Balancing trastuzumab's survival benefits and heart risks for women with breast cancer

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Adding trastuzumab (trade name Herceptin) to the treatment offered to women who have HER2-positive breast cancer, significantly increases the chance of life being prolonged, and reduces the chance of tumours reappearing once therapy stops. This is important, because about one-fifth of women who develop early breast cancer have HER2-positive tumours that, if untreated, are associated with a worse outlook than HER2-negative tumours. At the same time, however, women given trastuzumab have a higher risk of experiencing problems with their heart. These findings are the key conclusions of a systematic review published in *The Cochrane Library*.

Breast cancer is the most common diagnosed cancer in women. There are different types of breast cancer cells, but one feature is whether the tumour's cells produce excess quantities of a particular protein called the human epidermal growth factor receptor 2 (HER2). Cells which do are known as HER2-positive, while those with normal production are referred to as HER2-negative. Trastuzumab is a new-generation antibody based medicine that blocks the receptor and stops it triggering the excessive cell growth that causes tumours.

To provide clinicians and patients with accurate evidence of trastuzumab's harms and benefits, a team of researchers based in Milan and Modena, Italy, were keen to study available clinical trial data. They identified eight trials that involved 11,991 women with HER2-positive operable breast cancer who had been assigned randomly either to receive trastuzumab or not, in addition to other treatments. Women were

followed by clinicians for several years (three on average).

The overall finding was that breast cancer mortality was reduced by one-third, but the risk of heart toxicity went up five times for women receiving trastuzumab compared with women receiving standard therapy alone.

If 1000 women were given standard therapy with no trastuzumab then after three years about 900 would survive, but if 1000 women were treated with standard chemotherapy and trastuzumab for one year, about 933 would survive.

"This means that for every 1000 women treated with trastuzumab, 33 more women will have their lives prolonged," says lead researcher Lorenzo Moja who works in the Department of Public Health at the University of Milan. In addition, about 95 more women will remain disease-free once therapy has stopped.

However, the study showed that the treatment isn't free of problems. About 26 in 1000 women taking trastuzumab experienced serious heart toxicity. This is 21 more than the chemotherapy alone group.

"These heart toxicities are often reversible if the treatment is stopped straight away," says Moja.

The researchers conclude that in women at higher risk of recurrence and with no signs of a weak heart, trastuzumab offers far more benefits than risks.

The balance of risks to benefits is less clear and must be carefully evaluated in women at lower risk of recurrence, for example if they only have a small tumour, or those who are at increased risk for cardiac complications. "The oncologist should share the decision with the

patient, after careful consideration of the risks and benefits," says Roberto D'Amico, senior scientist at the Clinical Trial Unit of the Department of Oncology of the University of Modena.

More information: Moja L, Tagliabue L, Balduzzi S, Parmelli E, Pistotti V, Guarneri V, D'Amico R. Trastuzumab containing regimens for early breast cancer. Cochrane Database of Systematic Reviews 2012, Issue 4. Art.No.:CD006243. DOI: 10.1002/14651858.CD006243.pub2