo group, a reduction of 27 per cent.
- There was no reduction in the risk of ER-negative invasive tumours (35 vs. 35, but ER-positive breast cancers were reduced by 34 per cent in the tamoxifen group (87 vs. 129 cases)
- Among women who never used HRT or who only used HRT before the trial, there was a significant reduction in ER-positive breast cancers in the tamoxifen arm compared to the placebo arm (37 vs. 77 cases, a 52 per cent reduction. However, for women taking HRT during the trial no clear effect of tamoxifen was seen overall (64 vs. 68 cases) or for ER-positive tumours (40 vs. 43 cases)

### **IBIS-I Tolerability Results**

- Deep-vein thrombosis (DVT) and pulmonary embolism (PE) were more than twice as common in the tamoxifen group during treatment (52 vs. 23 cases). However, after ceasing active treatment the rates were equally distributed between the two treatment groups.
- A total of 28 endometrial cancers were reported (17 vs. 11 cases) Twelve of the endometrial cancers in the tamoxifen group were detected during the active treatment compared to only 3 in the placebo group. After stopping tamoxifen, slightly fewer women in the tamoxifen group reported endometrial cancer compared to those in the placebo group (5 vs. 8 cases).
- Gynaecological side effects such as abnormal bleeding or vaginal discharge, or hot flushes were much more common in the tamoxifen

group during active treatment compared to the placebo group. However, after active treatment was completed there were marked reductions in the tamoxifen group and the event rate was similar to the placebo group.

### **IBIS-2** (International Breast cancer Intervention Study 2)

IBIS-2 is being coordinated by Cancer Research UK and sponsored by Queen Mary, University of London. The trial is taking place in 21 countries, including Australia, India, Chile, Germany and Italy.

- The IBIS-2 Prevention part of the study aims to recruit 6,000 postmenopausal women who are at increased risk of developing breast cancer. A number of factors for increased risk can make a woman eligible to enter the study and these are set according to the different age groups. Women can take part in the trial if they are aged between 40-70 years and are not on HRT.
- IBIS-2 DCIS will recruit 4,000 postmenopausal women who have been diagnosed with and had surgery to remove DCIS (Ductal Carcinoma In Situ). This part of the trial is designed to determine which of the two drugs, anastrozole or tamoxifen, can best prevent new cancers, both in the breast affected by DCIS and in the opposite breast. Women who have had a mastectomy to remove their DCIS cannot join this arm of the trial but they can be part of IBIS-2 Prevention.