

Trastuzumab raises risk of heart problems in the elderly with history of heart disease or diabetes

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(Medical Xpress) -- The first study to investigate the effect of the breast cancer drug trastuzumab (Herceptin) on heart and vascular function in elderly patients has found that it increases the risk of heart problems, particularly in women with a history of heart disease, diabetes or both.

Authors of the study, published in the cancer journal, *Annals of Oncology*, looked at records for 45 women aged between 70 and 92 who had been treated with [trastuzumab](#) since 2005 and found that 26.7% (12) of the patients developed [heart problems](#) caused by the drug – a slightly higher rate than seen in earlier, clinical trials in younger, healthier women. Thirty-three percent of the women with a history of [heart disease](#) developed either asymptomatic and symptomatic heart problems as a result of taking trastuzumab, compared to only 9.1% of women without such a history, and 33.3% of women with [diabetes](#) developed problems compared to only 6.1% without the condition. When trastuzumab treatment was stopped, all but one of the women recovered fully and five of them were able to re-start the treatment.

Trastuzumab is the current standard of care for women diagnosed with the type of breast cancer that expresses the protein HER2 on the surface of the cancer cells (HER2 positive breast cancer). Although breast cancer is most common in elderly women, clinical trials of trastuzumab have been carried out in younger women, "ideal patients", who have few if any other health-related issues.

Dr César Serrano, who carried out the research while working as a clinical fellow at the Department of Medical Oncology Breast Cancer Centre at the Vall d'Hebron University Hospital in Barcelona, Spain, said: "This is the first study specifically to assess trastuzumab-related cardiac toxicity and the cardiovascular factors that are associated with an increased risk in a selected population of elderly breast cancer patients.

"Trastuzumab is generally well-tolerated and, although there are some concerns about it causing heart problems, until now few risk factors have been identified among patients in clinical trials, most of whom are usually younger than 70 years and have good general health. Our study has demonstrated a significantly increased incidence of cardiac events among patients aged 70 and over with cardiovascular risk factors such as a history of cardiac disease and diabetes.

"Approximately 70% of all newly diagnosed cancers occur in patients older than 65 and, given the expected increase in the absolute number of elderly cancer patients over the coming decades in Western countries, there is an unmet need for information about the efficacy and safety of anti-cancer treatments in daily clinical practice. Data obtained in this report can serve to advise clinicians to be aware of symptomatic and asymptomatic cardiac dysfunction in elderly patients. We think that it is reasonable to refer elderly breast cancer patients to a cardiologist if one or more cardiovascular risk factors are present before or during treatment with trastuzumab. Moreover, a closer surveillance of early symptoms and cardiac function is highly recommended."

Asymptomatic cardiotoxicity is defined as when there are no obvious symptoms of any heart problems, but assessment (usually via scanning or echocardiography) of the function of the heart's left ventricle shows an absolute drop of 10% or more, resulting in a left ventricle ejection fraction (LVEF) of less than 50% of normal its normal function, or an absolute drop of more than 20%. Symptomatic cardiotoxicity, such as

congestive heart failure, has obvious physical symptoms such as shortness of breath and swelling limbs.

Out of the 12 patients who developed heart problems, eight developed asymptomatic LVEF decline and four developed symptomatic congestive heart failure. All eight, asymptomatic patients recovered completely after they stopped taking trastuzumab, and then the drug was reintroduced in four patients. Only one of these had a repeat asymptomatic drop in LVEF, which improved without withdrawing the treatment.

"One of the main characteristics of trastuzumab cardiotoxicity is its reversibility. It is a well-known phenomenon that differs from other chemotherapeutic agents such as anthracyclines. Reversibility normally happens with treatment discontinuation, but also can also occur spontaneously," explained Dr Serrano. "The decision to reintroduce trastuzumab, or to continue with it, must be taken case-by-case together with a cardiologist."

Of the four patients who developed symptomatic congestive heart failure, three recovered their cardiac function after discontinuing trastuzumab and receiving standard cardiac therapy, and one was able to restart trastuzumab without any further problems. The fourth woman did not recover cardiac function, showing only a slight improvement and the doctors did not reintroduce any cancer treatment because of this. She died three months later due to progression of her cancer.

Dr Serrano, who is now working as a postdoctoral research fellow at the Brigham and Women's Hospital in Boston, USA, concluded: "It's important to be cautious when interpreting our data given the small number of women involved in the study and the very limited power to detect small differences. However, until safety cardiac data in [elderly patients](#) receiving trastuzumab becomes available from prospective

clinical trials, this study may contribute to identifying those elderly women with [breast cancer](#) who are most likely to develop heart problems during treatment with trastuzumab."

More information: "Trastuzumab-related cardiotoxicity in the elderly: a role for cardiovascular risk factors". *Annals of Oncology*.
[doi:10.1093/annonc/mdr348](https://doi.org/10.1093/annonc/mdr348)

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