Supplemental Materials

Supplemental Table 1: Changes in Diastolic Function Parameters Over Time According to Treatment Regimen

Echocardiographic Parameter	Time since initiation of cancer therapy	Doxorubicin Mean Change (95% CI)	P-value	Trastuzumab Mean Change (95% CI)	P-value	Doxorubicin+ Trastuzumab Mean Change (95% CI)	P-value
Deceleration time	6 months	-9.0 (-12.9, -5.0)	<0.001	-11.0 (-16.1, -5.8)	<0.001	-1.9 (-7.9, 40)	0.524
	12 months	-2.9 (-7.9, 2.2)	0.267	-6.0 (-11.6, -0.5)	0.034	4.8 (-0.9, 10.6)	0.101
	24 months	4.0 (-1.0, 9.0)	0.117	1.0 (-6.5, 8.4)	0.797	8.1 (-1.4, 17.6)	0.093
	36 months	7.0 (1.6, 12.4)	0.011	3.9 (-6.6, 14.4)	0.468	12.2 (0.3, 24.1)	0.044
IVRT (msec)	6 months	0.8 (-1.9, 3.5)	0.580	2.7 (-1.8, 7.2)	0.242	0.1 (-3.0, 3.2)	0.944
	12 months	4.5 (0.5, 8.5)	0.026	1.6 (-2.6, 5.8)	0.449	0.6 (-3.7, 4.9)	0.778
	24 months	2.5 (-0.7, 5.8)	0.130	4.1 (-2.9, 11.2)	0.250	1.4 (-3.3, 6.1)	0.568
	36 months	0.2 (-3.7, 4.1)	0.929	5.3 (-4.3, 14.8)	0.279	2.0 (-3.6, 7.7)	0.479
TR Velocity (m/s)	6 months	0.0 (-0.0, 0.0)	0.960	0.0 (-0.0, 0.1)	0.470	0.1 (0.0, 0.1)	0.014
	12 months	-0.0 (-0.1, 0.0)	0.419	0.0 (-0.1, 0.1)	0.896	0.0 (-0.0, 0.1)	0.117
	24 months	-0.0 (-0.1, 0.0)	0.627	-0.0 (-0.1, 0.1)	0.949	0.0 (-0.0, 0.1)	0.229
	36 months	0.0 (-0.0, 0.1)	0.553	0.0 (-0.1, 0.1)	0.852	0.0 (-0.0, 0.1)	0.185

Dox refers to doxorubicin, IVRT to isovolumic relaxation time Tras to trastuzumab, ,TR to tricuspid regurgitation

Supplemental Table 2: Associations between Baseline Abnormal Diastolic Function Grade and Change in LVEF, Time to CTRCD and Change in Longitudinal Strain

Variable	Change in LVEF*			Time to Subsequent CTRCD†			Change in Longitudinal Strain*		
	Beta	95% CI	P-value	HR	95% CI	P-value	Beta	95% CI	P-value
Baseline Diastolic Function Grade >0	-0.2	(-1.4, 1.0)	0.748	1.2	(0.6, 2.3)	0.647	0.5	(-0.0, 1.0)	0.070
Age (10 years)	-0.1	(-0.6, 0.4)	0.674	0.9	(0.7, 1.2)	0.377	0.4	(0.2, 0.6)	0.001
Hypertension	-0.8	(-2.0, 0.3)	0.154	1.5	(0.8, 2.8)	0.218	0.7	(0.2, 1.2)	0.005
Current smoker	0.3	(-2.2, 2.8)	0.797	0.7	(0.2, 2.3)	0.531	0.3	(-0.5, 1.2)	0.444
BMI (5 kg/m^2)	0.4	(0.0, 0.8)	0.042	0.9	(0.7, 1.1)	0.263	0.1	(-0.1, 0.3)	0.467
Baseline LVEF	-0.5	(-0.6, -0.4)	<0.001	1.0	(1.0, 1.1)	0.204	-	-	-
Baseline Longitudinal Strain	-	-	-	-	-	-	-0.8	(-0.8, -0.7)	<0.001

BMI refers to body mass index, CTRCD to cancer therapeutics-related cardiac dysfunction LVEF to left ventricular ejection fraction,.

*Generalized estimating equation beta coefficient reflects the mean difference in LVEF or longitudinal strain relative to baseline for each variable, adjusted for all variables included in this Table plus treatment regimen and time since cancer therapy initiation interacted with treatment, modeled using cubic splines. There are no effect estimates for treatment due to modeling strategies used.

† Cox proportional hazards model, HR for time to CTRCD, adjusted for all variables included in this Table, and using stratified baseline hazards for treatment regimen. There are no effect estimates for treatment due to modeling strategies used. 52 CTRCD events in this analysis.

Supplemental Table 3: Associations between Worsening Diastolic Function Grade and Subsequent Changes in LVEF, Time to CTRCD or Subsequent Changes in Longitudinal Strain

Variable	Change in LVEF*			Time to Subsequent CTRCD†			Change in Longitudinal Strain*		
	Beta	95% CI	P-value	HR	95% CI	P-value	Beta	95% CI	P-value
Worsening Diastolic Function Grade	-1.4	(-2.4, -0.4)	0.006	2.2	(1.1, 4.3)	0.028	0.3	(-0.1, 0.7)	0.195
Age (10 years)	-0.1	(-0.7, 0.5)	0.797	0.8	(0.6, 1.2)	0.256	0.5	(0.2, 0.7)	<0.001
Hypertension	-1.0	(-2.2, 0.2)	0.092	1.3	(0.7, 2.9)	0.464	0.8	(0.2, 1.3)	0.008
Current smoker	1.0	(-1.2, 3.2)	0.84	0.8	(0.2, 3.4)	0739	0.5	(-0.5, 1.5)	0.293
BMI (5 kg/m^2)	0.4	(-0.1, 0.9)	0.148	1.0	(0.7, 1.3)	0.827	0.1	(-0.1, 0.3)	0.272
Baseline LVEF	-0.4	(-0.6, -0.3)	<0.001	1.0	(0.9, 1.1)	0.951	-	-	-
Baseline Longitudinal Strain	-	-	-	-	-	-	-0.7	(-0.8, -0.7)	<0.001

BMI refers to body mass index, CTRCD to cancer therapeutics-related cardiac dysfunction, LVEF to left ventricular ejection fraction
Worsening diastolic function is defined by increase in diastolic function grade in patients with diastolic function grade <3 at baseline.
In all models, outcome evaluated at the subsequent and not the same visit.

*Generalized estimating equation beta coefficients reflect the mean difference in LVEF or longitudinal strain relative to baseline for each variable, adjusted for all variables included in this Table plus treatment regimen and time since cancer therapy initiation interacted with treatment, modeled using cubic splines. There are no effect estimates for treatment due to modeling strategies used.

†Cox proportional hazards model, HR for time to CTRCD, adjusted for all variables included in this Table, and using stratified baseline hazards for treatment regimen. There are no effect estimates for treatment due to modeling strategies used. 35 CTRCD events in this analysis.