Real-World Outcome of Neoadjuvant Chemotherapy vs Endocrine Therapy in ER+/HER2− and HER2-Low Early Breast Cancer: A single-instituation Retrospective Study

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Abstract

Background: Neoadjuvant chemotherapy (NAC) and endocrine therapy (NET) are both used for ER+/HER2− or HER2-low breast cancer, but comparative real-world data are scarce.
Methods: We retrospectively reviewed 100 hormone receptor–positive, HER2-negative/low early breast cancer patients treated at King Fahad Medical City (2021–2024): 53 received NAC and 47 received NET. Clinical, pathological, and survival outcomes were compared.
Results: NET patients were older (median 67 vs 59 years) with more comorbidities and worse ECOG, while NAC was used for more advanced and aggressive tumors. pCR rates were low and similar (4% vs 5.7%). Tumor downstaging and breast-conserving surgery rates were comparable; nodal downstaging favored NAC (22.7% vs 9.1%). At 20-month median follow-up, recurrence-free survival was similar.
Conclusion: NAC was selected for younger, high-risk patients, whereas NET was used in older or lower-risk cases. Both approaches achieved meaningful downstaging and comparable early survival outcomes.

Introduction

Neoadjuvant chemotherapy (NAC) and endocrine therapy (NET) are both used in ER+/HER2− or HER2-low breast cancer, yet comparative real-world data remain limited.
This study aimed to evaluate treatment patterns, pathological response, and clinical outcomes between NAC and NET in this setting

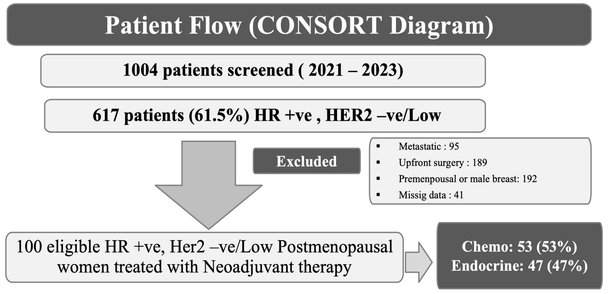


Figure 1. Patient Flow (CONSORT Diagram)

Methods and Materials

We retrospectively reviewed 100 hormone-positive, HER2-negative/low early breast cancer patients treated at King Fahad Medical City (Jan 2021– Dec 2024), comparing neoadjuvant chemotherapy (n=53) versus neoadjuvant endocrine therapy (n=47). Luminal subtype was defined by grade and Ki-67. Baseline variables were analyzed using χ^2/Fisher's exact and Mann–Whitney U tests. Outcomes included pCR, nodal and tumor downstaging, breast-conserving surgery conversion rate, and recurrence-free survival (RFS). pCR was defined as ypT0/is and ypN0. RFS was assessed using Kaplan–Meier with log-rank testing and Cox regression; significance set at p<0.05.

Characteristic	Chemotherapy (NAC) (n=53)	Endocrine (NET) (n=47)	P value
Age : Median (Range)	59.0 (range 50–71)	67.0 (range 53–90)	**<0.001**
ECOG ≥ 2	6 (11.3%)	11 (23.4%)	0.120
Comorbidities present	34 (64.2%)	37 (78.7%)	0.127
Clinical T3–4	29(54.7%)	21 (44.7%)	0.423
Clinical N+ at baseline	46 (86.8%)	30 (63.8%)	**0.0097**

Characteristic		Chemotherapy (NAC) (n=53)	Endocrine (NET) (n=47)	P value
Grade 3		12 (22.6%)	3 (6.4%)	**0.026**
Ki-67 ≥ 20%		34 (64.2%)	19 (40.4%)	**0.027**
Luminal Subtype	Luminal A	18 (34.0%)	27 (57.4%)	**0.025**
	Luminal B	35 (66.0%)	20 (42.6%)	

Table 1. Baseline Characteristics.

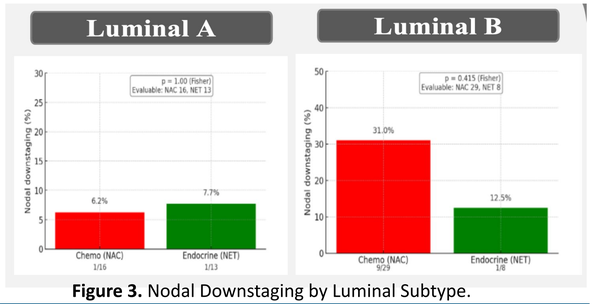


Figure 3. Nodal Downstaging by Luminal Subtype.

Results

NET patients were older (median 67 vs 59 years), had more comorbidities (37 vs 34), and worse ECOG ≥ 2 status (11 vs 6), whereas NAC was used more often for advanced disease (T3–T4: 29 vs 21; cN+: 46 vs 30; P=0.0097) and aggressive biology (grade 3: 12 vs 3; Ki-67 > 20%: 34 vs 19; luminal B: 35 vs 20; all statistically significant) (**Table 1**). pCR rates were low and similar (NAC 4% vs NET 5.7%) (**Figure 2**). Tumor downstaging was comparable overall (78% vs 80%), though in luminal B tumors it favored NAC (31% vs 13%) (**Figure 3**). Nodal downstaging occurred higher with NAC (22.7% vs 9.1%).
Breast-conserving surgery conversion rate was numerically slightly higher with NET but not statistically significant. At 20-month median follow-up, recurrence-free survival appeared comparable between the two groups (**Figure 4**).

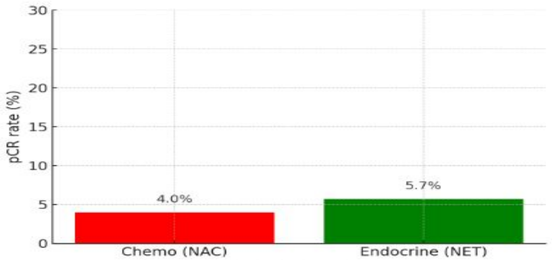


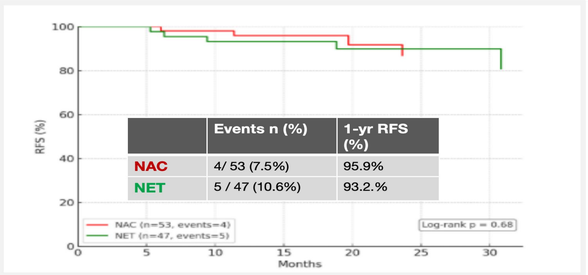
Figure 2. Pathologic Complete Response.

Discussion

In this comparative analysis, patients receiving endocrine therapy (ET) were notably older and exhibited a higher burden of comorbidities and poorer performance status, reflecting a population less suited for cytotoxic chemotherapy. Conversely, neoadjuvant chemotherapy (NAC) was preferentially administered in cases of more advanced disease and biologically aggressive subtypes, consistent with contemporary clinical practice patterns. Despite these baseline imbalances, the observed pathologic complete response (pCR) rates were low and comparable between the groups, aligning with prior evidence that hormone receptor–positive tumors seldom achieve pCR regardless of regimen. Tumor downstaging and breast-conserving surgery rates were similar, indicating that both NAC and neoadjuvant endocrine therapy (NET) can achieve meaningful locoregional control in selected patients. However, nodal downstaging and response in luminal B subtypes favored NAC, supporting its continued role in more proliferative or high-grade disease. At a median follow-up of 20 months, recurrence-free survival appeared comparable, suggesting that NET may represent a reasonable alternative to NAC for appropriately selected, lower-risk patients unfit for chemotherapy or with indolent tumor biology.

Conclusions

In this real-world study, NAC was favored in younger, fitter patients with aggressive tumor features, while NET was reserved for older patients or those with more favorable disease biology. pCR was comparable between NAC and NET while nodal response rates were higher in the NAC group numerically, but treatment selection reflected inherent baseline differences. Tumor downstaging and low recurrence rates were observed with both strategies.



	Events n (%)	1-yr RFS (%)
NAC	4/ 53 (7.5%)	95.9%
NET	5 / 47 (10.6%)	93.2.%

Figure 4. Recurrence & Follow-up.

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