

## HER2-TARGETED THERAPIES AND CARDIOTOXICITY

### Cardiotoxicities Associated With HER2-Targeted Therapies

- Heart failure (HF)
- Left ventricular ejection fraction (LVEF) decline

Prolonged trastuzumab therapy can increase the risk of cardiotoxicity 27% to 35%.<sup>1,2</sup> The risk of cardiotoxicity appears lower among patients treated with trastuzumab in the absence of anthracyclines, with LVEF decline and symptomatic heart failure occurring in 3.2 and 0.5%, respectively.<sup>3,4</sup>

### Patient Risk Factors

- Age
- Preexisting cardiovascular comorbid conditions (e.g., hypertension)
- Lower baseline LVEF
- Obesity
- Prior treatment with anthracycline chemotherapy

Trastuzumab-associated cardiotoxicity may occur at much higher rates (20% to 40% of patients) when used in combination with cardiotoxic chemotherapy (especially regimens containing anthracyclines) in high-risk patients.<sup>5</sup>

### Monitoring/Management Strategies

- Routine cardiac monitoring, including every-3-month echocardiogram during trastuzumab therapy, or tailor cardiac monitoring regimen based on an individual's risk of cardiotoxicity, as determined by baseline cardiovascular risk factors and the cardiotoxicity risk associated with the cancer treatment regimen.
  - Patients who exhibit diminished LVEF should be evaluated and followed by cardiology/cardio-oncology for management of cardiotoxicity.<sup>1</sup>
- Monitor and control existing cardiovascular risk factors (e.g., hypertension and diabetes).
- Possible benefit from beta-blocker and angiotensin-converting enzyme (ACE) inhibitor treatment; may allow longer duration of treatment with HER2-targeted therapies.<sup>6</sup>
- The use of biomarkers is unclear at this time, and more research is needed. Data show that early increases in biomarkers occur with breast cancer treatments, including troponin, NT-proBNP, and myeloperoxidase; these markers were noted to be associated with changes in LVEF.<sup>7</sup>
- *Prevention Measures*
  - Consider holding or discontinuing adjuvant trastuzumab in cases of mild, asymptomatic LV dysfunction.
  - Continuation of trastuzumab therapy in combination with intensive administration of cardiac medications (beta blockers and ACE inhibitors) and close clinical surveillance for progressive LVEF deterioration may be a safe alternative in patients with mild, asymptomatic LV dysfunction.

## References

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3. Tolaney SM, et al. *N Engl J Med.* 2015;372:134-41.
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