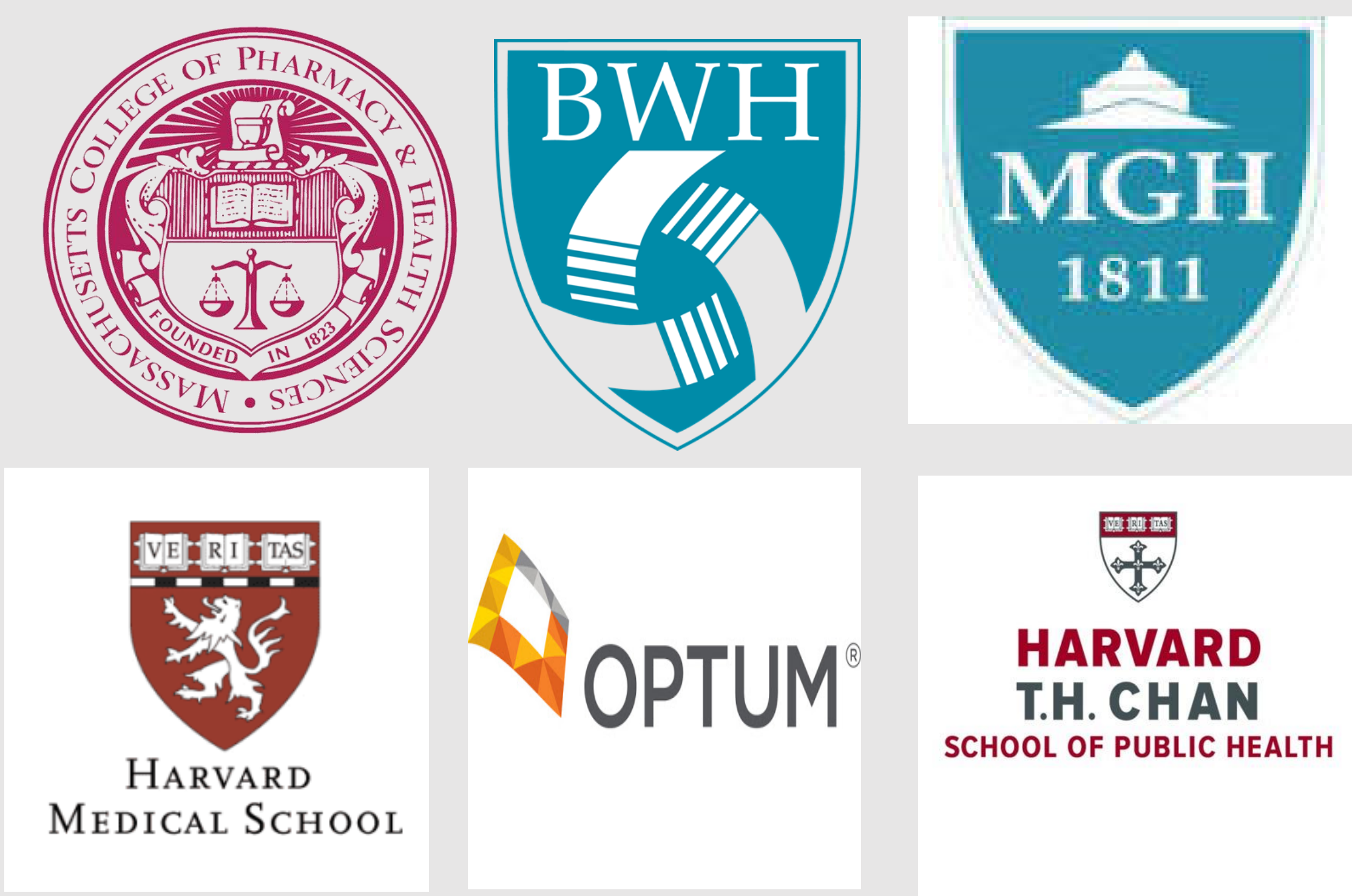


REAL-WORLD CARDIAC SAFETY OF ANTI-HER2 THERAPIES IN ELDERLY PATIENTS WITH HER2+/HR-METASTATIC BREAST CANCER: A RETROSPECTIVE COHORT STUDY USING SEER-MEDICARE DATA 2012-2016

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OBJECTIVES

Anti-HER2 therapies have significantly improved survival in human epidermal growth factor 2 (HER2)-positive metastatic breast cancer (mBC). However, clinical trials have identified increased cardiac risk with trastuzumab-based therapies. The purpose of our study was to assess the incidence of cardiac safety events after trastuzumab initiation among elderly HER2+ mBC patients in the real-world setting.

METHODS

We identified 73 eligible HER2+/hormone receptor-negative (HR-) mBC patients diagnosed between February 2013 and December 2015 (mean age at diagnosis, 75.0±7.7 years) from SEER and followed their MEDICARE records through December 2016 (**Figure1**) (**Table 1**). Fifty-six patients were treated with trastuzumab, and among them, five received ado-trastuzumab emtansine (T-DM1) as second-line therapy during the study period. We identified the occurrence of cardiac safety events 12 months before diagnosis through patient death or the end of observation. (**Figure 2**) We defined a cardiac safety event as inpatient or outpatient cardiomyopathy (CM) or heart failure (HF).

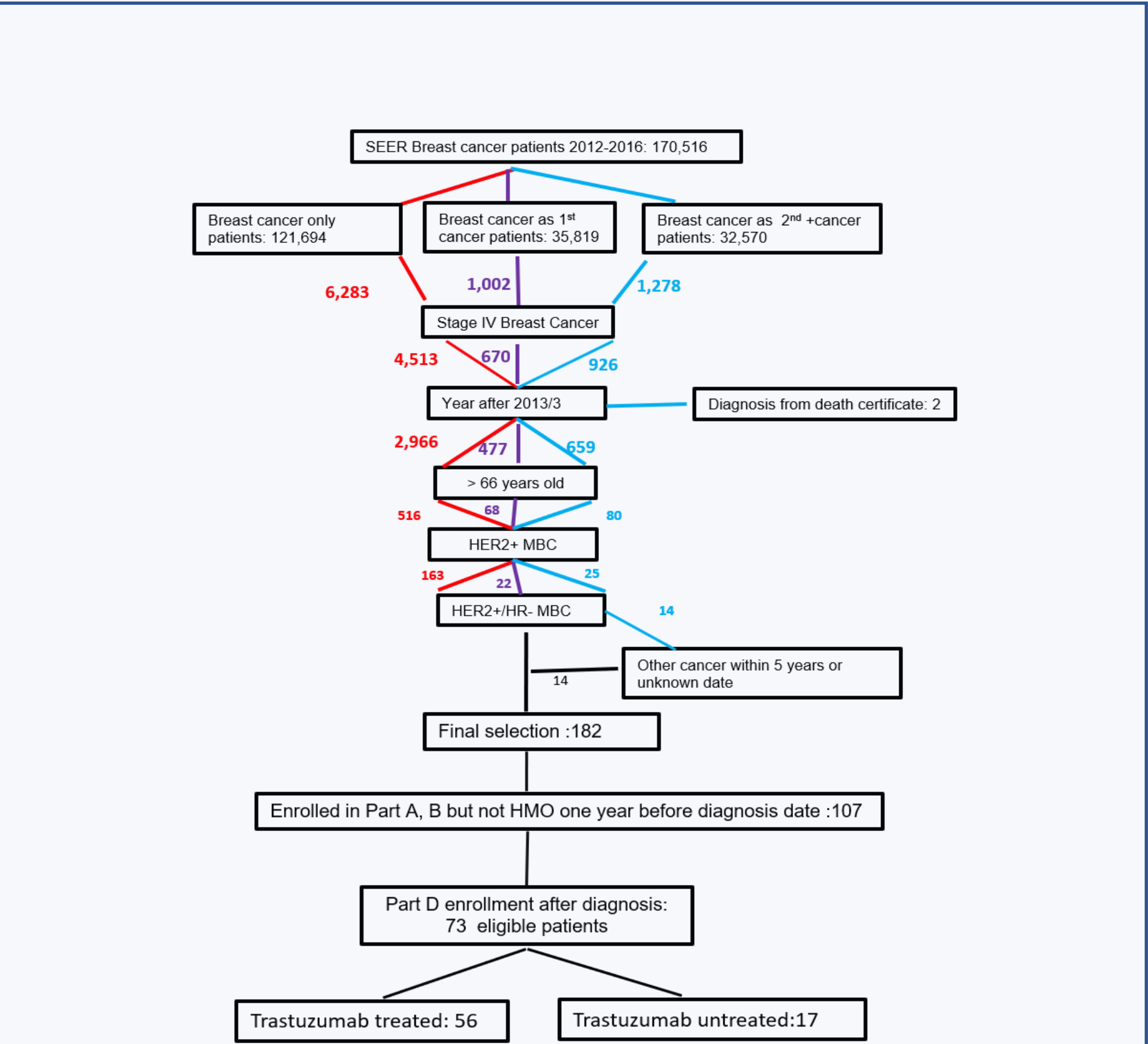


Figure 1. Consort diagram of study cohort

Cohort characteristics	All n=	%	Proportion of trastuzumab patients n=	%	Proportion of non-trastuzumab patients n=	%	p-value(two-tailed) n=8,95
Total sample	73	100	56	77	17	23	N/A
Age at diagnosis (yrs)							
mean, SD	75	±7.7	75	±7.7	74	±7.7	0.6405
median	75		72		74		
Age groups							
66-69	39	26	13	22	6	35	0.5487
70-74	21	29	18	32	3	18	0.6242
75-79	17	23	11	20	6	35	0.4966
80-84	7	10	7	13	0	0	N/A
≥85	9	12	7	13	2	12	0.9702
Race							
White	58	80	46	82	12	71	0.3508
Black	12	16	7	13	5	29	0.4918
API and others	3	4	3	5	0	0	N/A
Median household income							
<\$0,000	25	34	17	30	8	46	0.4343
\$0,000-100,000	33	45	29	52	4	24	0.2936
100,000-200,000	12	16	8	14	4	24	0.6662
200,000+	0	0	0	0	0	0	N/A
Unknown	3	4	2	4	1	6	N/A
Non-high school diplomas Percentage							
mean, SD	13	±9.9	13	±9.5	12	±7.6	0.7011
marital status							
Married	24	33	21	38	3	18	0.4983
Others	49	67	35	62	14	82	0.1762
SEER region							
Northeast	17	23	16	29	1	6	N/A
South	23	32	18	32	5	29	0.8982
Midwest	7	10	4	7	3	18	0.6543
West	26	35	18	32	8	47	0.4637
Location of residence							
Major metropolitan	45	62	34	61	11	65	0.8122
Metropolitan/Urban	22	30	17	30	5	29	0.9657
Less urban/rural	6	8	5	9	1	6	N/A
Year of MBC diagnosis							
2013	21	29	17	30	4	24	0.8117
2014	28	38	20	36	8	47	0.5901
2015	24	33	19	34	5	29	0.8324
presence of metastatic brain disease							
Yes	7	9	6	11	1	6	N/A
No	64	88	49	87	15	86	0.9191
Unknown	2	3	1	2	1	6	N/A

Table1. Characteristics of trastuzumab-treated and untreated patients

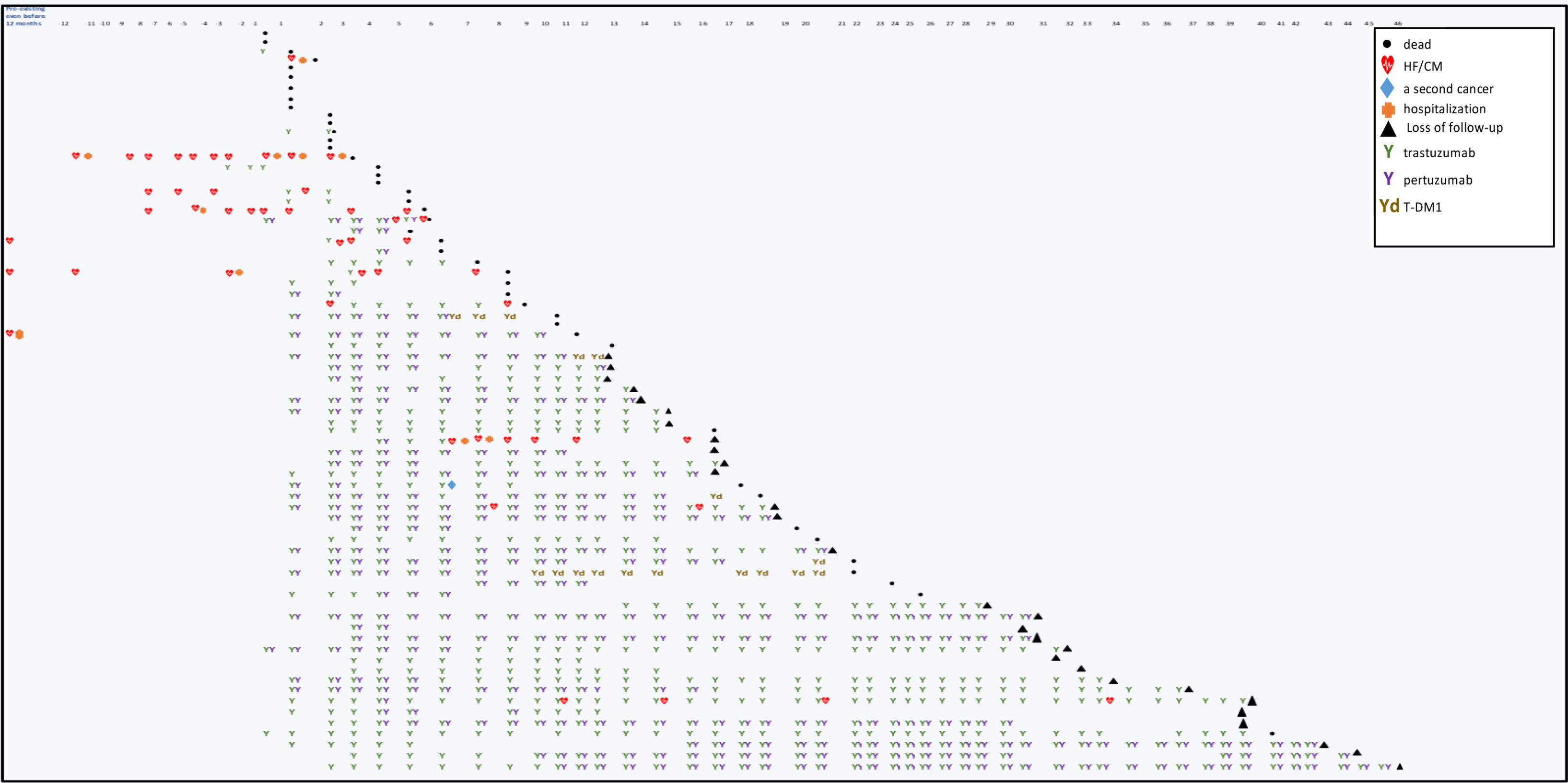


Figure 2. The 73 Patients' journey since mBC diagnosis

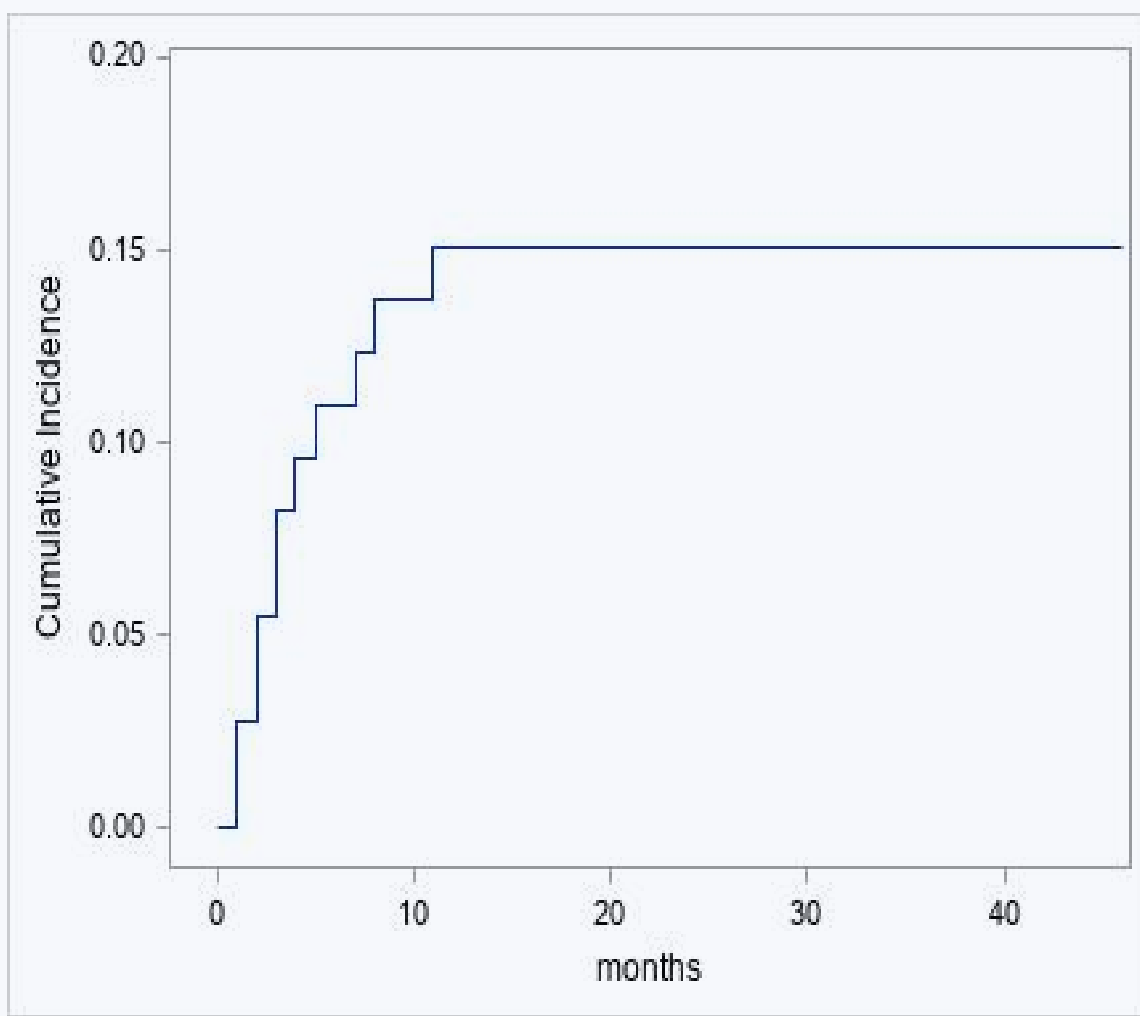


Figure 3. Probability of the cardiac safety event is 15% by 11 months for the 73 patients with death as a competing risk

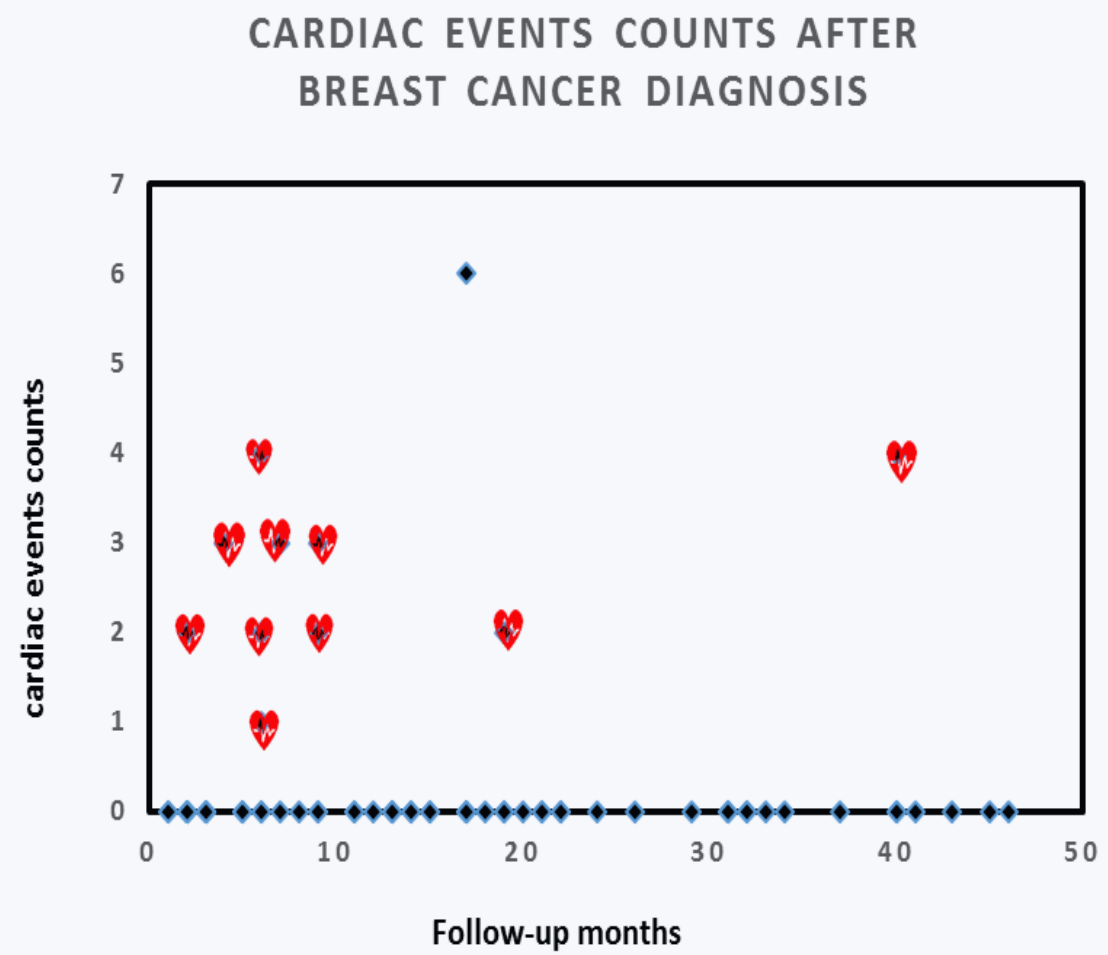


Figure 4. Patients who died within the first 12 months appeared to associate with more CM/HF events compared to patients who lived longer than one year

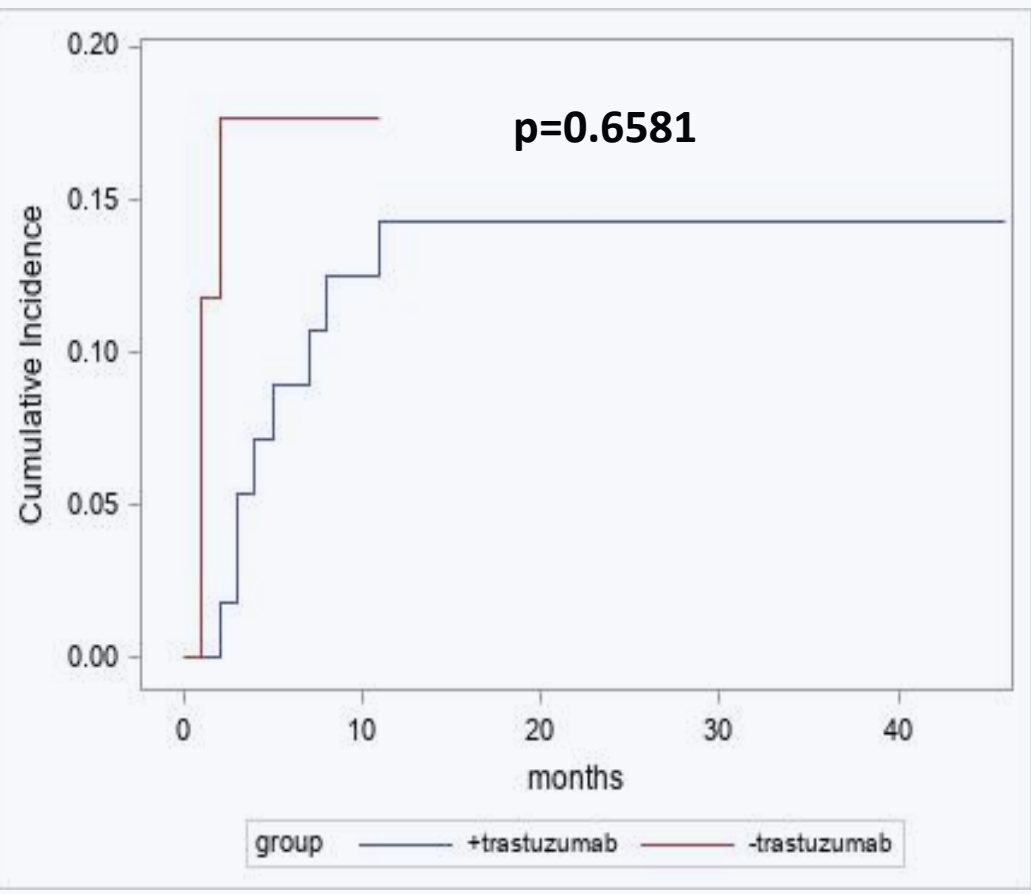


Figure 5a

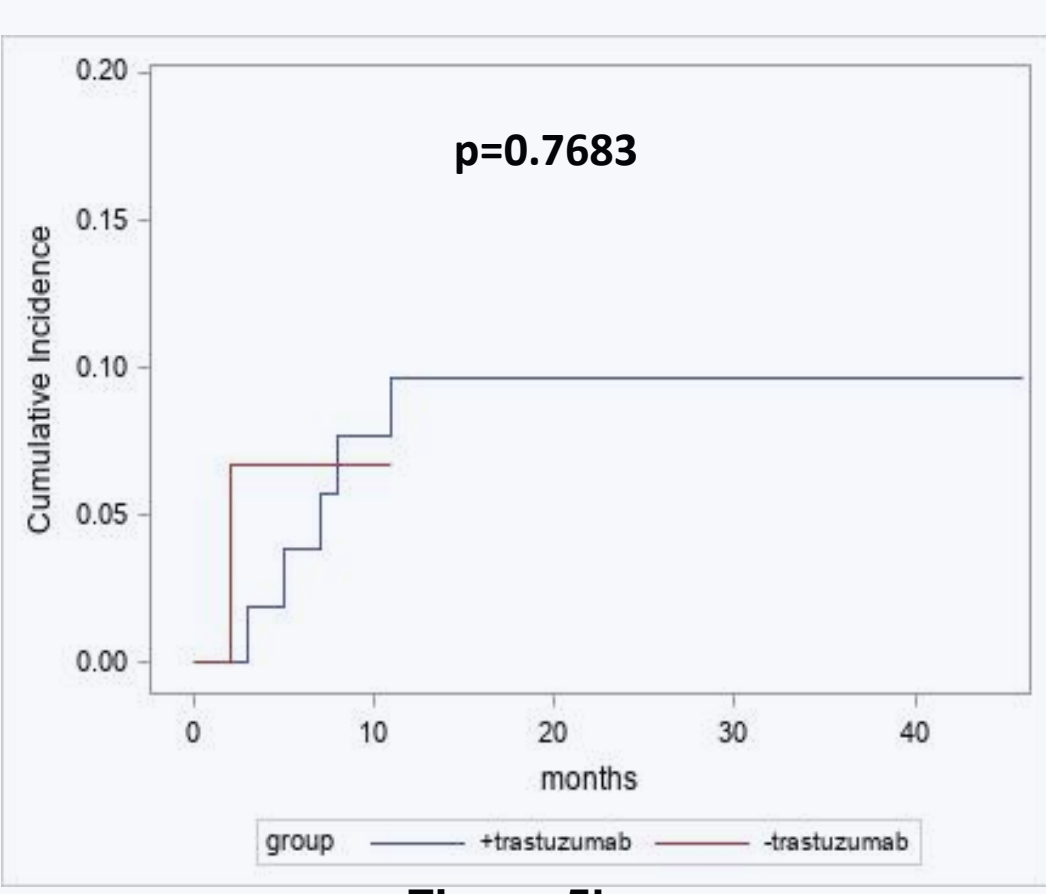


Figure 5b

Figure 5: Gray's Test for Equivalence of Cumulative Incidence showed that there is no significant difference of risk of cardiac events between patients treated or not treated. 5a: Patients with pre-existing CM/HF were included. 5b: Patients with pre-existing CM/HF were excluded

RESULTS

There were no significant baseline differences between patients treated with trastuzumab or not, except that the non-trastuzumab group had a higher proportion of patients with a prior history of CM/HF. (**Table 1**) (**Figure2**) Eight of the 56 patients (14.3%) developed CM/HF during or following trastuzumab treatment, including one HF hospitalization. (**Figure 2**) Three of the 8 patients (37.5%) who developed CM/HF had pre-existing cardiac conditions. (**Figure2**) Four of the 8 patients (50%) died within one month of developing CM/HF. (**Figure 2**) The average number of cardiac events per trastuzumab-treated patient was 2.9. (**Figure2**) Excluding patients with a history of CM/HF before mBC diagnosis, the incidence of CM/HF was 9.6% in patients treated with trastuzumab and 6.7% in patients without trastuzumab treatment (OR, 1.49; 95%CI, 0.16-13.83). Gray's Test for Equivalence of Cumulative Incidence showed that there is no significant difference of risk of cardiac events between patients treated or not treated. (**Figure 5**)

CONCLUSIONS

Our results suggest that elderly patients treated with trastuzumab-based therapies do not have an increased cardiac safety risk compared with patients with no trastuzumab-based treatment. However, our results are limited by the small size of our cohort.

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