Management of Cardiotoxicity Induced by Anthracyclines and HER2 Antagonists

AMERICAN COLLEGE of CARDIOLOGY

PROBLEM

Anthracyclines cause cardiomyopathy.

- ✖ Reduction in left ventricular ejection fraction (LVEF) can occur acutely or over years and may or may not be symptomatic.
- ✖ Incidence rises with increasing doses (7%, 18%, and 65% at cumulative doses of doxorubicin 150 mg/m2, 350 mg/m2, and 550 mg/m2, respectively).

HER2 agents cause cardiomyopathy, hypertension, peripheral edema, and arrhythmias.

- ✖ The risk of cardiomyopathy increases from 4.12 times to 7.19 times higher when used alone vs. sequentially after anthracyclines.

SOLUTION

- ✔ If cardiomyopathy is detected and treated within 3 months, the reduction in LVEF may be reversible.
- ✔ Cardiomyopathies attributed to HER2 agents are often reversible with cessation of therapy.
- ✔ If LVEF drops >10% to below 50%, or 20%, or if heart failure symptoms develop, consider holding therapy (in consultation with oncologist and discussion with the patient) and initiate treatment for heart failure with renin-angiotensin-aldosterone system (RAAS) inhibitor and beta-blocker, mineralocorticoid receptor antagonist (MRA) plus diuretic as needed.
- ✔ Identify high-risk patients: Age >60 years, baseline cardiac disease (LVEF 50-55% or history of myocardial infarction, moderate to severe valvular disease), ≥2 cardiac risk factors (smoking, hypertension, diabetes, dyslipidemia, obesity)
- ✔ Track cumulative dose, concomitant exposure to radiation and/or trastuzumab

INSTITUTE PREVENTATIVE STRATEGIES OUTLINED IN THE FOLLOWING TREATMENT TABLE:

Drug	Cardiotoxic Effects	Monitoring Strategies	Preventative Strategies
Anthracyclines	• Cardiomyopathy (7-65%) • Cumulative dose at which incidence rises:	• Assess baseline LVEF prior to therapy initiation • LVEF after 4 cycles for all patients • LVEF after each additional cycle beyond doses at which incidence of cardiomyopathy rises • Consider monitoring troponin or global longitudinal strain for early detection of cardiac injury in high risk patients • LVEF 6-12 months after completion of therapy • Long-term monitoring is not well defined	• Identify and treat modifiable risk factors • Anthracycline: Reduce dose, continuous infusion, use of liposomal doxorubicin • Consider dexrazoxane in high-risk patients • Data for prophylactic RAAS inhibitor, beta blocker, or statin in high-risk patients are limited
Doxorubicin	>250 mg/m^2		
Daunorubicin	>400-550 mg/m^2		
Epirubicin	>600 mg/m^2		
Idarubicin	>160 mg/m^2		
Mitoxantrone	>200 mg/m^2		
HER2 Inhibitors		• Assess baseline LVEF prior to therapy initiation • LVEF every 3 months during therapy and at completion • LVEF every 6 months for 2 years after completion of trastuzumab • LVEF every 4 weeks if agent held for cardiomyopathy • May resume following recovered LVEF • Permanently discontinue therapy if LVEF does not improve or heart failure develops • Consider global longitudinal strain monitoring to detect patients at higher risk for developing cardiomyopathy	• Identify and treat modifiable risk factors • Data for prophylactic RAAS inhibitor, beta blocker, or statin in high-risk patients are limited
Trastuzumab	• Cardiomyopathy: 3-28% • Arrhythmias: 5% • Hypertension: 4% • Peripheral edema: 5%		
Lapatinib	• Chemotherapy-related cardiac dysfunction: 2-5%		
Pertuzumab	• Chemotherapy-related cardiac dysfunction: 3-8% • Peripheral edema: 1-5%		
Ado-trastuzumab emtansine	• Chemotherapy-related cardiac dysfunction: 1-2% • Hypertension: 5-6% • Peripheral edema: 4-7%		
Fam-trastuzumab deruxtecan	• Chemotherapy-related cardiac dysfunction: 1%		

BEST PRACTICES

- ✔ Establish a cardio-oncology clinic in collaboration with oncology, as well as systematic protocols for identifying and monitoring high-risk patients for the early detection of cardiomyopathy.
- ✔ Treat cardiomyopathy with RAAS inhibitors, beta blockers, and MRA.

To download the infographic and see citations visit
ACC.org/Infographics