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MEDIA RELEASE

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RESEARCH OFFERS HOPE FOR LONG TERM BREAST CANCER PREVENTION

New results of a worldwide breast cancer prevention study¹, involving women from Australia and New Zealand, 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 that, after treatment has stopped, the protective effect of tamoxifen continues for several additional years while the risk of side effects returns to normal levels.

Initial IBIS-I results² released in 2002 showed tamoxifen reduced hormone receptor positive breast cancer by about one third in pre and post-menopausal women at 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, coordinated in Australia and New Zealand by the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG), and globally by Cancer Research UK, involved 7,154 pre and post-menopausal women in seven countries including 2,674 entered by the ANZ BCTG. All women on the trial had an increased risk of breast cancer; determined by family history of the disease, previous benign breast disease and other risk factors. 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.

Professor Jack Cuzick, Global Coordinator of the trial, 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.

John Forbes, Professor of Surgical Oncology at the University of Newcastle, Newcastle Mater Hospital and ANZ BCTG Study Chair for IBIS-I, said: "Previous studies have shown that tamoxifen lowers the risk of developing breast cancer during the active preventive treatment phase (five years). For the first time, we now have clear evidence on the benefits and side effects of tamoxifen after preventative treatment with the drug has stopped. These new findings suggest that the long term cost benefit of taking tamoxifen for prevention of breast cancer is substantially more favourable than we had thought."

Professor Forbes also said: "These new results are a wonderful tribute to, and a reward for, the women who took part in IBIS-I, and the ANZ BCTG researchers. Almost all the women chose to continue in the trial after the first results were released. Now they can see the gratifying results of their continued commitment. When we realise that this commitment of several thousand women, in a trial like IBIS-I, can ultimately provide global benefit for potentially millions of women, we are reminded how important clinical trials research is."

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 ANZ BCTG has commenced a new, global prevention trial called IBIS-II which is for post-menopausal women at increased risk of breast cancer. IBIS-II is investigating whether the aromatase inhibitor anastrozole is effective for prevention of breast cancer in post-menopausal women at increased risk. IBIS-II will also investigate whether anastrozole has fewer side effects than tamoxifen.

Women aged 40-70 who are at increased risk of breast cancer, usually because of a strong family history, can obtain more information regarding IBIS-II by telephoning Freecall 1800 640 709 in Australia.

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For interviews with Professor John Forbes concerning either the new IBIS-I results or the new IBIS-II trial, please contact:

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References

- * Cuzick J, Forbes JF, Sestak I, Cawthorn S, Hamed H, Holli K, et al. Long-Term Results of Tamoxifen Prophylaxis for Breast Cancer – 96 Month Follow-up of the Randomized IBIS-I Trial. JNCI 2007; 99:272-282.
- 1 IBIS-1, International **B**reast Cancer Intervention **S**tudy I
- 2 IBIS-I investigators, 2002, First results of the International Breast cancer Intervention Study (IBIS-I): a randomised prevention trial. Lancet. 2002 Sept 14; 360, p: 817-24.

NOTES TO EDITORS

Breast cancer

- In Australia, breast cancer is the most common invasive cancer diagnosed in women, with more than 12,000 new cases in 2002. It is projected that there will be over 13,000 new cases in 2007.

IBIS-I Patient Population

- A total of 7,154 women were included in this analysis.
- 97% of all women reported some family history whereas 8% 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 was 50.7 years and 54.7% were between the ages of 45 to 54 years. 53.8% were post-menopausal, 40.8% used HRT at some point before the trial, and 55.9% were overweight (BMI over 25) at entry.
- 2,674 women from Australia and New Zealand were entered by the ANZ BCTG.

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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 (OR=0.71 (0.56-0.89), P=0.002).
- There was no reduction in the risk of ER-negative invasive tumours (35 vs. 35, OR=0.99 (0.60-1.64)) but ER-positive breast cancers were reduced by 34% in the tamoxifen arm (87 vs. 129, OR=0.66 (0.49-0.88)).
- 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, OR=0.48 (0.31-0.72)). However, for women taking HRT during the trial no clear effect of tamoxifen was seen overall (64 vs. 68, OR=0.93 (0.65-1.34)) or for ER-positive tumours (40 vs. 43, OR=0.89 (0.56-1.41)).
- All cause mortality was non-significantly higher in the tamoxifen group (66 vs. 55, P=0.36). The excess is smaller than in the first report (25 vs. 11). No specific cause of death was elevated in the tamoxifen arm and this is probably a chance finding.

IBIS-I Tolerability Results

- Of the thromboembolic events, deep-vein thrombosis (DVT) and pulmonary embolism (PE) were the only adverse events elevated in the tamoxifen group on a significant level (52 vs. 23, P<0.001). However, after ceasing active treatment the rates were equally distributed between the two treatment arms (P=0.75).
- A total of 28 endometrial cancers were reported (17 vs. 11, OR=1.54 (0.68-3.65)). 12 of the endometrial cancers in the tamoxifen group were detected during the active treatment compared to only three in the placebo group (P=0.02). After stopping tamoxifen, slightly less women in the tamoxifen group reported endometrial cancer compared to those in the placebo group (5 vs. 8, P=0.4).
- Gynaecological side effects such as abnormal bleeding or vaginal discharge, or vasomotor side effects were significantly increased in the tamoxifen arm during active treatment compared to the placebo arm (all P<0.001). However, after active treatment an increase in hot flushes was seen in the placebo group, whereas reports in the tamoxifen group remained stable and no statistical difference was observed between the two groups post-treatment. Similar results were seen for abnormal vaginal bleeding. Overall, reports decreased after active treatment of the tamoxifen and no significant difference was observed between the two treatment groups.

IBIS-II (International Breast cancer Intervention Study II)

IBIS-II is being coordinated in Australia and New Zealand by the Australian New Zealand Breast Cancer Trials Group and globally by Cancer Research UK. The trial is taking place in 21 countries including Australia, New Zealand, India, Chile, Germany, Italy and the UK.

- The IBIS-II Prevention part of the study aims to recruit 6,000 post-menopausal 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 and 70 years and are not on HRT.
- IBIS-II DCIS will recruit 4,000 post-menopausal 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-II Prevention.
- Further information on IBIS-II is available at www.anzbctg.org.
- In Australia women can obtain more information on IBIS-II by telephoning 1800 640 709.