

**Supplementary Table 1.** Characteristics and clinical course in patients who developed asymptomatic LVEF decline or symptomatic heart failure

Age	Baseline CV Risk Factors	Baseline LVEF	Nadir LVEF	Time to cardiac event*	Severe HF (Y/N)	Trastuzumab Interruption	Clinical Details
<b>Significant LVEF Decline<sup>†</sup></b>							
71	HL, CAD, former smoker	60	48	7 months	N	Y (permanent)	At baseline, known CAD with history of PCI and mitral valve prolapse with mitral regurgitation. Asymptomatic LVEF decline at 7 months treated with ACE-I. H was permanently discontinued. LVEF recovered to 61% at 19 months after H discontinuation.
58	HTN, DM, smoking history	80	55	3 months	N	N	History of HTN treated with ramipril. No treatment interruption for asymptomatic LVEF decline.
76	HTN, HL, CAD, rheumatic heart disease, mitral and aortic valve replacement, chronic atrial fibrillation, BMI $\geq$ 30	52	33	3 months	N	Y (permanent)	Rheumatic heart disease and CAD status post mitral/aortic valve replacements and CABG. HTN treated with metoprolol, valsartan, and aliskiren. LVEF decline to 33% at 3 months, accompanied with NYHA class II symptoms. H permanently discontinued, and symptoms improved with diuretics. 2 months after H discontinuation, LVEF improved to 64%.

65	HL, DM, smoking history, non-ischemic cardiomyopathy, BMI $\geq$ 30	65	51	3 months	N	N	LBBB at baseline with history of LVEF decline to 50%, which normalized to 65% prior to breast cancer treatment. No H interruption.
48	None	67	46	6 months	N	N	Completed full course of H without interruption and with no heart failure symptoms.
73	HTN, HL, DM, CAD, active smoker	79	53	1 month	N	N	HTN controlled with enalapril at baseline. CAD with history of PCI.
76	HTN, DM, BMI $\geq$ 30	69	53	11 months	N	N	HTN treated with enalapril and amlodipine at baseline. Mild decline in LVEF after completion of H therapy. No cardiac meds initiated.
55	None	63	51	8 months	N	Y (permanent)	No cardiac medications started. 2 months after H discontinued, LVEF recovered to 57%. H was not reinitiated.
70	HTN, smoking history	67	48	3 months	N	Y (temporary)	HTN treated with losartan at baseline. H was held for 6 weeks and losartan was uptitrated. H reinitiated after LVEF improved to 63%. Patient completed full course of H with no recurrent LVEF decline.
42	None	77	52	3 months	N	Y (permanent)	H permanently discontinued for asymptomatic LVEF decline to 52%. No cardiac meds started. LVEF recovered to 60% at 2 months after H discontinuation.
<b><u>Symptomatic Heart Failure</u></b>							
55	Non-ischemic cardiomyopathy	66	47	7 months	Y	Y (permanent)	History of arrhythmogenic right ventricular cardiomyopathy and

	hy, smoking history						frequent PVCs, treated with BB. Developed NYHA class III HF. Treated with diuretics and ACE-I. 3 months after permanent discontinuation of H, LVEF improved to 56%.
76	HTN, HL, smoking history	52	20	5 months	Y	Y (permanent)	HTN controlled with CCB at baseline. Developed severe NYHA class IV HF after 5 months of H. Treated with BB, ACE-I, and diuretics. LVEF recovered to 58% at 15 months after discontinuation of H.

† LVEF decline without severe (NYHA class III/IV) heart failure

\* Time to onset of severe heart failure or LVEF decline after initiation of anti-HER2 therapy

ACE-I, angiotensin-converting enzyme inhibitor; BB, beta blocker; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DM, diabetes mellitus; H, trastuzumab; HF, heart failure; HTN, hypertension; HL, hyperlipidemia; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVC, premature ventricular contraction