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**MEDIA RELEASE**

**15 DECEMBER 2006**

**TAMOXIFEN CONTINUES TO HELP PREVENT BREAST CANCER  
EVEN AFTER TREATMENT IS COMPLETED**

New, long-term results of a worldwide breast cancer prevention study - called IBIS-I - confirm that tamoxifen, a well established treatment for breast cancer, also reduces the risk of hormone receptor positive breast cancer by 34% in women at increased risk of the disease, and that the benefit continues for at least several years even after treatment with the drug has stopped.

Initial IBIS-I results released in 2002 demonstrated that tamoxifen reduced hormone receptor positive breast cancer by about one third in pre and post-menopausal women at increased risk of the disease<sup>1</sup>. Today's findings presented at the San Antonio Breast Cancer Conference in Texas, USA, confirm that these benefits continue for at least another five years after treatment has stopped<sup>2</sup>.

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 from 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) daily 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 – a significant reduction in risk of 29%, (P=0.002), after an average follow-up of 96 months.

Professor Jack Cuzick, Global Coordinator of the trial, from the Cancer Research UK Centre for Epidemiology, Mathematics and Statistics, who presented the results at the conference 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 while the protective benefits of tamoxifen continue post-treatment, almost all of the side effects reported on tamoxifen do not occur in excess during that time."

Researchers have found that serious side effects like endometrial cancer and blood clots limit the use of tamoxifen in helping to prevent breast cancer. However, further IBIS-I data presented at the conference<sup>3</sup> demonstrated that these serious side effects stopped 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: "These new IBIS-I results are very pleasing – the prevention benefit continues long term after tamoxifen is stopped whereas the side effects experienced cease. This means that, with longer follow-up, the risk-benefit ratio has become more in favour of tamoxifen than previously believed and may further improve in the longer term. The results are also an important step towards the goal of effective prevention strategies for all women at risk of breast cancer and a sound scientific basis for further prevention research."

Professor Linda Reaby, Coordinator of the ANZ BCTG Consumer Advisory Panel 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."

### **Further evidence on combined use of HRT and tamoxifen in prevention**

Hormone Replacement Therapy (HRT) is known to increase the risk of oestrogen receptor positive breast cancer and many clinicians believe that tamoxifen can be used in combination with HRT to reduce that risk. However, the latest IBIS-I results suggest that women who took tamoxifen and HRT may not benefit from the protective benefits of tamoxifen. Professor Forbes said: "Previous research has suggested that women taking HRT together with tamoxifen have a lower risk of breast cancer compared to those not taking tamoxifen. The IBIS-I results are therefore very important and we must continue to examine these because they suggest the opposite; that women on tamoxifen and HRT may not benefit from taking the tamoxifen."

### **The future of breast cancer prevention**

Commenting on what the future of breast cancer prevention holds, Professor Jack Cuzick said: "The side effects of tamoxifen in the five years of treatment are a concern but we now know that these stop after treatment is completed. However, we must continue our search for a preventive option which is safer and more effective than tamoxifen from the commencement of treatment."

He concluded: "A new type of breast cancer treatment called an aromatase inhibitor, may be able to prevent up to 75% of hormone receptor positive breast cancers, and these drugs do not have the gynaecological or thromboembolic side effects of tamoxifen. They offer another attractive possibility for prevention."

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. Women 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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### **References**

- 1 Cuzick J, Forbes JF, Edwards R, Baum M, Cawthorn S, Coates A, Hamed A, Howell A, Powles T; IBIS investigators. First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial. *Lancet*. 2002 Sep 14;360(9336):817-24.
- 2 Jack Cuzick on behalf of the IBIS investigators. Long term efficacy of tamoxifen for chemoprevention - results of the IBIS-I study. Presented at San Antonio Breast Cancer Symposium, 16 December 2006.
- 3 Sestak I, Forbes JF, Kealy R, Edwards R, Howell A, Cuzick J. Comparison of side effect profiles during active treatment versus follow-up in the IBIS-I tamoxifen prevention study. Poster Presentation: San Antonio Breast Cancer Symposium 15 December.

## 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 2006.

### 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 postmenopausal, 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.

### 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 3 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.