

# Trastuzumab Cardio-Oncology: Lessons Learned

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Treatment with the humanized monoclonal antibody trastuzumab can significantly improve outcomes for patients with early or metastatic HER2-positive breast cancer. In a small proportion of patients, trastuzumab is associated with an increased risk of cardiac dysfunction. Although the mechanisms have yet to be fully established, trastuzumab may block HER2 signaling in cardiomyocytes, which is believed to be important for protecting the cardiomyocytes from stress such as that induced by treatment with anthracyclines. The risk of trastuzumab-associated cardiac dysfunction can be reduced if patients are evaluated thoroughly for risk factors before treatment (e.g., hypertension, low ejection fraction at onset, hyperglycemia, prior congestive heart failure). In addition, cardiac function must be assessed before and during the treatment period. If cardiac dysfunction occurs during treatment, early intervention can expand the possibilities of reinstitution of trastuzumab treatment. The integration of nonanthracycline adjuvant regimens offers opportunities for cardiac-compromised patients.

**M**any chemotherapeutic regimens have the potential to adversely affect the heart (Jones, Haykowsky, Swartz, Douglas, & Mackey, 2007). The clinical benefits of using a particular chemotherapeutic agent must be weighed against its potential risk for producing adverse cardiac effects. The degree of risk considered acceptable depends upon a number of factors, including whether the patient has early-stage cancer or metastatic disease. In the adjuvant setting, treatment is given with curative intent; therefore, the risk of long-term cardiac complications should be minimized whenever possible. By contrast, a greater degree of cardiac risk is acceptable for patients with metastatic disease if the treatment is associated with a significant survival benefit.

Table 1 summarizes the potential risks associated with some adjuvant systemic therapies used in breast cancer. Most notable are the long-term effects associated with anthracycline therapy, namely a progressive decline in left ventricular (LV) function and congestive heart failure (CHF) (Jones et al., 2007). Trastuzumab treatment also has been associated with LV dysfunction and CHF; however, distinct differences exist between the clinical characteristics of and biologic mechanisms associated with the cardiovascular adverse effects of anthracyclines and those of trastuzumab (Ewer & Lippman, 2005).

Although they are the mainstay of treatment for early breast cancer, anthracyclines are associated with cardiac dysfunction (CD) (Bird & Swain, 2008). It can manifest acutely as arrhythmias and chest pain shortly after administration of an anthracycline or as heart failure months or years after administration (referred to as subacute and long-term toxicity, respectively) (Love & Steingart, 2007; Pinder, Duan, Goodwin, Hortobagyi, &

## At a Glance

- ◆ Trastuzumab is the standard of care for treatment of patients with early or metastatic HER2-positive breast cancer. Its use can be associated with cardiac dysfunction, the nature of which is believed to be different than that of anthracycline-related cardiac toxicity.
- ◆ Optimal cardiac safety is achieved when patients are evaluated thoroughly for cardiac risk factors before receiving trastuzumab and closely monitored for cardiac function throughout the treatment period and subsequently for at least two years.
- ◆ One way nurses can help minimize the risk of cardiac dysfunction is by educating patients about lifestyle changes that promote cardiac health.

Giordano, 2007). The risk of a patient experiencing cardiotoxic effects from anthracycline therapy is influenced by a number of treatment- and patient-related factors, including cumulative dose (doxorubicin 300 mg/m<sup>2</sup> or higher or epirubicin 600 mg/m<sup>2</sup> or higher), associated therapy (mediastinal radiation therapy or

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