

Supplementary Information

Supplemental Table 1. Summary of iDFS and OS within our two- and three-arm comparisons when classified by T1a versus T1b/c substage

	T1a iDFS	T1b/c iDFS	T1a OS	T1b/c OS
Univariate analysis				
Trastuzumab +/- chemotherapy vs. untreated	HR 0.63 95% CI 0.33-1.19 $p=0.154$	HR 0.68 95% CI 0.51-0.89 $p=0.004^{**}$	HR 1.21 95% CI 0.37-3.96 $p=0.756$	HR 0.50 95% CI 0.31-0.79 $p=0.002^{**}$
Trastuzumab vs. untreated	HR 0.28 95% CI 0.09-0.95 $p=0.041^{**}$	HR 0.55 95% CI 0.34-0.89 $p=0.014^{**}$	HR 1.02 95% CI 0.20-5.27 $p=0.981$	HR 0.35 95% CI 0.14-0.90 $p=0.027^{**}$
Combination vs. untreated	HR 0.88 95% CI 0.44-1.73 $p=0.707$	HR 0.71 95% CI 0.53-0.94 $p=0.016^{**}$	HR 1.33 95% CI 0.36-4.95 $p=0.673$	HR 0.53 95% CI 0.33-0.86 $p=0.001^{**}$
Combination vs. trastuzumab	HR 3.08 95% CI 0.88-10.83 $p=0.079$	HR 1.30 95% CI 0.80-2.09 $p=0.287$	HR 1.3 95% CI 0.24-7.11 $p=0.761$	HR 1.53 95% CI 0.60-3.94 $p=0.375$
Overall test on treatment effect	$p=0.094$	$p=0.01^{**}$	$p=0.906$	$p=0.007^{**}$
Multivariate analysis				
Trastuzumab +/- chemotherapy vs. untreated	HR 0.53 95% CI 0.26-1.09 $p=0.084$	HR 0.69 95% CI 0.52-0.92 $p=0.012$	N/A	N/A
Trastuzumab vs. untreated	HR 0.23 95% CI 0.06-0.84 $p=0.026^{**}$	HR 0.62 95% CI 0.37-1.02 $p=0.061$		
Combination vs. untreated	HR 0.78 95% CI 0.35-1.73 $p=0.544$	HR 0.70 95% CI 0.52-0.95 $p=0.023^{**}$		
Combination vs. trastuzumab	HR 3.36 95% CI 0.86-13.21 $p=0.082$	HR 1.14 95% CI 0.70-1.86 $p=0.602$		
Overall test on treatment effect	$p=0.084$	$p=0.037^{**}$		

Notes: ******Denotes statistical significance between comparator groups. Multivariate analysis using a Cox proportional hazard model was used to control for the following factors: age, race, ethnicity, BMI, hormone receptor status, tumor grade, histology type, T1 substage, BRCA mutation status, geographical region, functional status, and smoking history.

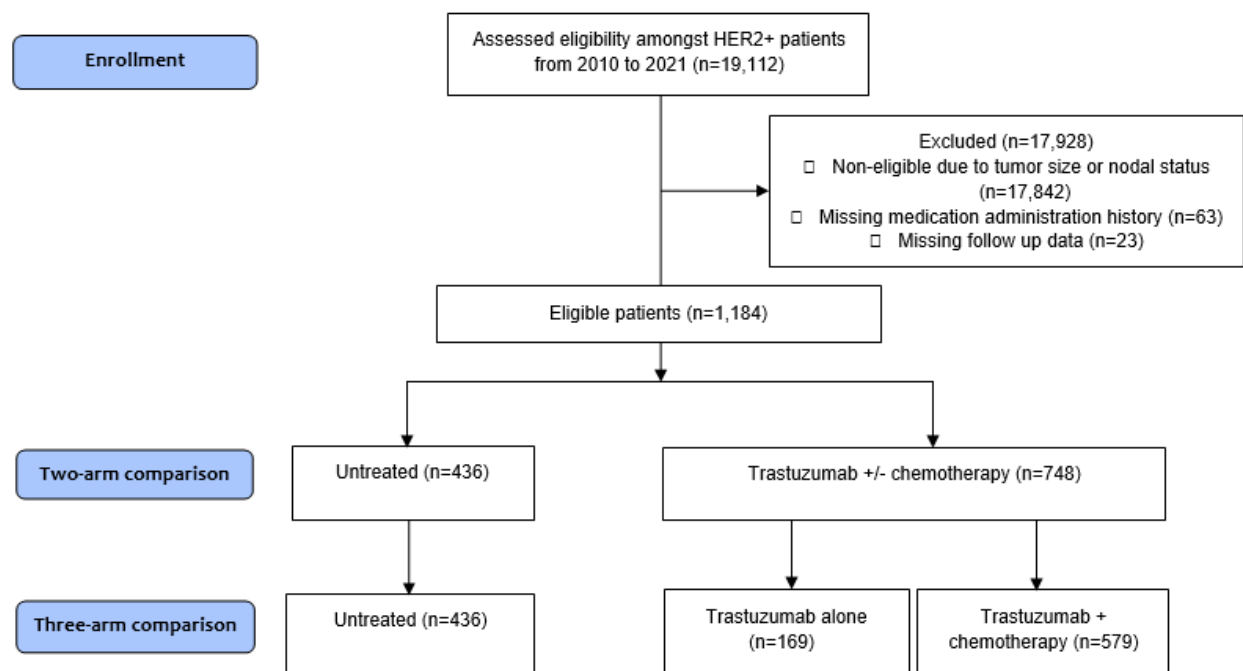
Abbreviations: CI = confidence interval, iDFS = invasive disease-free survival, OS = overall survival

Supplemental Table 2. Summary of iDFS and OS within our two- and three-arm comparisons for each T1 sub-categorization

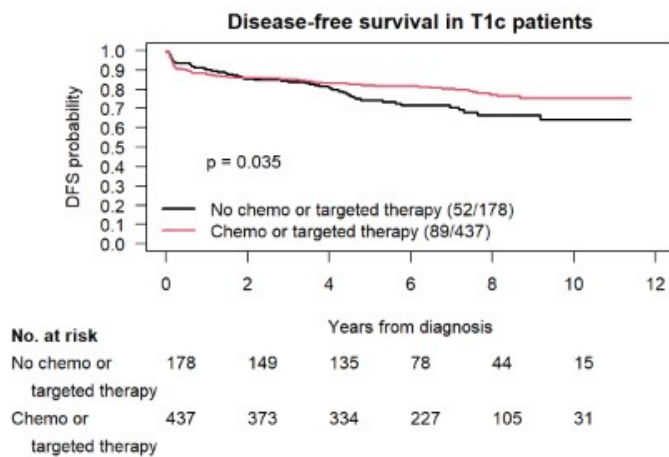
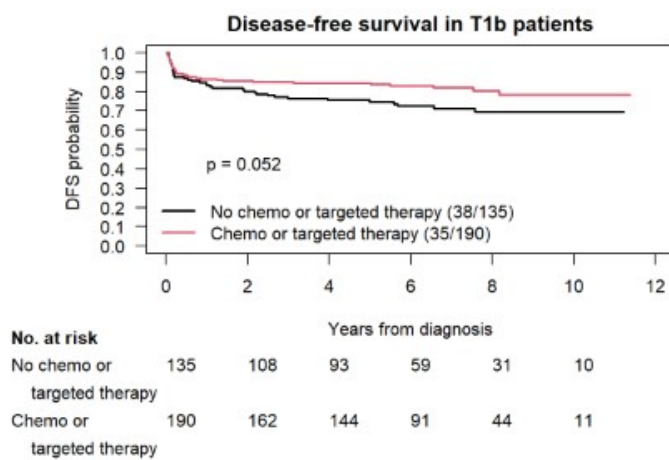
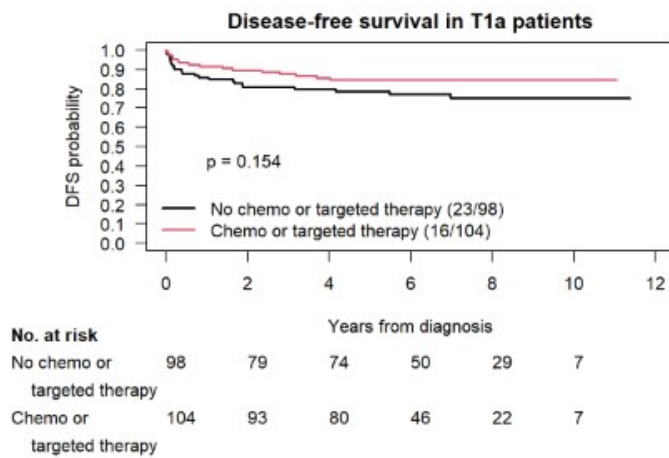
	T1a iDFS	T1b iDFS	T1c iDFS	T1a OS	T1b OS	T1c OS
Univariate analysis						
Trastuzumab +/- chemotherapy vs. untreated	HR 0.63 95% CI 0.33-1.19 <i>p</i> =0.154	HR 0.64 95% CI 0.4-1.01 <i>p</i> =0.052	HR 0.69 95% CI 0.49-0.98 <i>p</i> =0.035**	HR 1.21 95% CI 0.37-3.96 <i>p</i> =0.756	HR 0.50 95% CI 0.2-1.25 <i>p</i> =0.133	HR 0.46 95% CI 0.27-0.79 <i>p</i> =0.004**
Trastuzumab vs. untreated	HR 0.28 95% CI 0.09-0.95 <i>p</i> =0.041**	HR 0.59 95% CI 0.25-1.39 <i>p</i> =0.226	HR 0.53 95% CI 0.3-0.96 <i>p</i> =0.036**	HR 1.02 95% CI 0.20-5.27 <i>p</i> =0.981	HR 1.01 95% CI 0.28-3.62 <i>p</i> =0.99	HR 0.16 95% CI 0.04-0.68 <i>p</i> =0.013**
Combination vs. untreated	HR 0.88 95% CI 0.44-1.73 <i>p</i> =0.707	HR 0.65 95% CI 0.4-1.05 <i>p</i> =0.079	HR 0.74 95% CI 0.52-1.05 <i>p</i> =0.089	HR 1.33 95% CI 0.36-4.95 <i>p</i> =0.673	HR 0.39 95% CI 0.13-1.12 <i>p</i> =0.079	HR 0.54 95% CI 0.13-1.12 <i>p</i> =0.026**
Combination vs. trastuzumab	HR 3.08 95% CI 0.88-10.83 <i>p</i> =0.079	HR 1.1 95% CI 0.46-2.66 <i>p</i> =0.827	HR 1.38 95% CI 0.78-2.44 <i>p</i> =0.267	HR 1.3 95% CI 0.24-7.11 <i>p</i> =0.761	HR 0.38 95% CI 0.09-1.61 <i>p</i> =0.191	HR 3.32 95% CI 0.79-13.99 <i>p</i> =0.102
Overall test on treatment effect	<i>p</i> =0.094	<i>p</i> =0.149	<i>p</i> =0.063	<i>p</i> =0.906	<i>p</i> =0.167	<i>p</i> =0.005**
Multivariate analysis						
Trastuzumab +/- chemotherapy vs. untreated	HR 0.53 95% CI 0.26-1.09 <i>p</i> =0.084	HR 0.68 95% CI 0.41-1.15 <i>p</i> =0.155	HR 0.65 95% CI 0.45-0.94 <i>p</i> =0.02**	N/A	N/A	
Trastuzumab vs. untreated	HR 0.23 95% CI 0.06-0.84 <i>p</i> =0.026**	HR 0.60 95% CI 0.23-1.55 <i>p</i> =0.295	HR 0.57 95% CI 0.3-1.05 <i>p</i> =0.071			
Combination vs. untreated	HR 0.78 95% CI 0.35-1.73 <i>p</i> =0.544	HR 0.70 95% CI 0.41-1.21 <i>p</i> =0.204	HR 0.67 95% CI 0.46-0.98 <i>p</i> =0.039**			
Combination vs. trastuzumab	HR 3.36 95% CI 0.86-13.21 <i>p</i> =0.082	HR 1.16 95% CI 0.45-2.99 <i>p</i> =0.752	HR 1.19 95% CI 0.65-2.18 <i>p</i> =0.576			
Overall test on treatment effect	<i>p</i> =0.084	<i>p</i> =0.348	<i>p</i> =0.06			

Notes: **Denotes statistical significance between comparator groups. Multivariate analysis using a Cox proportional hazard model was used to control for the following factors: age, race, ethnicity, BMI, hormone receptor status, tumor grade, histology type, T1 substage, BRCA mutation status, geographical region, functional status, and smoking history.

Abbreviations: CI = confidence interval, iDFS = invasive disease-free survival, OS = overall survival

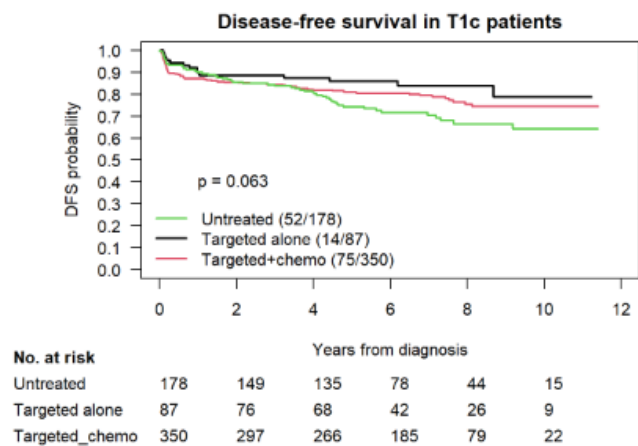
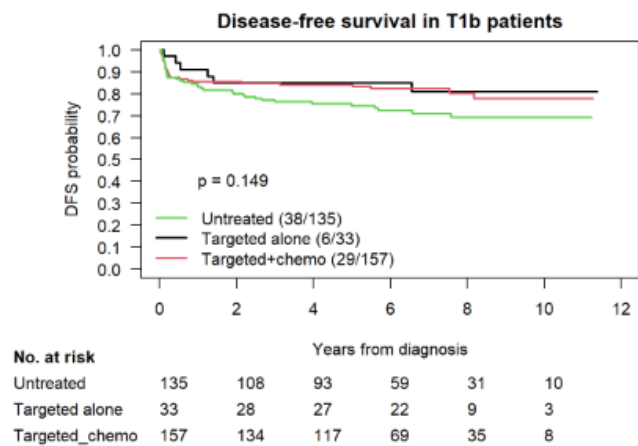
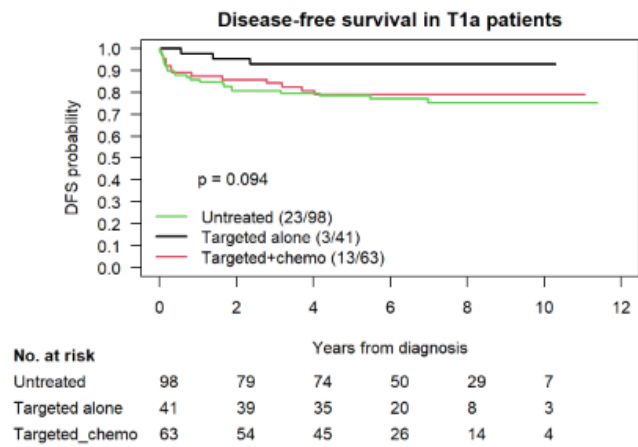


Supplemental Figure 1. CONSORT diagram highlighting the patient selection process for this retrospective study



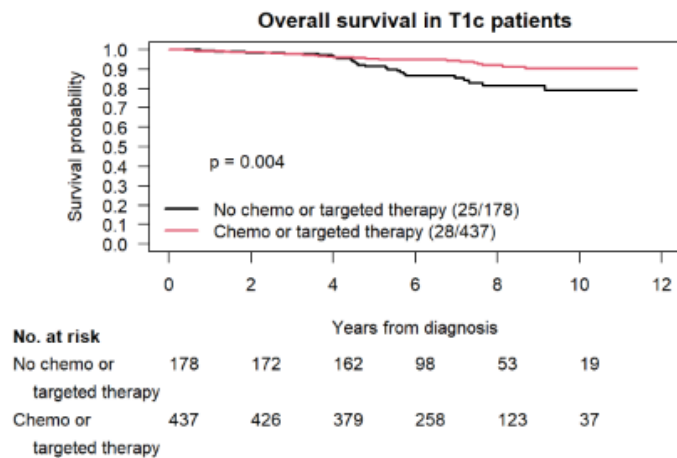
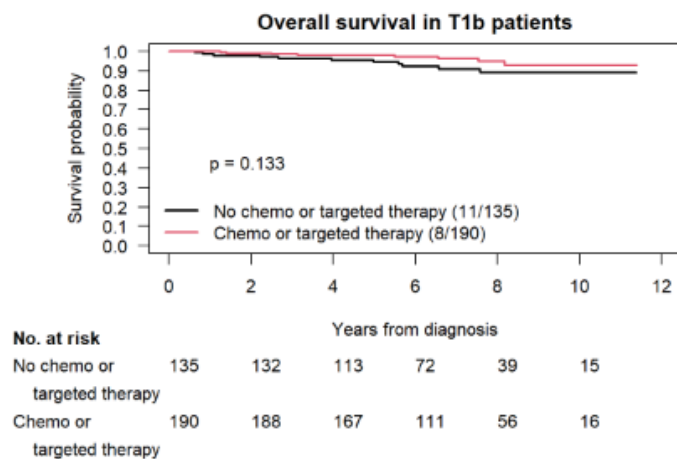
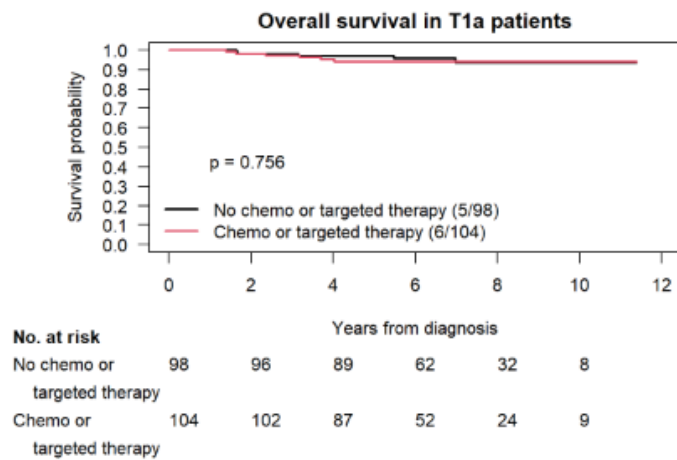
Abbreviations: iDFS = invasive disease-free survival, chemo = chemotherapy

Supplemental Figure 2. Univariate analysis of iDFS among T1 sub-categorizations in our two-group comparison of locoregional therapy alone versus trastuzumab with or without chemotherapy



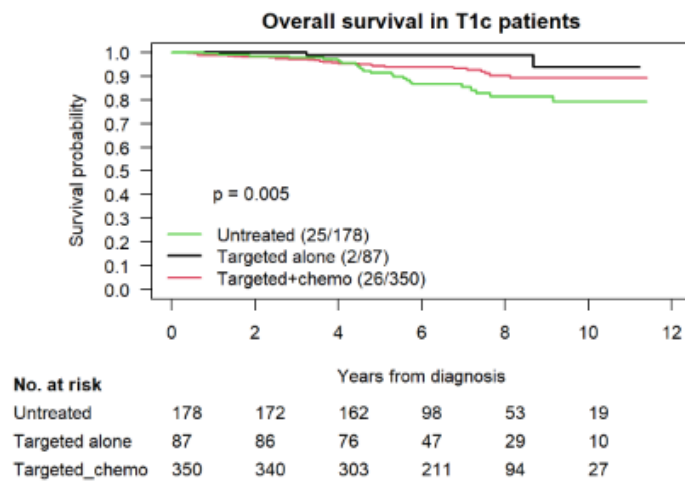
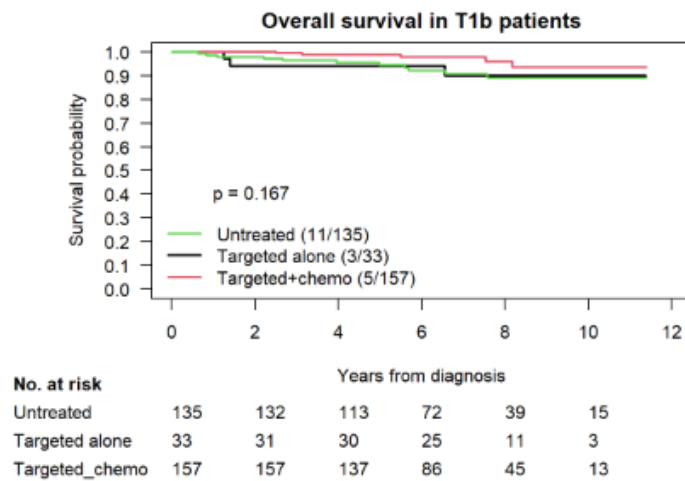
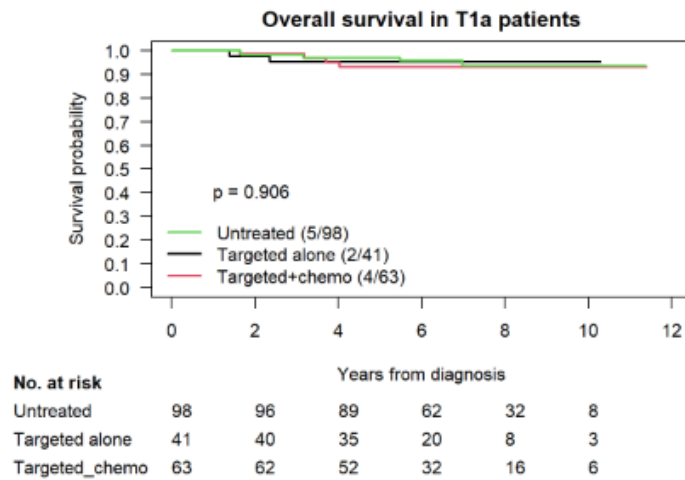
Abbreviations: iDFS = invasive disease-free survival, chemo = chemotherapy

Supplemental Figure 3. Univariate analysis of iDFS among T1 sub-categorizations in our three-group comparison of locoregional therapy alone versus trastuzumab with or without chemotherapy



Abbreviations: OS = overall survival, chemo = chemotherapy

Supplemental Figure 4. Univariate analysis of OS among T1 sub-categorizations in our two-group comparison of locoregional therapy alone versus trastuzumab with or without chemotherapy



Abbreviations: OS = overall survival, chemo = chemotherapy

Supplemental Figure 5. Univariate analysis of OS among T1 sub-categorizations in our three-group comparison of locoregional therapy alone versus trastuzumab with or without chemotherapy