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.