Trastuzumab-induced cardiotoxicity: Risk factors, pharmacologic prevention and cardiotoxicity of novel agents

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Despite great success as a targeted breast cancer therapy, trastuzumab use may be complicated by heart failure and loss of left ventricular contractile function. Cardiovascular disease risk factors, advanced age and previous anthracycline treatment predispose to trastuzumab-induced cardiotoxicity (TIC), with anthracycline exposure being the most significant risk factor. Cardiac biomarkers such as troponins and pro-BNP and imaging assessments such as echocardiogram before and during trastuzumab therapy may help in early identification of TIC. Initiation of beta-adrenergic antagonists and angiotensin converting enzyme inhibitors may prevent TIC. Cardiotoxicity rates of other HER2-targeted treatments, such as pertuzumab, T-DM1, lapatinib, neratinib, tucatinib, trastuzumab deruxtecan and margetuximab appear to be significantly lower as reported in the pivotal trials which led to their approval.

Risk assessment for TIC should include cardiac imaging assessment and should incorporate prior anthracycline use the strongest risk factor for TIC. Screening and prediction of cardiotoxicity, referral to a cardio-oncology specialist and initiation of effective prophylactic therapy may all improve prognosis in patients receiving HER2-directed therapy. Beta-blockers and ACE inhibitors appear to mitigate risk of TIC. Anthracycline-free regimens have been proven to be efficacious in early HER2-positive breast cancer and should now be considered the standard of care for early HER2-positive breast cancer. Newer HER2-directed therapies appear to have significantly lower cardiotoxicity compared to trastuzumab, but trials are needed in patients who have experienced TIC and patients with pre-existing cardiac dysfunction.

Biography

Naomi Dempsey is a hematologist/oncologist with a focus on breast cancer with the Center for Hematology and Oncology at the Lynn Cancer Institute in Boca Raton, FL. She graduated from University of Miami Miller School of Medicine as a Doctor of Medicine in 2014. She then completed her internal medicine residency at Jackson Memorial Hospital in Miami in 2018. She also has experience in breast cancer basic science research, which she conducted during medical school and residency. She graduated from hematology/oncology fellowship in June 2021. She now leads the breast cancer clinical trials initiative at the Lynn Cancer Institute.