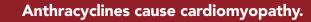
## Management of Cardiotoxicity Induced by Anthracyclines and HER2 Antagonists







- **★** 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.
- ✓ If cardiomyopathy is detected and treated within 3 months, the reduction in LVEF may





- ✓ 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	<ul><li>Cardiomyopathy (7-65%)</li><li>Cumulative dose at which incidence rises:</li></ul>	<ul> <li>Assess baseline LVEF prior to therapy initiation</li> <li>LVEF after 4 cycles</li> </ul>	<ul> <li>Identify and treat modifiable risk factors</li> <li>Anthracycline: Reduce</li> </ul>
Doxorubicin	>250 mg/m²	<ul><li>for all patients</li><li>LVEF after each additional cycle beyond doses</li></ul>	dose, continuous infusion, use of liposomal doxorubicin
Daunorubicin	>400-550 mg/m²	at which incidence of cardiomyopathy rises	Consider dexrazoxane in high-risk patients
Epirubicin	>600 mg/m²	Consider monitoring troponin or global longitudinal strain for early detection of cardiac injury	<ul> <li>Data for prophylactic RAAS inhibitor, beta blocker, or statin in high- risk patients are limited</li> </ul>
Idarubicin	>160 mg/m²	<ul><li>in high risk patients</li><li>LVEF 6-12 months after completion of therapy</li></ul>	
Mitoxantrone	>200 mg/m²	Long-term monitoring is not well defined	
HER2 Inhibitors		<ul> <li>Assess baseline LVEF prior to therapy initiation</li> </ul>	<ul> <li>Identify and treat modifiable risk factors</li> </ul>
Trastuzumab	<ul><li>Cardiomyopathy: 3-28%</li><li>Arrhythmias: 5%</li><li>Hypertension: 4%</li><li>Peripheral edema: 5%</li></ul>	<ul> <li>LVEF every 3 months during therapy and at completion</li> <li>LVEF every 6 months for 2 years after completion</li> </ul>	<ul> <li>Data for prophylactic RAAS inhibitor, beta blocker, or statin in high- risk patients are limited</li> </ul>
Lapatinib	Chemotherapy-related cardiac dysfunction: 2-5%	<ul> <li>LVEF every 4 weeks if agent held for cardiomyopathy</li> </ul>	
Pertuzumab	<ul><li>Chemotherapy-related cardiac dysfunction: 3-8%</li><li>Peripheral edema: 1-5%</li></ul>	<ul> <li>May resume following recovered LVEF</li> <li>Permanently discontinue</li> </ul>	
Ado-trastuzumab emtansine	<ul> <li>Chemotherapy-related cardiac dysfunction: 1-2%</li> <li>Hypertension: 5-6%</li> <li>Peripheral edema: 4-7%</li> </ul>	therapy if LVEF does not improve or heart failure develops  • Consider global longitudinal	
Fam-trastuzumab deruxtecan	Chemotherapy-related cardiac dysfunction: 1%	strain monitoring to detect patients at higher risk for developing cardiomyopathy	

## **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.