ER expression and age as key determinants of pathologic complete response (pCR) following neoadjuvant chemotherapy in patients with hormone receptor-positive, her2-negative early breast cancer. Real world data

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Background

- Neoadjuvant chemotherapy is vital in early-stage breast cancer and enhances survival.
- Pathological complete response (pCR) is a key surrogate for improved outcomes and a common trial endpoint.
- pCR rates are generally low in hormone receptor–positive, HER2-negative tumors.
- Identifying factors influencing pCR in this subgroup is essential for optimizing treatment.

Methods and Materials

- Retrospective cohort study using electronic clinical and pathological data from a single institution.
- Included patients with early-stage HR+/HER2-negative breast cancer (AJCC 8th edition, stages I–III).
- Estrogen receptor (ER) expression categorized as: high (>50%), intermediate (11–50%), low (1–10%), or negative (0%).
- Multivariable logistic regression used to identify independent predictors of pathological complete response (pCR).

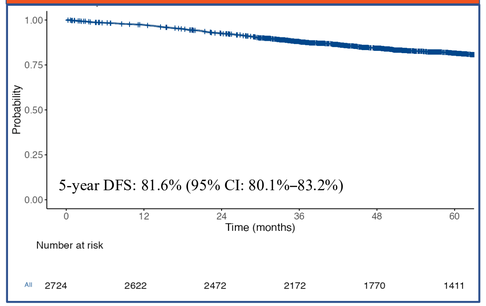
Results

- Among 2,724 patients analyzed, 1,039 received neoadjuvant chemotherapy; median age was 50 years (range 22–83).
- Most had invasive ductal carcinoma (IDC, 83.1%), and 8.8% had invasive lobular carcinoma (ILC).
- ER expression: high 83.7%, intermediate 4.2%, low 5.6%, and ER-negative/PR-positive 6%.
- Clinical node-positive disease was present in 72.9%.
- Overall pCR rate = 10.9% (n = 114).
- Younger age correlated with higher pCR: 15.0% (<45 yrs), 8.7% (45–64 yrs; OR 0.52, p = 0.004), 4.9% (≥65 yrs).
- Histology not predictive: ILC 5.4% vs IDC 10.5% (p = 0.838).
- ER expression strongly predicted pCR: low ER 42.4% (OR 10.35, p < 0.001); ER-negative/PR-positive 39.7% (OR 8.96, p < 0.001); intermediate ER 18.2% (OR 2.40, p = 0.042).
- Nodal status not independently associated with pCR.
- HER2-zero tumors showed higher, though non-significant, pCR rates versus HER2-low disease.

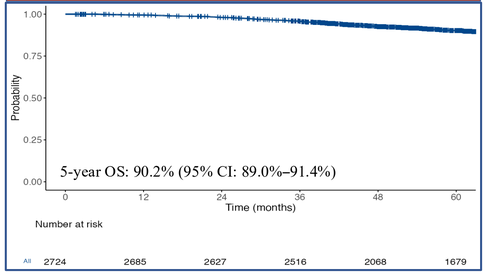
Baseline Characteristics

Overall (N=2724)		Grade	
Age groups		Missing	107
<45	845 (31.0%)	1	373 (14.3%)
45-64	1444 (53.0%)	2	1505 (57.5%)
≥65	435 (16.0%)	3	739 (28.2%)
Histology group		Clinical Tumor Stage	
IDC	2220 (81.5%)	cT1	580 (21.3%)
ILC	284 (10.4%)	cT2	1310 (48.1%)
others	220 (8.1%)	cT3	460 (16.9%)
Estrogen Receptor		cT4	141 (5.2%)
High Expression	2419 (88.8%)	cTx	233 (8.6%)
Intermediate	89 (3.3%)	Clinical Nodal Status	
Low	82 (3.0%)	cN+	1206 (44.3%)
Negative	91 (3.3%)	cN0	1296 (47.6%)
Unknown	43 (1.6%)	cNx	222 (8.1%)

Disease-Free Survival



Overall Survival



Multivariable Logistic Regression Analysis of Predictors of pCR

Variable	Category	OR (Multivariable)
Sex	Female	Reference
	Male	0.00 (NA-.4×10^{19}, p=0.986)
Age Group (years)	<45	Reference
	45–64	**0.52 (0.33–0.81, p=0.004)**
	≥65	0.37 (0.10–1.02, p=0.084)
Histology	IDC	Reference
	ILC	0.90 (0.30–2.19, p=0.838)
	Other	2.58 (1.33–4.84, p=0.004)
ER Expression	High	Reference
	Intermediate	**2.40 (0.97–5.35, p=0.042)**
	Low	**10.35 (5.47–19.57, p<0.001)**
	Negative	**8.96 (4.87–16.40, p<0.001)**
	Unknown	0.00 (NA–4.9×10^{84}, p=0.992)
HER2 IHC Score	0	Reference
	1+	0.77 (0.47–1.26, p=0.309)
	2+ (FISH–)	0.66 (0.30–1.35, p=0.281)
Clinical T Stage	cT1	Reference
	cT2	1.33 (0.55–3.69, p=0.557)
	cT3	0.95 (0.38–2.72, p=0.920)
	cT4	0.49 (0.14–1.75, p=0.268)
	cTx	1.14 (0.16–6.99, p=0.895)
Clinical N Stage	cN+	Reference
	cN0	1.31 (0.81–2.08, p=0.268)
	cNx	0.61 (0.07–3.50, p=0.611)

Conclusions

- Our analysis showed consistent findings with previously published data worldwide informing a low rate of pCR in this population.
- This confirms that HR+ breast cancer carries a significant resistance to chemotherapy and validates ER-expression as an important biomarker for responsiveness to chemotherapy.
- Younger age and lower ER-expression are strong independent predictors of response.
- Such findings could influence tailored treatment approaches and the use of personalized therapeutics, as well as exploring different neoadjuvant strategies using targeted agents among others.

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2. This review discusses how achieving pCR after neoadjuvant chemotherapy has been correlated with improved survival and its role as a surrogate marker.
3. Conforti, F., et al. "Surrogacy of Pathologic Complete Response in Trials of Neoadjuvant Therapy for Early Breast Cancer." JAMA Oncology, 2022.
4. This paper addresses the regulatory support for pCR as a surrogate endpoint in early breast cancer trials, and also highlights the limitations in certain subgroups (e.g. HR+).
5. Huppert, L. A., et al. "Pathologic Complete Response and Distant Recurrence-Free Survival in Patients With HR-Positive/HER2-Negative Early-Stage Breast Cancer Receiving Neoadjuvant Therapy." Annals of Oncology, 2025.
6. This original study analyzes pCR rates and their association with distant recurrence–free survival specifically in HR+ / HER2– breast cancer.

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