MedicalXpress

Breast cancer survival rates improved by novel drug sequence, say researchers

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Changing the way women are treated for breast cancer could improve their overall chance of survival, according to research published today in the *Lancet*. The new paper shows that switching to a drug called exemestane, two to three years after commencing standard therapy with the drug tamoxifen, can cut the risk of death for certain women by a further 17% compared with using tamoxifen alone.

Postmenopausal women with early-stage hormone-sensitive primary breast cancer are usually treated with tamoxifen for five years, once they are free of disease, to reduce the risk of their cancer recurring. This therapy was once viewed as the ‘gold-standard' treatment and it has been shown to cut the risk of death by 34%.

Over recent years, increasing numbers of these women have been receiving treatment with tamoxifen followed by Aromatase Inhibitors such as exemestane.

The Intergroup Exemestane Study (IES), which involved women from 37 different countries, has been examining the benefits of taking tamoxifen for two to three years and then switching to exemestane for the remainder of the five-year period. This new research is the first to show that early benefits of the tamoxifen and exemestane treatment sequence are maintained after treatment has stopped.

The majority of breast cancer cases are hormone-sensitive, meaning that the cancer cells respond to oestrogen and die when they are deprived of

the hormone. Tamoxifen works by preventing oestrogen from acting on cancer cells, whereas exemestane is an Aromatase Inhibitor, which works by stopping the body's production of oestrogen.

The researchers believe that during treatment with tamoxifen, some cancer cells can become resistant to the effects of the drug. Exemestane is subsequently able to kill these resistant cells by withdrawing the oestrogen from circulation.

The researchers examined 2,352 postmenopausal women with early-stage breast cancer who switched to exemestane, compared with another group of 2,372 women who were treated with tamoxifen alone. The women were halfway through their five-year tamoxifen treatment when they joined the study and they were followed up for a median of 56 months after this point.

The study found that the women taking exemestane had a 15% lower risk of dying than those taking only tamoxifen. When women whose tumours were found not to be hormone sensitive were excluded (8% of the total), the improvement increased to 17%.

The results of the study also suggest that sequential use of tamoxifen and exemestane is safe and well tolerated.

Professor Charles Coombes, lead author of the paper from the Cancer Research UK Department of Cancer Medicine at Imperial College London, and based at Hammersmith Hospital, said: "This study shows that, in order to get best results, patients need to be treated with a sequence of anti-hormonal treatments. Just giving one or other drug, such as has been done in some other studies, has not been shown to give added benefit in terms of improved survival. The task now is to determine what other drugs should be given in sequence to prevent cancer cells that have become resistant to exemestane from growing."

Professor Judith Bliss, Director of The Cancer Research UK Clinical Trials and Statistics Unit at The Institute of Cancer Research said: "This trial is an excellent example of how international collaborations between researchers and clinicians can be quickly translated into a cost effective treatment strategy providing patient benefit. To the many postmenopausal breast cancer patients around the world this new research offers the hope of improved treatment options."

Current practice is to give patients treatment for a period of time after surgery and then stop. Following this, doctors wait for a recurrence of the cancer, at which point it is often impossible to cure the disease.

Professor Coombes added: "The other challenge is to find a way of monitoring breast cancer to find a blood test that can tell us when some cancer cells are once more growing. This will allow us to time the sequence of treatment more accurately. A test for early resistance would give us a chance of curing the disease whilst it is still at an early stage."

Source: Imperial College London