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Pathological complete response rates, treatment patterns, and survival outcomes in high-risk, neoadjuvant-treated HER2-positive early breast cancer: a Canadian chart review

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Objectives

- To describe the pathologic complete response (pCR) rates in patients with high-risk, neoadjuvant-treated, Human epidermal growth factor receptor 2 (HER2) overexpressing early breast cancer (eBC) in Alberta, Canada, and describe their treatment patterns within the overall target population and by achievement of pCR.
- To describe event-free survival (EFS) and overall survival (OS) in this population overall and by achievement of pCR, and to examine the healthcare resource utilization (HCRU) in this population overall and by achievement of pCR.

Conclusions

- pCR following neoadjuvant therapy (NAT) is a key milestone for patients with high-risk HER2+ eBC. In this chart review study, patients who achieved pCR had previously received less invasive surgery, and had lower subsequent mortality, and experienced reduced healthcare utilization, emphasizing the clinical and patient-centered relevance of pCR as a meaningful endpoint.
- Given the observed clinical benefits of pCR, it should be noted that the pCR rates in this cohort, which largely reflect the recent standard-of-care in Alberta, Canada, remain suboptimal. Improvements in NAT approaches are warranted to improve outcomes in high-risk eBC.

Plain language summary

Why did we perform this research?

- Breast cancer is the most common cancer and second leading cause of cancer death among women in Canada.
- Maintaining high quality, equitable care for patients with HER2+ early breast cancer remains essential as the number of eligible patients for novel neoadjuvant therapies is expected to grow.
- In Canada, there is limited evidence on contemporary treatment patterns and clinical outcomes associated with the management of HER2+, high-risk eBC.

How did we perform this research?

This was a study using existing real-world data from patients in Alberta, Canada who were diagnosed with non-metastatic, high risk HER2+ eBC. Through manual chart abstraction, this study collected and analyzed clinical outcomes of patients treated with neoadjuvant therapy.

What were the findings of this research?

Patients who achieved a complete response were less likely to develop disease recurrence, and previously had less invasive surgeries, and were associated with lower HCRU.

What are the implications of this research?

These results highlight the importance of pCR as a milestone in the treatment of HER2+ eBC cancer and support the need to promote efficient and sustainable access to novel treatments for this disease.

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Poster presented at the 2025 San Antonio Breast Cancer Symposium by Dr. Jan-Willem Henning. Corresponding author email address: janwillem.henning1@astrazeneca.com. Dr. Henning's contributions to the study as an author were completed prior to his joining AstraZeneca.

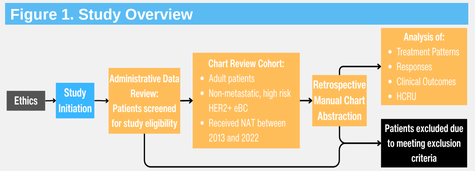
Introduction

- Breast cancer was estimated to be the second leading cause of cancer deaths among women in Canada in 2024.[1]
- HER2 is overexpressed in approximately 15-20% of breast cancers and is associated with increased cancer growth rate and metastases while decreasing overall survival.[2-4] The prognosis for patients with HER2+ eBC has improved with the expansion of HER2-directed therapies to eBC.[5]
- Patients with high-risk early breast cancer may benefit from HER2-directed NAT, which can be used to reduce tumor size, assess treatment response, and may allow for de-escalation of surgery where it was initially not possible.[6]

Methods

- We conducted a retrospective chart review of all adults (≥18 years at diagnosis) with non-metastatic, high risk (T0-4N1-3M0 or T3-4N0M0) HER2+ (classified as IHC3+ or IHC2+/ISH+) eBC who received NAT (including anti-HER2 with anthracycline-containing or non-anthracycline-containing chemotherapy) from 17 Alberta cancer centres between 2013 and 2022, identified in the Oncology Outcomes database. Patients were followed up until death, last known date of follow-up, or the administrative end of the study (August 2024).
- The study overview is displayed in **Figure 1**.
- All analyses were descriptive in nature. The primary objectives included the estimation of pCR (ypT0/Tis ypN0) and characterization of neoadjuvant and post-neoadjuvant treatment patterns (overall and by pCR). Secondary objectives included the estimation of event free survival (EFS) and overall survival (OS), overall and by pCR.
- Time to event outcomes were evaluated using unadjusted Kaplan Meier methods with date of diagnosis as the index date, while healthcare resource utilization rates (HCRU) were reported by pCR status. Kaplan Meier survival curves were plotted with 95% confidence intervals.

Figure 1. Study Overview



Results

- The chart review included 606 neoadjuvant-treated women who were diagnosed with HER2+ early-stage breast cancers in Alberta between 2013 and 2022. The median follow-up time was 4.6 years. The characteristics of patients who achieved a pCR are described in **Table 1** below, while the proportions of post-neoadjuvant treatments by pCR status are described in **Table 2**.

Table 1. pCR status by patient characteristics

Characteristic (N=606)	Achieved a pCR
	n = 268 (46.9)[a]
Age (mean [SD])	51.5 (11.2)
Year of diagnosis (n [%])	
2013	17 (42.5)
2014	24 (51.1)
2015	19 (54.3)
2016	24 (48.9)
2017	23 (48.9)
2018	33 (44.0)
2019	33 (55.9)
2020	28 (48.3)
2021	37 (51.4)
2022	30 (36.1)
HR status (n [%])	
Negative	113 (57.4)
Positive	155 (41.4)
Type of surgery (n [%])	
Breast conserving	105 (53.3)
Mastectomy	163 (43.6)
Received node dissection (n [%])	60 (58.3)
TNM group (n [%])	
T0-4, N1-3, M0	254 (47.4)
T3-4, N0, M0	14 (40.0)
Stage at diagnosis (n [%])	
IIA	46 (65.7)
IIB	119 (48.6)
IIIA	52 (39.1)
IIIB	37 (46.2)
IIIC	14 (32.6)
Neoadjuvant treatment[b] (n [%])	
Anti-HER2+ without anthracycline	185 (49.6)
Anti-HER2+ with anthracycline	83 (41.9)

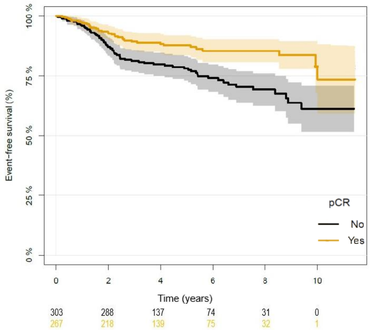
a: pCR status could not be obtained for 35 patients (n=571)
b: Anti-HER2+ regimens were trastuzumab for >95% of patients. Non-anthracycline chemotherapy complements were either carboplatin and docetaxel, or paclitaxel in >90% of patients. Anthracycline chemotherapy complements were cyclophosphamide, epirubicin and fluorouracil, or cyclophosphamide and doxorubicin, with both combinations accounting for >90% of patients receiving anthracycline-containing NAT.

Table 2. Patient characteristics

Post-neoadjuvant treatment[a]	No pCR n (%)	pCR n (%)
Trastuzumab	220 (72.6)	237 (88.4)
Pertuzumab + trastuzumab	*Suppressed*	12 (4.5)
T-DM1	61 (20.1)	*Suppressed*

a: Not all regimens observed are listed. In addition, cells are suppressed if they contained <10 observations. Percentages are by column.

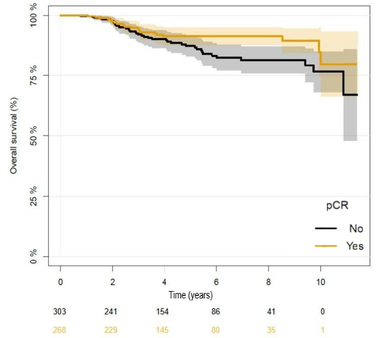
Figure 2. Event-free survival by pCR status



	EFS at 2-years (95% CI)	EFS at 3-years (95% CI)	EFS at 5-years (95% CI)
pCR	**92.8%** (89.7-95.9)	**89.4%** (85.6-93.2)	**87.8%** (83.6-91.9)
No pCR	**87.2%** (83.4-91.0)	**81.3%** (76.7-85.9)	**78.2%** (73.1-83.2)

- pCR status was obtainable for 571 (94.2%) patients. Among these patients, 268 (46.9%) achieved pCR. Nodal dissection was less frequent in patients who received breast conserving surgery (132 [27.4%]) as opposed to patients who received mastectomy (350 [72.6%]).
- Patients who received breast conserving surgery were more likely to obtain pCR (53.5%) than patients who received mastectomy (43.6%).

Figure 3. Overall survival by pCR status



	OS at 2-years (95% CI)	OS at 3-years (95% CI)	OS at 5-years (95% CI)
pCR	97.3% (95.3-99.3)	94.3% (91.4-97.2)	91.3% (87.6-95.0)
No pCR	97.6% (95.9-99.4)	92.0% (88.7-95.3)	87.3% (83.0-91.7)

- 583 (96.2%) of patients received post-neoadjuvant therapy, with trastuzumab mostly commonly used (484 [79.9%]). T-DM1 was used almost exclusively as a post-neoadjuvant therapy in patients without pCR.
- Among the 303 patients who did not achieve a pCR, 63 (20.8%) developed disease recurrence, whereas among the 268 patients who achieved a pCR, only 27 (10.1%) developed disease recurrence.

Table 3. HCRU during recurrence-free period over 5 years by pCR status

	Year 1		Year 2		Year 3		Year 4		Year 5	
Resource Type	**pCR**	**No pCR**	**pCR**	**No pCR**	**pCR**	**No pCR**	**pCR**	**No pCR**	**pCR**	**No pCR**
Inpatient hospitalizations per person-year	0.67	0.86	0.19	0.25	0.12	0.15	0.11	0.16	0.07	0.11
Outpatient emergency visits per person-year	1.69	1.99	0.50	0.76	0.40	0.51	0.30	0.68	0.48	0.64
Outpatient non-emergency visits per person-year	10.61	12.65	3.27	3.99	2.03	3.06	2.01	2.59	1.20	1.94

Healthcare Resource Utilization

- **Table 3** summarizes the rates of inpatient hospitalizations, outpatient emergency visits, and outpatient non-emergency visits over a 5-year horizon after initiation of NAT, stratified by pCR.
- The HCRU rates suggest that achieving pCR corresponds with fewer hospitalizations and inpatient visits throughout all 5 years following NAT initiation.
- The high number of hospitalizations, emergency visits, and outpatient visits in the first year of follow-up highlights the intensive healthcare needs of this patient population.

Discussion

- Our findings underscore the clinical significance of achieving a pCR in patients with HER2+ eBC while highlighting economic benefits associated with the achievement of pCR.
- Patients who achieved a pCR were less likely to have had received invasive surgical procedures compared to patients who did not achieve pCR.
- Patients receiving neoadjuvant treatment for HER2+ eBC had worse clinical outcomes if they did not achieve a pCR.
- The low uptake of neoadjuvant pertuzumab in this study reflects the lack of public access in Canada during the study period.

Limitations

- Analyses conducted using chart review data may be subject to information bias due to errors in data abstraction.
- The descriptive differences in clinical outcomes must be interpreted with caution as they do not take differences in prognostic factors.

Disclosures

JWH has received research funding from AstraZeneca, Pfizer, Rethink Breast Cancer and Novartis. JWH's contributions as an author for this work was completed prior to joining AstraZeneca. SS, ZSM, and MB are employees of AstraZeneca. AN was an employee of AstraZeneca during the time of their contributions. Oncology Outcomes (O2) received funding from AstraZeneca for the conduct of this study.

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