



Media Release

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## **' First IBIS results show tamoxifen reduces breast cancer in healthy high-risk women – but still too early to know if benefits outweigh risks '**

First results from the long-awaited IBIS trial<sup>i</sup> into the use of tamoxifen to prevent breast cancer in healthy women at high risk have firmly established that the drug can indeed cut the incidence of the disease.

These preliminary results were presented on Wednesday 20 March at the 3<sup>rd</sup> European Breast Cancer Conference in Barcelona together with an overview of the four breast cancer prevention trials<sup>ii</sup>. Results from the previous studies have been mixed.

In addition, nine trials using tamoxifen for treatment of breast cancer patients and who were therefore at high risk of developing a second cancer in the opposite breast, were also reviewed.

IBIS lead investigator Professor Jack Cuzick, who is from Cancer Research UK, told the conference that the incidence of breast cancer was reduced by a third in the women taking tamoxifen in the IBIS trial with 68 cases of breast cancer compared with 101 among those taking the placebo. When the results of all the prevention trials were combined the overall reduction was 38%. The trials of the adjuvant treatment of breast cancer in patients showed a slightly greater (46%) reduction in the incidence of second cancers in the opposite breast.

IBIS is an international study which is conducted in Australia and New Zealand by the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG)<sup>iii</sup>. The ANZ BCTG is Australia's national breast cancer research body conducting research for prevention, treatment and cure of breast cancer through a collaborative national and international clinical trials research program.

The reduction in incidence of breast cancer in IBIS was found only in oestrogen receptor (ER) positive (hormone sensitive) breast cancers with no effect on cancers that were oestrogen receptor (ER) negative. The benefit was the same whatever the age of the woman, whatever the level of risk and whether or not she was taking hormone replacement therapy.

However, while the benefits of tamoxifen for treating breast cancer patients are indisputable, there is still no conclusive answer as to whether the benefits outweigh the side effects for prevention in healthy women, according to Professor Cuzick. "All along the line, we have kept the volunteers in the trial fully informed of developments. That is why we and the Independent Data Monitoring Committee felt it was right to report these preliminary findings at this point. But, I stress that these results are preliminary and it is essential to continue to follow the participants to see if a particular high risk group of healthy high-risk women can be identified for whom the benefits of tamoxifen clearly outweigh any risks."

It is also too early, he said, to judge the ultimate effect on breast cancer deaths among the prevention trials in healthy women. In the IBIS trial only four breast cancer deaths have been reported so far – two in the tamoxifen arm and two in the placebo arm. However, the likely potential mortality benefit could be calculated if certain factors<sup>iv</sup> were assumed. "For high risk women, we calculate that deaths from breast cancer within 10 years of diagnosis would be reduced by 18%."

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Professor John Forbes, IBIS Study Coordinator for Australia and New Zealand agreed with Professor Cuzick. "It seems very likely from the IBIS data that future breast cancer deaths may be avoided. We must continue the follow up of women on IBIS to first learn what happens to breast cancer risk after tamoxifen is stopped."

Other key findings from IBIS were also generally in line with the other tamoxifen trials, confirming that there was a 2 to 3-fold increase in the risk of endometrial cancer and a 2 to 3-fold increase in the risk of thromboembolism for women taking tamoxifen.

For all of the prevention trials combined there was no effect on all-cause mortality with 112 deaths in the tamoxifen arms and 122 in the placebo arms. However, there were variations, with statistically non-significant reductions in death in two trials, no difference in one trial and a statistically significant excess of deaths in the IBIS trial.

Professor Cuzick said: "In IBIS there were more deaths in the tamoxifen arm with 25 against 10 in the placebo arm. Deaths from cancers other than the breast were higher, but the numbers of these cancers were not increased, suggesting this was likely to be a chance finding. Also, with the exception of venous thromboembolic events, other vascular and cardiac events were not increased. This suggests that, apart from two possible deaths from pulmonary embolism (PE), the increases in other vascular and cardiac deaths were also chance findings."

Professor Cuzick said that in the prevention trials overall, non breast cancer deaths appeared to be similar, but the small excess of PE deaths in IBIS and one other trial – the American P1 study– indicated that thromboembolism was the most important complication of tamoxifen use.

"Every effort should be made to reduce this risk, although we must keep it in perspective. It is about the same level of risk as that faced by a woman taking HRT, and if you are a breast cancer patient taking tamoxifen for treatment it is absolutely essential that you continue the treatment. Tamoxifen is a lifesaver and the single most effective medical treatment for breast cancer. Any risks from tamoxifen used for treatment are far outweighed by the benefits. There are many more thousands of breast cancer patients alive today because of tamoxifen."

Professor Cuzick concluded: "We need, however, to be aware of the potential risks of blood clots in women taking tamoxifen. We know that there is a link between blood clots and surgery, with 40% of all the clotting events in our trial occurring within three months of surgery or following immobility. Most of these events were in the tamoxifen arm. Thus, it would seem a wise precaution to discontinue tamoxifen before any major surgery, to ensure that appropriate anti-clotting treatments are provided during surgery and not to recommence tamoxifen until at least one month after surgery. Similar precautions would also be appropriate for women who become immobile for any reason."

Professor Forbes stressed the importance of learning more about side effects. "We need longer follow up to identify which women benefit most from tamoxifen; both in terms of breast cancer prevention and minimising risks for individual women".

"The IBIS results mark the end of the beginning of breast cancer prevention. We now know that we can prevent some breast cancers. We can now go forward to test new prevention strategies with the ultimate goal of prevention of all breast cancer with minimum risks to women."

"We expect to begin testing the new agent anastrozole which has been shown to be better than tamoxifen for prevention of new contralateral breast cancer in women diagnosed with breast cancer" he said.

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Professor Forbes acknowledged the contributions of participants to IBIS. "I wish to pay tribute to those women in Australia and New Zealand who have participated in this trial, the results of which have potential benefits for many women worldwide. We will advise women on IBIS that results have been presented and keep them informed at every step".

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Abstract no: 20

<sup>i</sup> The International Breast Cancer Intervention Study (IBIS) involves more than 7,000 healthy women at increased risk of breast cancer. Half are taking the drug tamoxifen and half are taking a placebo (dummy) tablet. It is a randomised double-blind trial i.e. one in which neither the volunteers nor the doctors know which women are taking tamoxifen or placebo. It is coordinated by the British charity Cancer Research UK and the countries taking part are the UK, Finland, Switzerland, Belgium and Australia and New Zealand through the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG).

<sup>ii</sup> The three other prevention trials are:

- NSABP P1 Tamoxifen Prevention Trial (USA)
- The Royal Marsden Hospital chemoprevention trial
- The Italian National Trial

<sup>iii</sup> IBIS was conducted by the ANZ BCTG in 19 participating institutions throughout Australia and New Zealand contributing 37% of total international accrual (2,674 participants). Australia was the first country to randomise a participant to IBIS (April 1992), and also randomised the last participant in March 2001. This study has been funded in Australia by the National Health and Medical Research Council (NHMRC).

<sup>iv</sup> The assumptions when estimating the potential effect on breast cancer mortality were:

- an incidence rate of 6/1000 breast cancer per year
- 25% of the breast cancers would be ER negative
- tamoxifen reduces the incidence of ER positive cancers by 50% for five years and 30% in the next five years
- tamoxifen is ineffective for ER negative cancers
- 10 year survival for ER positive cancers in the placebo arm is 75%
- 10 year survival for ER positive cancers in the tamoxifen arm is 70%
- 10 year survival for ER negative tumours is 60%

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**Spokespeople from the ANZ BCTG are available for comment on these results. Further information can be sourced at [www.anzbctg.org](http://www.anzbctg.org)**

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