



MEDIA RELEASE

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Study involving Australian women suggests letrozole reduces the risk of post-surgery recurrence of early breast cancer when compared with tamoxifen

An international clinical trial in which the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG) is making a major contribution, has established that in postmenopausal women with early breast cancer, the drug letrozole offers better post-surgery protection against breast cancer recurrence than does tamoxifen, the current standard of care.

Results from the trial, Breast International Group (BIG) 1-98, which involved the largest number of women from Australia recruited to an international breast cancer treatment trial, have been published in the *New England Journal of Medicine*.

The BIG 1-98 trial studied the effectiveness of two drugs, the well-established anti-oestrogen agent, tamoxifen, and the newer aromatase inhibitor, letrozole. The trial is uniquely designed to study two important questions for the treatment of postmenopausal women with early breast cancer who have the type of breast cancer that responds to endocrine treatments such as tamoxifen and letrozole (oestrogen receptor positive or progesterone receptor positive):

- 1) Is a five-year program of letrozole better than a five-year program of tamoxifen?
and
- 2) Is a five-year program of letrozole better than a sequence that begins with tamoxifen for the first two years followed by letrozole for three years, or better than a sequence that begins with letrozole for the first two years followed by tamoxifen for three years?

In 2005 this clinical trial showed that letrozole for five years was superior to tamoxifen for five years in preventing breast cancer recurrence, especially distant recurrence. This 2009 update shows a continued significant reduction (12%) in recurrences (including second malignancies and deaths prior to cancer event), and evidence of a reduction (13%) in deaths. The difference in outcomes between these two treatment programs is diluted because one quarter of the patients on the tamoxifen program “crossed over” and began to take letrozole after the early results were presented in 2005. The trend toward improved survival benefit has not been observed in other trials comparing five years of tamoxifen to other aromatase inhibitors.

Professor Alan Coates, Scientific Committee Co-Chairman of the International Breast Cancer Study Group which coordinated the trial, put the results in perspective, saying “The results of BIG 1-98 are of great importance for the majority of patients with breast cancer. We already knew from our earlier results that letrozole alone is more effective than tamoxifen alone, but we did not know if giving both of the agents in a sequence (of letrozole followed by tamoxifen or tamoxifen followed by letrozole) would show superior results. We found that it seems the best - or the most promising - strategy to start with letrozole, but if necessary patients can switch to tamoxifen after two years without loss of efficacy.”

Professor John Forbes, University of Newcastle, Study Chair of BIG 1-98 for the ANZ BCTG and a Member of the BIG 1-98 International Steering Committee said “Together with optimal surgery, followed by chemotherapy and radiotherapy if needed, incorporation of letrozole early in the treatment plan is the best way to control the disease, especially for patients with a higher likelihood of recurrence, such as cancer that has spread to the lymph nodes near the breast. The trend for reduction in mortality with letrozole for five years compared with tamoxifen for five years reinforces our earlier results and confirms the need for careful long-term follow up and reporting of clinical trials, even after treatment has been completed.”

The BIG 1-98 trial compares:

- Tamoxifen for two years followed by letrozole for three years versus five years of letrozole
- Letrozole for two years followed by tamoxifen for three years versus five years of letrozole
- Five years of tamoxifen versus five years of letrozole

Methods and Results

BIG 1-98 is a multinational Phase III double-blind, randomised, multicentre trial that is being conducted in 27 countries and involves more than 8,000 postmenopausal women with early breast cancer.

The ANZ BCTG conducted the BIG 1-98 study in 29 centres in Australia and New Zealand and recruited 804 women, 10% of the worldwide total.

The primary goal of the study was to determine if letrozole could reduce the risk of a disease-free survival event (breast cancer recurrence, occurrence of a second primary cancer or death without recurrence having occurred) compared with tamoxifen. Many breast cancers depend on oestrogen for their growth. Letrozole is an aromatase inhibitor, a type of drug that blocks production of oestrogen in postmenopausal women. Tamoxifen works by blocking the effect of oestrogen at the tumour cell.

The primary conclusions of BIG 1-98 are:

- Updated results of BIG 1-98 suggest superior overall survival with letrozole compared with tamoxifen
- Adjuvant endocrine therapy should start with letrozole especially for patients at higher risk for early recurrence
- Patients commenced on letrozole can be switched after two years to tamoxifen, if required
- Safety is consistent with known safety profiles of each agent
- Improved therapeutic approaches beyond five years are required to control late recurrence

Professor Forbes said “BIG 1-98 is an impressive international collaboration involving Australian researchers to extend the evidence base for adjuvant therapy of breast cancer. The trial shows clearly that this population of women had a better outcome if their treatment commenced with letrozole rather than with tamoxifen. It adds to our knowledge of the advantages of the aromatase inhibitors in this role, and will assist women and their doctors in reaching appropriate treatment choices.”

Professor Forbes concluded, “We are indebted to the women from Australia and worldwide who are taking part in the trial. The commitment of these women involved in the trial will lead to a better outcome for many thousands of other women throughout the world.”

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For further information on this media release and to arrange interviews with Professor Coates, Professor Forbes and other ANZ BCTG researchers, please contact:

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NOTES TO EDITORS

About the BIG 1-98 trial

BIG 1-98 is being conducted under the auspices of the Breast International Group (BIG) and coordinated and managed by the International Breast Cancer Study Group (IBCSG). The IBCSG is an active member of the BIG organisation. In Australia and New Zealand the trial is being conducted by the Australian New Zealand Breast Cancer Trials Group (ANZ BCTG), based at the University of Newcastle.

About the Australian New Zealand Breast Cancer Trials Group

The Australian New Zealand Breast Cancer Trials Group (ANZ BCTG) is Australia's national breast cancer research group. It is dedicated entirely to breast cancer research through the conduct of multi-institution and international clinical trials for the treatment and prevention of breast cancer. Working in collaboration with 300 researchers in more than 80 of the leading medical institutions in Australia and New Zealand, and with similar research groups in 15 countries internationally ensures Australia and New Zealand are at the forefront of breast cancer research progress and this delivers benefits to women immediately. Additional information can be found at www.anzbctg.org.

About the International Breast Cancer Study Group

The International Breast Cancer Study Group (IBCSG), created as the 'Ludwig Breast Cancer Study Group' in 1977, is dedicated to innovative clinical research designed to improve the outcome of women with breast cancer. Additional information regarding BIG 1-98 or the IBCSG can be found at www.ibcsg.org.

About the Breast International Group

The Breast International Group (BIG) is an international non-profit organisation dedicated to coordinating large breast cancer trials among its membership. These include well-established clinical research and cooperative groups based in Europe, Australia, New Zealand, South Africa and Canada, with affiliated centres around the world. Additional information about the BIG can be found at www.breastinternationalgroup.org.