

Manuscript Title: Impact of stopping trastuzumab in early breast cancer: a population-based study in Ontario, Canada

SUPPLEMENTARY MATERIALS

Supplementary Methods

Data Sources

Our dataset used in our study was linked by ICES using the following data sources. The Ontario Health Insurance plan (OHIP) is a publicly funded provincial health insurance that covers medical costs for all residents in Ontario. The OHIP database was used to identify outpatient visits, physician visits, echocardiogram and MUGA testing through billing codes in our patients. The Ontario Cancer Registry (OCR) was used to confirm BC diagnosis and to obtain cancer stage, estrogen receptor (ER) status, and progesterone receptor (PR) status information. Patients treated with trastuzumab were identified through the New Drug Funding Program (NDFP), a public health program which captures information on trastuzumab administration. The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD), CIHI same-day surgery, the National Ambulatory Care Reporting System (NACRS) database, and ICES-derived cohorts for pre-treatment Charlson co-morbidity index scores, treatment location (community vs. teaching hospital), ambulatory and emergency department visits and hospitalizations for heart failure, pulmonary edema and cardiomyopathy, income demographics and cause of death were collected. We did not have access to LVEF values or clinic notes.

Supplementary Table 1: Hazard ratio estimates with 95% confidence limits from multivariable analysis calculated for disease free survival in primary analysis.

Analysis of Maximum Likelihood Estimates					
Parameter		Hazard Ratio	95% Hazard Ratio Confidence Limits		p*
Age at first treatment	40-49	0.77	0.55	1.08	0.13
Age at first treatment	50-59	0.97	0.71	1.33	0.84
Age at first treatment	60-69	1.17	0.85	1.61	0.34
Age at first treatment	70-79	1.99	1.42	2.78	<.0001
Age at first treatment	>=80	3.63	2.22	5.94	<.0001
Charlson Comorbidity Index	1 - 2	1.24	0.96	1.60	0.10
Charlson Comorbidity Index	>=3	1.33	1.10	1.62	0.00
Rural	Yes	1.04	0.82	1.32	0.73
ER positive	Positive	0.62	0.48	0.81	0.00
Stage at diagnosis	Stage II	1.74	1.30	2.32	0.00
Stage at diagnosis	Stage III	3.30	2.43	4.50	<.0001
Completed chemotherapy	No	1.62	1.09	2.41	0.02
Cardiologist visit history	yes	0.81	0.63	1.04	0.10
Anthracycline treatment history	yes	1.23	0.86	1.78	0.26

* two-sided P values were calculated using chi-square test

Supplementary Table 2: Hazard ratio estimates with 95% confidence limits from multivariable analysis calculated for overall survival in in primary analysis

Analysis of Maximum Likelihood Estimates					
Parameter		Hazard Ratio	95% Hazard Ratio Confidence Limits		p*
Age at first treatment	40-49	0.76	0.53	1.09	0.14
Age at first treatment	50-59	0.96	0.68	1.36	0.83
Age at first treatment	60-69	1.11	0.78	1.59	0.56
Age at first treatment	70-79	1.97	1.36	2.84	0.00
Age at first treatment	>=80	3.63	2.18	6.03	<.0001
Charlson Comorbidity Index	1 - 2	1.41	1.08	1.84	0.01
Charlson Comorbidity Index	>=3	1.43	1.16	1.77	0.00
Rural	Yes	1.10	0.86	1.40	0.44
ER positive	Positive	0.61	0.46	0.81	0.00
Stage at diagnosis	Stage II	1.77	1.28	2.46	0.00
Stage at diagnosis	Stage III	3.80	2.70	5.35	<.0001
Completed chemotherapy	No	1.67	1.12	2.49	0.01
Cardiologist visit history	yes	0.76	0.58	1.00	0.05
Anthracycline treatment history	yes	1.40	0.98	2.01	0.07

* two-sided P values were calculated using chi-square test

Supplementary Table 3: Hazard ratio estimates with 95% confidence limits from multivariable analysis calculated for disease free survival in sensitivity analysis.

Analysis of Maximum Likelihood Estimates					
Parameter		Hazard Ratio	95% Hazard Ratio Confidence Limits		p*
Age at first treatment	40-49	0.83	0.58	1.20	0.33
Age at first treatment	50-59	0.95	0.67	1.35	0.78
Age at first treatment	60-69	1.21	0.85	1.72	0.29
Age at first treatment	70-79	2.14	1.48	3.11	<.0001
Age at first treatment	>=80	4.15	2.37	7.24	<.0001
Charlson Comorbidity Index	1 - 2	1.16	0.87	1.54	0.32
Charlson Comorbidity Index	>=3	1.32	1.06	1.63	0.01
Rural	Yes	0.99	0.76	1.30	0.97
ER positive	Positive	0.68	0.50	0.92	0.01
Stage at diagnosis	Stage II	1.55	1.14	2.10	0.01
Stage at diagnosis	Stage III	2.85	2.05	3.97	<.0001
Completed chemotherapy	No	1.40	0.90	2.18	0.13
Cardiologist visit history	yes	0.89	0.68	1.17	0.40
Anthracycline treatment history	yes	1.12	0.73	1.72	0.61

* two-sided P values were calculated using chi-square test

Supplementary Table 4: Hazard ratio estimates with 95% confidence limits from multivariable analysis calculated for overall survival in sensitivity analysis

Analysis of Maximum Likelihood Estimates					
Parameter		Hazard Ratio	95% Hazard Ratio Confidence Limits		P*
Age at first treatment	40-49	0.78	0.52	1.17	0.23
Age at first treatment	50-59	0.90	0.61	1.32	0.59
Age at first treatment	60-69	1.10	0.75	1.63	0.62
Age at first treatment	70-79	2.10	1.40	3.16	0.00
Age at first treatment	>=80	3.97	2.24	7.04	<.001
Charlson Comorbidity Index	1 - 2	1.33	0.99	1.79	0.06
Charlson Comorbidity Index	>=3	1.42	1.13	1.79	0.00
Rural	Yes	1.05	0.80	1.38	0.74
ER positive	Positive	0.68	0.49	0.95	0.02
Stage at diagnosis	Stage II	1.52	1.08	2.15	0.02
Stage at diagnosis	Stage III	3.28	2.28	4.72	<.001
Completed chemotherapy	No	1.50	0.96	2.34	0.07
Cardiologist visit history	yes	0.87	0.64	1.17	0.35
Anthracycline treatment history	yes	1.40	0.92	2.12	0.12

* two-sided P values were calculated using chi-square test