

## **An evaluation of cardiovascular and oncologic outcomes associated with interruption vs. continuation of adjuvant trastuzumab following the development of mild left ventricular dysfunction.**

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**Background:** While trastuzumab has been proven effective in treating HER2 positive breast tumors, it may also be associated with an acute decline in left ventricular (LV) function. Managing trastuzumab therapy in the setting of mild LV dysfunction is a commonly encountered scenario that currently is guided by expert opinion. The objectives of this study were to retrospectively assess how trastuzumab was managed immediately after the development of mild LVD and evaluate associated cardiovascular (CV) and oncologic outcomes.

**Methods:** Heart function imaging data of patients who received adjuvant trastuzumab for breast cancer between September 2005 and September 2010 in British Columbia were evaluated. Patients who experienced a drop in LV ejection fraction (LVEF) to 40-49% or a greater than 15% drop in LVEF from their pre-chemotherapy baseline to a final LVEF  $\geq$ 50% were identified. The charts of these patients were reviewed for demographic information, comorbidities, trastuzumab dosing regime, CV events, and breast cancer outcomes.

**Results:** A total of 171 patients were included in this study. 121 (70.8%) patients had an immediate hold in their trastuzumab therapy while the remaining 50 (29.2%) continued with their next scheduled dose. The number of patients who experienced a cancer relapse event in the therapy interruption and continuation groups were 21 (17.4%) and 5 (10.0%), respectively ( $P = 0.25$ ). CV events in the therapy interruption group included a subsequent drop in LVEF to  $<$ 40% in 11 (9.1%) patients, congestive heart failure (CHF) in 2 (1.7%) patients, and 1 (0.9%) death related to CHF. CV events in the therapy continuation group included a subsequent drop in LVEF to  $<$ 40% in 3 (6.0%) patients and CHF in 1 (2.0%) patient.

**Conclusions:** When compared to holding trastuzumab immediately after the development of mild LVD, continuing trastuzumab did not appear to be associated with an increased risk of long-term CV events but did appear to be associated with a 7.4% absolute risk reduction in breast cancer recurrence. While these results are not statistically significant, they underscore the need for further investigation.

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