Efficacy of Neoadjuvant Endocrine Therapy Versus Neoadjuvant Chemotherapy in ER-positive Breast Cancer: Results From a Prospective Institutional Database

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Abstract

Data comparing the efficacy of neoadjuvant endocrine therapy with neoadjuvant chemotherapy are scarce. This retrospective analysis compared the efficacy of endocrine therapy with chemotherapy to downstage tumors in a matched cohort analysis of 176 patients. Down-staging of the primary tumor was achieved in 39% with chemotherapy and 22% with endocrine therapy ($P = .032$). Pathologic complete response was achieved in 2% of all cases. This study highlights the need to develop and validate biomarkers that can discern differences in biology and better predict responses to preoperative treatment for patients with estrogen receptor-positive breast cancer.

Background: Although neoadjuvant chemotherapy (NACT) has been established as a standard for medically fit patients with locally advanced breast cancer, there has been renewed interest in utilizing neoadjuvant endocrine therapy (NET) for women with estrogen receptor-positive, human epidermal growth factor receptor 2-negative breast cancer. Rates of pathologic complete response (pCR) are known to be low, but data regarding down-staging and long-term outcomes are inconsistent. **Patients and Methods:** A prospective institutional database of patients with breast cancer treated with neoadjuvant therapy from 2012 to 2017 was analyzed to identify patients with estrogen receptor-positive, human epidermal growth factor receptor 2-negative breast cancer. Patients who received NET were compared with those who received NACT. A matched analysis (age, stage, grade) was performed to compare rates of down-staging, pCR, breast conserving surgery, and CPS+EG scores. **Results:** A total of 176 patients met eligibility criteria. Of these, 111 (63%) patients received NACT, 51 (29%) received NET, and 14 (8%) received both sequentially. Women prescribed NET were older (65.5 vs. 51.2 years; $P < .0001$) and presented with lower clinical stage ($P < .0001$). The median duration of NET was 90 days. When matched, clinical down-staging was more frequent with NACT (20/51; 39%) compared with NET (11/51; 22%) ($P = .032$). Of these, 2% achieved pCR in each cohort. Conversion rates to breast conserving surgery eligibility were low (8% and 13% with NET and NACT; $P = .70$). No significant differences in CPS+EG scores were identified. **Conclusions:** Significantly higher rates of down-staging were achieved with NACT compared with NET when patients were matched. This study highlights the importance of establishing tumor biology and the need for biomarkers that can be used as predictive tools to inform treatment.

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Introduction

The use of neoadjuvant chemotherapy (NACT) in the treatment of early stage breast cancer has been established as a standard option for selected, medically fit patients.[1-4] NACT is most often utilized to improve surgical options through tumor downsizing or to render inoperable cancers operable. This may, in turn, improve the chances of obtaining clear surgical margins with the first surgery and allow for higher rates of breast conserving surgery (BCS).[5,6] Further, pathologic complete response (pCR) has been recognized as a surrogate endpoint for improved disease-free and overall survival after NACT,[7-9] but the ability to achieve a pCR in patients with estrogen receptor-positive (ER^+) breast cancer is significantly lower than those with triple negative or human epidermal growth factor receptor 2-positive ($HER2^+$) breast cancer.[10-12] Indeed, the pCR rate reported in patients with hormone receptor-positive (HR^+), HER2-negative ($HER2^-$) disease treated with NACT are in the range of 5% to 15%.[7,11]

Owing to this low rate of pCR in response to NACT, there has been renewed interest in utilizing neoadjuvant endocrine therapy (NET) for the treatment of women with HR^+, $HER2^-$ breast cancer.[10,11,13-15] However, the relative efficacy of NET compared with NACT for these patients has been difficult to elucidate. NET has historically been offered to frail or elderly patients whose comorbidities may have contributed to relative contraindication to surgery.[1,14,16,17] Direct comparisons of the efficacy of NET with NACT have been attempted in small phase II studies, although these were fraught with a number of issues, such as small sample size,[18,19] short duration of NET,[20] and the lack of incorporating information on HER2 status.[20] Despite the challenges of direct comparisons with chemotherapy, the use of NET has been supported by a number of clinical trials, such as the Immediate Preoperative Anastrozole, Tamoxifen, or Combined with Tamoxifen (IMPACT) multicenter double-blind randomized trial, the Preoperative treatment of postmenopausal breast cancer patients with letrozole (P024) trial and the Efficacy of six month neoadjuvant endocrine therapy in postmenopausal, hormone receptor-positive breast cancer patients (TEAM IIA) trial.[21-23] These larger randomized studies and others[16,24,25] reported similar pCR rates as those obtained with NACT in this population, but with less toxicity.

This does, however, bring into question the validity of pCR as a clinically meaningful surrogate endpoint, especially in patients with ER^+ disease. One promising endpoint with potentially improved clinical applicability, particularly in ER^+ breast cancer, is the CPS+EG staging system in the setting of neoadjuvant therapy, which utilizes baseline clinical stage, final pathologic stage, the ER status, and the nuclear grade. The score is established after surgery and has demonstrated an ability to further sub-stratify patients who do not achieve a pCR based on degree of response[26] to estimate 5-year distant metastasis-free survival and disease-specific survival. This has been validated prospectively in patients with HR^+, $HER2^-$ breast cancer[27] and is currently used as a criterion for eligibility in some post-NACT residual disease intervention studies.

Despite the proof of concept, large prospective randomized trials comparing NACT directly with NET have not been carried out. This is partially owing to reluctance to randomization from patients and physicians alike. Consequently, large trials are thought to be unfeasible given the slow accrual observed in prior randomized feasibility studies.[19] Further, as pCR is not often achieved in this subgroup of patients, the selection of an alternate, clinically meaningful, endpoint is needed. This issue has been widely debated, but a clear consensus has yet to emerge.

Studies of real-world outcomes assessing the use of NET compared with NACT in a medically fit group are needed to determine if, indeed, clinically meaningful endpoints are improved with less toxicity in those receiving NET compared with those receiving NACT. Given the difficulties and the low likelihood of a large randomized study to be feasible, we sought to assess the relative effectiveness of NET compared with NACT in down-staging, improving surgical options, and in improving CPS+EG scores in a real-world setting.

Patients and Methods

Study Design

Cancer control in British Columbia (BC) is mandated through the British Columbia Cancer Agency (BCCA) and overseen by the Provincial Health Services Authority (PHSA). Within this mandate, the BCCA has created a number of databases to document baseline clinical, pathologic, and long-term outcome data for patients with cancer within the province. One of the newest databases includes the locally advanced breast cancer prospective database, established in 2012. Data is acquired in a locally advanced breast cancer clinic by trained personnel, ensuring ongoing maintenance and accuracy of the data, and is utilized for quality initiatives, safety reviews, and research purposes.

The prospective institutional database of patients with breast cancer who received neoadjuvant therapy between January 2012 and September 2017, at the British Columbia Cancer Agency – Vancouver Centre, was analyzed to identify all patients with HR^+, $HER2^-$ breast cancer. Only patients who were medically fit to undergo surgery at presentation and went on to have surgical resection were included in the final cohort. Clinical trial patients were excluded. No additional exclusion criteria were applied. Database accuracy was routinely ensured by ongoing quarterly quality assessment in which 10 to 20 charts were randomly selected for an in-depth audit, and percent agreement among data managers was reported quarterly. This database was maintained on an encrypted server, only accessible to the database managers. Data utilized for research purposes was then de-identified prior to analyses. This project was conducted in accordance and approval with the University of British Columbia BCCA Research Ethics Board.

Outcome Assessment and Statistical Analyses

Data from the database pertaining to baseline demographics, including age, baseline clinical tumor size, nodal involvement, nuclear grade, and HR status was extracted. Details on final pathologic stage, rates of pCR, and rates of BCS, in addition to the type and duration of treatment received, were collected for assessment of outcomes. In order to compare outcomes between NET and NACT and overcome selection bias, a matched cohort of cases (NET) and controls (NACT) was created using a propensity scoring method accounting for age, clinical stage, and tumor grade. Matched groups

were balanced for all covariates with a standard difference of 0.1. Independent sample *t* tests was used to assess for statistical significance for continuous variables, whereas the χ^2 test was performed for categorical variables.

For outcome assessment between these 2 groups, data pertaining to duration and type of treatment received (NACT vs. NET), clinical response, final pathologic stage, pCR, and type of surgery were extracted from the database. CPS+EG scores were also calculated for all patients, including those who did not achieve pCR. Rates of down-staging, clinical complete response, pCR, BCS, and CPS+EG scores were then compared using the Pearson χ^2 test or independent sample *t* tests. Down-staging was defined as a difference in baseline clinical stage as compared with final pathologic stage, whereby each stage was attributed a numerical value and down-staging was defined as a decrease in the numerical value of the final pathologic stage compared with the baseline clinical stage; clinical complete response was defined as the resolution of palpable disease within the breast or axilla, whereas pCR was defined as the absence of any invasive cancer within the breast and lymph nodes. BCS was defined as partial mastectomy, with or without sentinel lymph node biopsy or axillary lymph node dissection. Statistical analyses were performed using both IBM SPSS Software (Version 25) and Statistical Analysis Software (SAS software version 9.2; SAS Institute, Cary, NC).

Results

Cohort Characteristics

From 2012 to 2017, a total of 176 patients met eligibility criteria for this study. The median age was 56 years (range, 26-87 years), with 9.1% below the age of 40, 50.0% between the ages of 41 and 60, 35.8% between the ages of 61 and 80, and 5.1% who were 81 years or older (Table 1). A total of 87.6% had a T2 or greater size tumor, and 63.1% of patients had clinical axillary nodal involvement at baseline assessment. Overall, 76.2% of patients had clinical stage 2b or greater disease at presentation. Nuclear grade was available for 158 of the 176 patients, which included 58.7% of nuclear grade 1 to 2 and 30.1% of nuclear grade 3 invasive carcinoma. ER receptor status was reported as Allred 8/8 in 85.2% of patients, whereas PR status was more widely distributed (Table 1).

Of all patients, 51 (29.0%) received NET as compared with 111 (63.1%) who received NACT and 14 (7.9%) who received a combination of both sequentially, while awaiting definitive management. Median duration of treatment with NET was 90 days (range, 9-366 days). Median duration of treatment with NACT was 103 days (range, 64-178 days). The median age of women offered NET was 65.5 years as compared with 50.1 years with NACT ($P < .0001$; 95% confidence interval [CI], 10.4-18.3). With regard to tumor characteristics, 45.2% of those who received NET had stage I or IIa disease, compared with 16.2% of those who received NACT. Conversely, 54.9% who received NET had stage IIb or III disease, compared with 83.7% who received NACT. Overall, patients receiving NET presented with a lower clinical stage ($P < .0001$; 95% CI, −1.07 to −0.354) compared with those who received chemotherapy. With regard to grade, 36.5% of patients with grade 1 to 2 tumors received NET and 63.5% received NACT. For grade 3 tumors, 16.0% received NET and 84.0% received NACT. Overall, NET patients had a lower nuclear grade on initial core biopsy ($P = .004$; 95% CI −0.530 to −0.104). With regard to receptor status, all patients were ER^+, and no significant difference in ER positivity level was observed between the 2 groups. Likewise, progesterone receptor (PR) status, although more variable overall, was similar in both groups (Table 1). Baseline rates of BCS-eligible patients were similar between groups, 23.5% for those who received NET and 23.4% for those who received NACT ($P = .99$). The percentage of patients eligible for BCS at the end of treatment were similar, 31.4% with NET and 29.7% with NACT ($P = .83$). Rates of conversion from BCS-ineligible to BCS-eligible were similar between those who received NET and NACT (10.3% and 8.2%, respectively; $P = .72$).

Matched Cohort Characteristics

A matched propensity cohort based on age, baseline clinical stage, and nuclear grade was created, resulting in a matched cohort of 51 patients treated with NET and 51 matched controls treated with NACT (Table 2). Matched groups were balanced for all covariates with a standard difference of 0.1. When matched for age, baseline clinical stage, and nuclear grade, rates of down-staging were 21.6% (11/51) with NET and 39.2% (20/51) with NACT, ($P = .032$) (Table 3). Rates of clinical complete response were 3.9% (2/51) with NET and 37.3% (19/51) with NACT ($P < .0001$). pCR was achieved in 2 patients in the whole cohort, 1 patient with NET (2.1%) and the other with NACT (2.1%). Rates of partial mastectomy were 25.5% (13/51) for patients receiving NET as compared with 27.5% for those receiving NACT (14/51) ($P = .05$). No significant difference in CPS+EG scores were identified when comparing NET with NACT ($P = .296$), although numerically, 37.3% and 21.6% of NET patients had a score of "1" and "2," compared with 17.6% and 45.1% with NACT, respectively. Baseline rates of BCS-eligible patients were 22.9% for those who received NET and 33.3% for those who received NACT ($P = .26$). Patients eligible for BCS at the end of treatment were similar: 29.2% with NET and 41.7% with NACT ($P = .20$). Rates of conversion from BCS-ineligible to BCS-eligible were similar between those who received NET and NACT (8.1% and 12.5%, respectively; $P = .70$) (Table 3).

Discussion

In this matched analysis of patients with breast cancer, the use of NACT compared with NET was significantly associated with greater down-staging of tumors and higher rates of clinical complete response. These results are clinically meaningful because they challenge the perception that patients with luminal tumors (ER^+, $HER2^-$) achieve similar rates of down-staging with NET compared with NACT when a relatively short course of NET is used, with a median duration of 90 days in this study. Although these results differ from a phase II study that included patients who were $HER2^+$,[20] they are also different from 2 other small phase II studies that included comparable patient cohorts. Both of these studies enrolled a small number of patients and were not powered to detect significant differences in clinical response, as they were designed as feasibility studies[19] with exploratory analyses.[18] Further, these studies used radiologic response and pathologic response rates as endpoints, making direct comparisons difficult.[18-20]

Table 1 Whole Cohort Baseline Characteristics

Characteristic	Whole Cohort (N = 176), n (%)	NET (N = 51), n (%)	NACT (N = 111), n (%)
Age at Diagnosis, y			
Median	56	65	50
Range	26-87	41-87	26-75
Age Group, y			
<40	16 (9.1)	0 (0)	16 (14.4)
41-50	48 (27.3)	7 (13.7)	39 (35.1)
51-60	40 (22.7)	11 (21.6)	28 (25.2)
61-70	41 (23.3)	13 (25.5)	23 (22.5)
71-80	22 (12.5)	11 (21.6)	5 (4.5)
>81	9 (5.1)	9 (17.6)	0 (0)
Size of Initial Tumor			
TX	7 (4.0)	2 (3.9)	4 (3.6)
T1	15 (8.6)	5 (9.8)	9 (8.1)
T2	71 (40.4)	26 (51.0)	43 (38.7)
T3	59 (33.6)	15 (29.4)	40 (36.0)
T4	24 (13.6)	3 (5.9)	15 (13.5)
Baseline Nodal Status			
N0	65 (36.9)	32 (62.7)	29 (26.1)
N1	92 (52.3)	18 (35.3)	68 (61.3)
N2	15 (8.5)	1 (2.0)	13 (11.7)
N3	4 (2.3)	0 (0)	1 (0.9)
Baseline Clinical Stage			
1a	7 (4)	3 (5.9)	3 (2.7)
1b	0 (0)	0 (0)	0 (0)
2a	35 (19.9)	20 (39.3)	15 (13.5)
2b	68 (38.7)	20 (39.2)	46 (41.4)
3a	40 (22.7)	5 (9.8)	31 (27.9)
3b	22 (12.5)	3 (5.9)	15 (13.5)
3c	4 (2.3)	0 (0)	1 (0.9)
Nuclear Grade			
1	14 (8)	6 (11.8)	7 (6.3)
2	91 (51.7)	29 (56.9)	54 (48.6)
3	53 (30.1)	8 (15.7)	42 (37.8)
Unavailable	18 (10.2)	7 (13.7)	8 (7.2)
ER Allred Score			
4	2 (1.1)	0 (0)	2 (1.8)
5	5 (2.8)	2 (3.9)	3 (2.7)
6	3 (1.7)	0 (0)	3 (2.7)
7	16 (9.1)	4 (7.8)	11 (9.9)
8	150 (85.2)	45 (88.2)	92 (82.9)
PR Allred Score			
0	24 (13.6)	6 (11.8)	16 (14.4)
1	0 (0)	0 (0)	0 (0)
2	3 (1.7)	2 (3.9)	1 (0.9)
3	3 (1.7)	1 (2.0)	2 (1.8)
4	8 (4.5)	4 (7.8)	3 (2.7)
5	17 (9.7)	2 (3.9)	14 (12.6)
6	22 (12.5)	3 (5.9)	18 (16.2)
7	24 (13.6)	12 (23.5)	9 (8.1)
8	75 (42.6)	21 (41.1)	48 (43.2)

Abbreviations: ER = estrogen receptor; NACT = neoadjuvant chemotherapy; NET = neoadjuvant endocrine therapy; PR = progesterone receptor.

Table 2 Matched Cohort Baseline Characteristics

Characteristic	NET, n (%)	NACT, n (%)
Age at Diagnosis, y		
Median	64.6	60.1
Range	41.4-87.3	40.3-77.2
Age Group, y		
<40	0 (0)	2 (3.9)
41-50	9 (17.6)	7 (13.7)
51-60	10 (19.6)	17 (33.3)
61-70	14 (27.5)	21 (41.2)
71-80	10 (19.6)	4 (7.8)
>81	8 (15.7)	0 (0)
Baseline Clinical Stage		
1a	3 (5.9)	2 (3.9)
1b	0 (0)	0 (0)
2a	20 (39.3)	12 (23.5)
2b	20 (39.2)	23 (45.1)
3a	5 (9.8)	10 (19.6)
3b	3 (5.9)	4 (7.8)
3c	0 (0)	0 (0)
Nuclear Grade		
1	6 (11.8)	6 (11.8)
2	29 (56.9)	29 (56.9)
3	8 (15.7)	10 (19.6)
Unavailable	7 (13.7)	6 (11.8)

Abbreviations: NACT = neoadjuvant chemotherapy; NET = neoadjuvant endocrine therapy.

The differences observed between this real-world prospective cohort and clinical trial patients may in part be owing to patient selection factors. Overall, the observed pCR rates were low and occurred at equal frequency in both the NACT and NET groups on matched analysis, although the study was not powered for this endpoint. In the absence of long-term outcomes for these patients, pCR remains one of the few surrogate endpoints used to predict better long-term outcomes.[28-30] However, it is well-recognized that ER-positivity predicts for much lower rates of pCR.[31] For this reason, CPS+EG scores were also assessed and revealed a numerically different proportion of score CPS+EG score of "1" and "2," which likely represents patients' favorable characteristics at baseline in addition to treatment received. Yet, the difference observed was not statistically significant, suggesting similar long-term outcomes for patients included in the matched analysis, albeit with a small sample size. This should be interpreted with caution, as the scoring system has not been validated with the use of NET and cannot replace long-term follow-up.

Finally, one of the most widely acknowledged goals of neoadjuvant therapy is to increase the rates of BCS.[2,3,5,6] Our study reveals low rates of conversion from BCS ineligibility to BCS eligibility of 8.1% and 12.5% with the use of NET and NACT, which is lower than what has been described in the literature.[6,10,11] It should also be noted that some patients deemed BCS-eligible went on to have a mastectomy. It is difficult to directly ascertain

Table 3 Rates of Down-staging, pCR, and CPS+EG Scores in the Matched Cohort Analysis

Characteristic	NET, n (%)	NACT, n (%)	*P* Value
Baseline Clinical Stage			
1a	3 (5.9)	2 (3.9)	
1b	0 (0)	0 (0)	
2a	20 (39.3)	12 (23.5)	
2b	20 (39.2)	23 (45.1)	
3a	5 (9.8)	10 (19.6)	
3b	3 (5.9)	4 (7.8)	
3c	0 (0)	0 (0)	
Final Clinical Stage			
Clinical complete response	2 (3.9)	19 (37.3)	**<.0001**
1a	8 (15.7)	10 (19.6)	
1b	0 (0)	0 (0)	
2a	13 (25.5)	13 (25.5)	
2b	8 (15.7)	1 (2.0)	
3a	1 (2.0)	6 (11.8)	
3b	1 (2.0)	1 (2.0)	
3c	0 (0)	0 (0)	
Undetermined	18 (35.3)	1 (2.0)	
Final Pathologic Stage			
pCR	1 (2.0)	1 (2.0)	NS
1a	6 (118)	8 (15.7)	
1b	1 (2.0)	1 (2.0)	
2a	13 (25.5)	14 (27.5)	
2b	14 (27.5)	8 (15.7)	
3a	8 (15.7)	13 (25.5)	
3b	3 (5.9)	1 (2.0)	
3c	5 (9.8)	5 (9.8)	
Proportion of Change			
Down-staged	11 (21.6)	20 (39.2)	**.032**
No change	20 (39.2)	19 (37.3)	
Up-staged	20 (39.2)	12 (23.5)	
BCS			
Yes	13 (25.5)	14 (27.5)	**.05**
No	37 (72.5)	35 (68.6)	
Axillary mass excision	1 (2.0)	2 (4.0)	
Conversion to BCS-eligible	3 (8.1%)	4 (12.5%)	**.70**
CPS+EG Score			**.296**
0	3 (5.9)	3 (5.9)	
1	19 (37.3)	9 (17.6)	
2	11 (21.6)	23 (45.1)	
3	10 (19.6)	9 (17.6)	
4	1 (2.0)	1 (2.0)	
N/A	7 (13.7)	6 (11.8)	

Bolded values denote statistical significance.
Abbreviations: BCS = breast conserving surgery; NACT = neoadjuvant chemotherapy; NET = neoadjuvant endocrine therapy; NS = not significant; pCR = pathologic complete response.

the reason for such a high proportion of mastectomies, as the data collected was based on the recommendations of the surgical oncologists, who often did not indicate if the mastectomy was owing to patient preference or medical necessity. Although it is suspected that many of them were indicated for medical reasons, many patients had a preference for a mastectomy with reconstruction to achieve the desired cosmetic outcome. Nonetheless, no difference was found between groups with regards to the rate of BCS conversion rates despite higher rates of clinical complete response and down-staging of tumors with NACT.

There were a number of limitations associated with this prospective cohort study. Notably, given that this is a real-world study, patients were not randomized, and the sample size was relatively small. Another pertinent limitation is patient selection for NET as compared with NACT. Although age, stage, and grade were identified as the factors most likely to influence the choice of treatment, comorbidities and other intangible factors may also account for patient selection. Nonetheless, this bias of comorbid disease was mitigated by selecting only patients who were medically fit to undergo surgery at the time of presentation and went on to have surgical resection. Another point to highlight is that the median duration of endocrine therapy was 90 days in the NET arm, whereas it is recognized that rates of regression are slow and warrant a minimum of 4 to 6 months of endocrine therapy to achieve a maximal response.[32-35] Moreover, it remains unclear if rates of down-staging predict better outcomes for patients. In the absence of a better surrogate endpoint, CPS+EG scores were calculated and suggested similar long-term outcomes, albeit with a small sample size. Although these findings are interesting, the scoring system has not been validated with NET and has not been widely adopted as a clinical tool. Further, it should be noted that a certain degree of subjectivity is associated with clinical assessment of down-staging. It may be helpful to combine this data with similar data collected by others to determine if the rates of difference are preserved with a larger cohort.

Moving forward, the identification of appropriate goals for this patient population should be explored, given that pCR is rarely achieved and it remains unclear if clinical down-staging is predictive of long-term outcomes. The focus of neoadjuvant studies will likely shift toward the development and validation of biomarkers, in an attempt to discern differences in biology and simultaneously develop better predictive tools.[36-41] To this effect, our group has opened a prospective trial using the Oncotype DX assay to optimize treatment selection for patients with ER^+ breast cancers considered for neoadjuvant treatment.[42] In addition, novel agents (such as CDK 4/6 inhibitors, PIK3CA inhibitors, and checkpoint blockade inhibitors) are also likely to make their way to the forefront of research in the neoadjuvant setting, both in combination with endocrine therapy and chemotherapy.

In conclusion, significantly higher rates of down-staging were achieved with NACT as compared with NET when patients were matched for age, clinical stage, and nuclear grade. The adoption of NET was generally low in this cohort, and, based on this finding, the approach may be best reserved for those patients who have comorbidities precluding their eligibility for surgery or chemotherapy. Future work assessing the potential benefit of neoadjuvant combinations of endocrine therapy may translate in to better outcomes, although the best endpoint to predict long-term outcomes has yet to be elucidated.

Clinical Practice Points

- The use of NET has been postulated as a reasonable alternative to NACT, although data on the comparative efficacy to chemotherapy is scarce.
- The use of NACT was significantly associated with greater down-staging of tumors and higher rates of clinical complete response compared with NET.
- These results are clinically meaningful because they challenge the perception that patients with luminal tumors (ER^+, $HER2^-$) achieve similar rates of down-staging with neoadjuvant endocrine therapy compared with chemotherapy.
- This study highlights the need to develop and validate biomarkers that can discern differences in biology and inform the development of predictive tools.

Disclosure

N. LeVasseur reports an advisory role for Pfizer and TerSera and a grant from Abbvie; S. Chia reports an advisory role for Novartis, Pfizer, Roche, and Lilly; C. Simmons reports an advisory role for Pfizer, Eisai, Lilly, and TerSera. All other authors state that they have no conflicts of interest.

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