Cardioprotective Therapy: Intervention	Author (Study; Study Type) Year[Ref]	Cohort (Number) Follow-Up	Cardiotoxic Chemotherapy	Primary Outcome	Results	Additional Findings
Neurohormonal therapy: ACEi and/or beta-blocker	Leong et al. (SCHOLAR; prospective, uncontrolled) 2019[12]	Breast cancer (n = 20) Follow-up: 1 year	Trastuzumab	Cardiovascular death, LVEF <40% and HF symptoms, or LVEF <35%	2 patients (or 10%), no cardiovascular deaths.	
Neurohormonal therapy: Beta-blocker and/or ACEi/ARB and close cardiac monitoring	Lynce et al. (SAFE-HEART; prospective, uncontrolled) 2019[13]	Breast cancer (n = 31) Follow-up: 6 months after completion of chemotherapy	Trastuzumab, pertuzumab, or ado-trastuzumab emtansine	Completion of chemotherapy without developing cardiac events (HF, myocardial infarction, arrhythmia, cardiac death, or significant asymptomatic worsening of LVEF)	27 patients (or 90%) completed planned therapy, 3 patients experienced a cardiac event.	
Neurohormonal therapy: Carvedilol vs. placebo	Kalay et al. (randomized, controlled) 2006[3]	Breast cancer, lymphoma, other (n = 50) Follow-up: 6 months	Anthracyclines	LVEF	LVEF baseline vs. follow-up: carvedilol cohort 70.5% vs. 69.7% (p-value = 0.3); control cohort 68.9% vs. 52.3% (p-value <0.001).	
Neurohormonal therapy: Carvedilol vs. control	El-Shitany et al. (randomized, controlled) 2012[32]	Children with acute lymphocytic leukemia (n = 50) Follow-up: 1 week after completion of chemotherapy	Anthracyclines	Two-dimensional echocardiographic parameters, pulsed tissue Doppler, longitudinal strain	Fractional shortening baseline vs. follow-up: carvedilol cohort 34 ± 4.53 vs. 39.466 ± 6.28 (p-value ≤0.05); control cohort 40 ± 4.62 vs. 33.5 ± 6.24 (p-value ≤0.05). Global peak systolic strain baseline vs. follow-up: carvedilol cohort 17.44 ± 2.92 to 19.3 ± 1.96 (p-value ≤0.05); control	Carvedilol was associated with lower cTnI and lactate dehydrogenase levels.

					cohort 18.65 ± 2.9 to 15.1 ± 1.769 (p-value ≤0.05). No change in LV diastolic function, E, A, E/A, s, e, a, e/a.	
Neurohormonal therapy: Enalapril and carvedilol vs. control	Bosch et al. (OVERCOME; randomized, controlled) 2013[11]	Leukemia or malignant hemopathies undergoing autologous hematopoietic stem cells (n = 90) Follow-up: 6 months	Various	LVEF	Change in LVEF: intervention cohort no change; control cohort -3.1% by echocardiography and -3.4 by MRI.	
Neurohormonal therapy: Perindopril, bisoprolol, placebo (1:1:1)	Pituskin et al. (MANTICORE; randomized, controlled) 2017[7]	Breast cancer (n = 99) Follow-up: Approximately 52 weeks	Trastuzumab	Left ventricular remodeling (LV end diastolic volume index on MRI)	LV end diastolic volume index: placebo +4 ± 11 mL/m2; perindopril +7 ± 14 mL/m2; bisoprolol +8 ± 9 mL/m2 (p-value = 0.36).	LVEF decline was attenuated on bisoprolol treatment relative to perindopril and placebo.
Neurohormonal therapy: Carvedilol vs. placebo	Nabati et al. (randomized, controlled) 2017[5]	Breast cancer (n= 91) Follow-up: 6 months	Anthracyclines	LVEF	LVEF baseline to follow-up: carvedilol cohort 58.72 ± 4.69% to 57.44 ± 7.52%; control cohort 61.13 ± 4.97% to 51.67 ± 6.01% (p-value inter-group comparison <0.001).	Control cohort showed increase in LV end systolic volume, left atrial diameter, pulmonary vein peak atrial

						reversal velocity, E/e' and decrease in e', s'. No variables were adversely changed in the carvedilol cohort. Troponin was significantly higher in control group.
Neurohormonal therapy: Carvedilol vs. placebo	Avila et al. (CECCY; randomized, controlled) 2018[4]	Breast cancer (n = 200) Follow-up: 6 months	Anthracyclines	Prevention of LVEF reduction ≥10%	% patients with primary endpoint: carvedilol cohort 14.5%; placebo group 13.5% (p-value = 1.0).	Carvedilol cohort had lower levels of troponin and lower incidence of diastolic dysfunction.
Neurohormonal therapy: Candesartan vs. placebo	Boekhout et al. (randomized, controlled) 2016[10]	Breast cancer (n = 210) Follow-up: 21 months	Trastuzumab	LVEF reduction ≥15% or absolute value <45%	% patients with LVEF reduction: candesartan cohort 19%; placebo cohort 16% (p-value = 0.58).	Candesartan did not affect N-terminal pro-B-type natriuretic peptide or troponin levels.
Neurohormonal therapy: Metoprolol or candesartan vs. placebo	Gulati et al. (PRADA; randomized, controlled [2 x 2 factorial]) 2016[6]	Breast cancer (n = 130) Follow-up: 61 weeks	Anthracycline with or without trastuzumab	LVEF (MRI)	LVEF decline: candesartan cohort 0.8%; placebo cohort 2.6% (p-value = 0.026). No difference was observed in LVEF in metoprolol vs. placebo.	

Neurohormonal therapy: Enalapril vs. control	Cardinale et al. (randomized, controlled) 2006[9]	Patients with cancer with troponin elevation (n = 114). Acute myeloid leukemia, breast cancer, Ewing sarcoma, myeloma, non-Hodgkin's lymphoma, Hodgkin's lymphoma Follow-up: 1 year	High-dose chemotherapy	LVEF decrease >10% with a decline below the normal limit	Cardiac event rate: control cohort 43%; enalapril cohort 0% (p-value <0.001).	
Neurohormonal therapy: Enalapril vs. placebo	Silber et al. (randomized, controlled) 2004[2]	Survivors of pediatric cancer with at least one cardiac abnormality (n = 135) Follow-up: 34.6 months	Anthracyclines	Maximum cardiac index	Maximum cardiac index: enalapril cohort 0.30 L/min/m2; placebo cohort 0.18 L/min/m2 (p-value = 0.55).	Enalapril reduced LV end systolic wall stress.
Neurohormonal therapy: Spironolactone vs. placebo	Akpek et al. (randomized, controlled) 2015[14]	Breast cancer (n = 83) Follow-up: 24 weeks	Anthracyclines	LVEF	LVEF baseline vs. follow-up: spironolactone cohort 67 ± 6.3% vs. 65.7 ± 7.4% (p-value = 0.094); control cohort 67.7 ± 6.3% vs. 53.6 ± 5.8% (p-value <0.001).	
Neurohormonal therapy: Lisinopril or carvedilol vs. placebo	Guglin et al. (Randomized, controlled) 2019[8]	Breast cancer (n = 468) Follow-up: 2 years	Trastuzumab	Rate of cardiotoxicity (LVEF >10% or >5% if below 50%)	No change in rate of cardiotoxicity: placebo 32%; carvedilol 29%; lisinopril 30%.	Patients treated with lisinopril or carvedilol had lower rates of chemotherapy interruption. Patients with prior

						anthracycline exposure had lower rates of LVEF decline on either lisinopril or carvedilol.
Neurohormonal therapy: Metoprolol or enalapril vs. control	Georgakopoulos et al. (randomized, controlled) 2010[33]	Lymphoma (n = 147) Follow-up: 36 months	Anthracyclines	HF	No significant change in HF events with metoprolol or enalapril compared to control.	
Neurohormonal therapy: Enalapril vs. placebo	Janbabai et al. (randomized, controlled) 2017[34]	Breast cancer, Hodgkin's lymphoma, Wilms tumor, lung cancer, sarcoma (n = 69) Follow-up: 6 months	Anthracyclines	Prevention of anthracycline-induced cardiomyopathy	Change in LVEF: enalapril cohort 0.55 ± 5.60%; placebo cohort -13.30 ± 7.38% (p-value <0.001).	
Neurohormonal therapy: Beta-blocker, ACEi/ARB, or mineralocorticoid receptor antagonists	Vaduganathan et al. (meta-analysis) 2019[15]	Adult patients who underwent chemotherapy and neurohormonal therapy Follow-up: ≥4 weeks	Predominantly anthracyclines	LVEF	Neurohormonal therapy: 3.96% less decline in LVEF compared to placebo but with significant heterogeneity among studies.	Neurohormonal therapy had a nonsignificant trend toward lower adverse clinical events.
Dexrazoxane	Vrooman et al. (prospective, uncontrolled) 2011[26]	Children with acute lymphocytic leukemia (n = 553) Follow-up: 3.8 years (median)	Anthracyclines	Secondary malignant neoplasm	Cumulative incidence of secondary malignant neoplasm was rare (0.24 ± 0.24%).	

Dexrazoxane	van Dalen et al. (meta-analysis) 2011[23]	Children or adult patients with cancer receiving anthracyclines and a cardioprotective agent (10 studies, n = 1,619) Follow-up: Variable	Anthracyclines	Prevention of heart damage	Dexrazoxane: Relative risk for HF = 0.29. No difference in response rate or survival between dexrazoxane and control group.	No significant difference in occurrence of secondary malignancy.
Dexrazoxane: Dexrazoxane vs. placebo	Swain et al. (randomized, controlled) 1997[22]	Advanced breast cancer (2 studies, n = 534)	Anthracyclines	LVEF, congestive HF	Hazard ratio for placebo to dexrazoxane = 2.0-2.63.	In study 088001, objective response rate for dexrazoxane was 46.8% vs. 60.5% for placebo. Study 088006 showed no difference. Time to progression and survival were not statistically significant.
Dexrazoxane: Dexrazoxane vs. placebo	Tebbi et al. (randomized, controlled) 2007[25]	Hodgkin's lymphoma (n = 478) Follow-up: 58 months	Anthracyclines	Acute myeloid leukemia/myelodysplastic syndrome, secondary malignant neoplasm	Standardized incidence rate for acute myeloid leukemia/myelodysplastic syndrome: dexrazoxane 613.6; placebo 202.4 (p-value = 0.0990). Standardized incidence rate for all secondary malignant neoplasm: dexrazoxane 41.86; placebo 10.8 (p-value = 0.0231).	

Dexrazoxane: Dexrazoxane vs. control	Asselin et al. (randomized, controlled) 2016[24]	T-cell acute lymphocytic leukemia, lymphoblastic non-Hodgkin's lymphoma (n = 537) Follow-up: 3 years	Anthracyclines	LV fractional shortening, wall thickness, and thickness-to-dimension ratio	Dexrazoxane vs. control: ΔLV fractional shortening z-score -0.05 vs. -0.77 (p-value = 0.005); ΔLV wall thickness z-score -0.13 vs. -0.69 (p-value = 0.014); ΔLV thickness-to-dimension ratio z-score -0.09 vs. 0.75 (p-value = 0.006).	Dexrazoxane was not associated with worse antitumor efficacy, frequency of toxicities, or secondary malignancies.
Dexrazoxane: Dexrazoxane vs. control	Ganatra et al. (case series) 2019[27]	Hodgkin's lymphoma, ovarian cancer, non-Hodgkin's lymphoma, breast cancer, diffuse large B-cell lymphoma, acute myeloid leukemia, peripheral T-cell lymphoma (n = 8) Follow-up: 13.5 months	Anthracyclines	LVEF, symptomatic HF, cardiac biomarkers	LVEF baseline vs. follow-up: dexrazoxane 39% vs. 34%; control 42.5% to 18%. None of the 5 patients in the dexrazoxane group had symptomatic HF or elevated biomarkers. All 3 patients who did not receive dexrazoxane had symptomatic HF requiring hospitalization; 2 died from cardiogenic shock and multiorgan failure.	
Cardiac resynchronization therapy	Singh et al. (MADIT-CHIC; prospective, uncontrolled) 2019[30]	Chemotherapy-induced cardiomyopathy with LVEF <35% (n = 30). Breast cancer, lymphoma/leukemia, sarcoma Follow-up: 6 months	Predominantly anthracyclines	LVEF	Mean LVEF improved from 28% to 39%.	
Statin: Statin vs. control	Acar et al. (randomized,	Non-Hodgkin's lymphoma, multiple myeloma, leukemia	Anthracyclines	LVEF <50%	% patients with LVEF <50%: statin cohort 5%;	Statin use was associated with maintenance of

	controlled) 2011[28]	(n = 40) Follow-up: 6 months			control cohort 25% (p-value = 0.18).	LVEF compared to placebo.
Statin	Seicean et al. (retrospective, propensity-matched) 2012[35]	Breast cancer (n = 628) Follow-up: 2.55 years	Anthracyclines	HF hospitalization	HF event: statin cohort 6%; control cohort 17.2% (p-value = 0.04).	