The European Research Journal 2025;11(5):858-867 Original Article

DOI: https://doi.org/10.18621/eurj.1704067 *Medical Oncology*

Evaluating the role of HER2-low versus HER2-0 status in predicting response to neoadjuvant chemotherapy in hormone receptor-positive breast cancer

Alper Topal, Mustafa Başak

Department of Internal Medicine, Division of Medical Oncology, Faculty of Medicine, Tokat Gaziosmanpaşa University, Tokat, Türkiye.

ABSTRACT

Objectives: The classification of human epidermal growth factor receptor 2 (HER2)-low breast cancer has gained clinical relevance following the success of antibody-drug conjugates in this subgroup. However, its prognostic and predictive role, particularly in hormone receptor-positive (HR+) early breast cancer treated with neoadjuvant chemotherapy (NACT), remains unclear. This study aimed to evaluate the impact of HER2-low versus HER2-0 status on pathological complete response (pCR) and disease-free survival (DFS) in HR+ breast cancer patients undergoing NACT.

Methods: A total of 216 HR+ and HER2-negative early breast cancer patients treated with NACT at Tokat Gaziosmanpasa University Hospital between January 2014 and January 2024 were retrospectively analyzed. HER2-low was defined as IHC 1+ or 2+ without gene amplification by FISH. pCR was assessed via the Miller-Payne grading system. Survival analyses were conducted using the Kaplan-Meier method; multivariate analyses were performed using Cox regression.

Results: Of the 216 patients, 30 (13.9%) achieved pCR. There was no statistically significant difference in pCR (P=0.83) or DFS (P=0.12) between HER2-0 and HER2-low groups. However, patients with ER <10% had significantly higher pCR rates (P=0.005). Achieving pCR was associated with longer DFS (P=0.045).

Conclusions: HER2-0 and HER2-low subgroups exhibited similar responses to NACT in HR+ breast cancer. Low ER expression was independently associated with higher pCR. Larger prospective studies are warranted to further define the biological and clinical implications of HER2 expression levels in early-stage HR+ breast cancer.

Keywords: Neoadjuvant chemotherapy, HER2-low, breast cancer, pathologic complete response

The second leading cause of mortality for women and the most frequent type of cancer overall is breast cancer (BC) [1]. Consequently, a large proportion of patients are detected at an early stage thanks to early screening programmes in many countries [2]. Hormone receptor-positive (HR+) BC, defined by the expression of immunohistochemical positivity for the estrogen (ER) and/or progesterone (PR) receptor, is the most common subtype. It accounts for approximately 70% of all breast cancer patients [3, 4]. Neoadjuvant chemotherapy (NACT) is used primarily in individuals with biolog-

Received: May 22, 2025 **Accepted:** August 1, 2025 **Available Online:** August 6, 2025 **Published:** September 4, 2025

How to cite this article: Topal A, Başak M. Evaluating the role of HER2-low versus HER2-0 status in predicting response to neoadjuvant chemotherapy in hormone receptor-positive breast cancer. Eur Res J. 2025;11(5):858-867. doi: 10.18621/eurj.1704067

Corresponding author: Alper Topal, MD., Asisst. Prof., Phone: +90 356 252 16 16, E-mail: dralpertopal@gmail.com

Available Online at https://dergipark.org.tr/en/pub/eurj

ically aggressive tumours, including triple-negative breast cancer (TNBC), human epidermal growth factor receptor 2 (HER2)-positive BC, and in individuals having ER (+)/HER2 (-) BC diagnosed with high-risk clinicopathological features. NACT reduces the stage of the tumour and allows breast and axillary surgery to be reduced. It is increasingly being used to enable breast-conserving surgery (BCS) to be performed, thus avoiding mastectomy [5].

Although response to NACT is prognostic in all tumour types, TNBC and HER2 (+) BC had notably greater pathological complete response (pCR) rates than luminal subtypes [6]. pCR rates are much lower in ER (+)/HER2 (-) breast cancer. It is linked to a pathological full reaction, improved survival and lower recurrence rates [7]. Therefore, pCR is a surrogate marker.

In the light of information from anti-HER2 antibody-drug conjugate (trastuzumab deruxtecan) research studies, new subsets such as HER2-low and HER2-ultra-low have emerged [8-10]. There are studies in the literature suggesting that the biology, histological, and proliferative values of HER2-low and HER2-0 tumors vary [11, 12]. The effect of HER2-low/HER2-0 status in reaction to neoadjuvant treatment is of interest. In our research, our aim was to investigate the effect of HER2-0/HER2-lowistatus on pCR and disease-free survival (DFS) after NACT in HR (+) BC.

METHODS

Patient Selection

The data of patients who were identified and handled for BC at Tokat Gaziosmanpasa University Hospital between January 2014 and January 2024 were retrospectively evaluated. ER, PR, HER2 and Ki67 values were analysed immunohistochemically. Patients with HER2 immunohistochemistry (IHC) values of 0, 1+ and 2+ and no amplification of genes determined by fluorescent situ hybridisation (FISH) were considered HER2-negative. Individuals having HER2 values of 1+ and 2+ were categorised as 'HER2-low'. All patients underwent clinical staging with ultrasound and mammography preoperatively.

BC individuals determined as PRipositive or negative, ER positive, HER2 negative or low expression, and who received neoadjuvant chemotherapy (NACT) were analyzed in the research. Individuals having bilateral BC, male gender and distant metastatic disease were excluded. Variables such as tumour size, menopausal status, age, pathological axillary lymph node (ALN) count, clinical stage, receptor status, HER2 status, Ki67 level, and histological grade were analysed.

Neoadjuvant Chemotherapy (NACT)

A standard taxane and anthracycline-based chemotherapy regimen was applied in the study. The treatment protocol was four courses of doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²) followed by weekly paclitaxel (80 mg/m²) or four courses of docetaxel (75-100 mg/m²) for 12 weeks. Postoperatively, all patients had adjuvant endocrine treatment, and all individuals who had BCS were advised to get adjuvant radiation.

Evaluation of NACT Response

Response to chemotherapy was evaluated with the routinely used Miller-Payne grading system. The Miller-Payne system is given in the following:

(1) Grade 1: No change or some alteration to individual malignant cells but no reduction in overall cellularity.

(2) Grade 2: A minor loss of tumour cells but overall cellularity still high; up to 30% loss.

(3) Grade 3: Between an estimated 30% and 90% reduction in tumour cells.

(4) Grade 4: A marked disappearance of tumour cells such that only small clusters or widely dispersed individual cell remain; more than 90% loss of tumour cells.

(5) Grade 5: No malignant cells identifiable in sections from the site of the tumour; only vascular fibroelastic stroma remains often containing macrophages. However, ductal carcinoma in situ (DCIS) may be present [12].

In the postoperative histopathological evaluation, tumour stage (ypT), lymph node stage (ypN), residual tumour size, surgical margins, number of removed and metastatic ALNs were analysed after NACT. pCR has been described as a lack of invasive tumor in breast tissue and metastasis in lymph nodes (ypT0, ypN0).

Statistical Analysis

SPSS 22.0 software was used for the statistical an-

alyze of the data (SPSSiInc., Chicago, Illinois). For comparative data, Fisher's exact test and chi-square tests were employed. Amongst the numerical parameters across two independent conditions, those with normal distribution were analysed by Student's t-test, and those without normal distribution were analysed by the Mann-Whitney U test. The univariate log-rank test was used to assess the impact of prognostic variables on pathological complete response. The 95% confidence interval (CI) was used to compute the hazard ratio (HR). The Cox proportional hazards model was used for multivariate analysis to assess the impact of prognostic variables on pathological complete response. To make an assessment regarding the prognostic variables influencing pathological complete response, both univariate and multivariate analyses were conducted using a logistic regression model. Survival studies were conducted using the Kaplan-Meier technique. DFS was defined as the interval between the first diagnosis and the death or recurrence of the disease. The significance level was set as ≤ 0.05.

Table 1. Data on pathological and clinical characteristics

			HER2 status		
		Total (n=216)	HER2-0 (n=63)	HER2-Low (n=153)	P value
Diagnosis age (year)	Median (min-max)	50 (28-87)			
	<50 years, n (%)	113 (52.3)	27 (42.9)	86 (56.2)	0.099
	≥50 years, n (%)	103 (47.6)	36 (57.1)	67 (43.8)	
Menopausal status, n (%)	Premenopausal	112 (51.8)	23 (36.5)	89 (58.2)	**0.004**
	Postmenopausal	104 (48.2)	40 (63.5)	64 (41.8)	
N stage, n (%)	NX and N0	18 (8.3)	7 (11.7)	11 (7.5)	0.414
	N1-N2-N3	189 (87.5)	53 (88.3)	136 (92.5)	
T stage, n (%)	TX and T1	62 (28.7)	19 (31.1)	43 (29.3)	0.868
	T2-T3-T4	146 (67.5)	42 (68.9)	104 (70.7)	
Clinical stage, n (%)	I	4 (1.8)	2 (3.4)	2 (1.4)	0.631
	II	125 (57.8)	35 (59.3)	90 (62.1)	
	III	75 (34.7)	22 (37.3)	53 (36.5)	
Grade (n=189), n (%)	Grade 1 and 2	154 (71.2)	43 (79.6)	111 (75.5)	0.579
	Grade 3	47 (21.7)	11 (20.4)	36 (24.5)	
ER Status	1-9%	5 (2.3)	3 (4.8)	2 (1.3)	0.307
	10-40%	11 (5.2)	3 (4.8)	8 (5.2)	
	>40%	200 (92.5)	57 (90.4)	143 (93.5)	
PR Status	Positive	186 (86.1)	55 (88.7)	131 (86.2)	0.823
	Negative	28 (12.9)	7 (11.3)	21 (13.8)	
Ki-67 (n=199), n (%)	<20 %	79 (36.5)	26 (45.6)	53 (37.3)	0.337
	≥20 %	120 (55.5)	31 (54.4)	89 (62.7)	
Surgery type, n (%)	Mastectomy	136 (62.9)	42 (66.7)	94 (61.4)	0.536
	Breast conserving	80 (37.1)	21 (33.3)	59 (38.6)	
pCR	Yes	30 (13.9)	8 (12.7)	22 (14.4)	0.831
	No	186 (86.1)	55 (87.3)	131 (85.6)	

Data are shown as median (minimum-maximum) or n (%). ER=estrogen receptor, PR=progesterone receptor, HER2=human epidermal growth factor receptor 2

RESULTS

The study included 216 patients. The median follow-up (mFU) time was 37 months. The median age of the participants was 50 years (min-max: 28-87). The number of premenopausal patients was 112 (51.8%). The number of patients with positive lymph nodes (N1-2-3) was 189 (87.5%). The clinical and pathological characteristics are presented in Table 1. There were 5(2.3%) patients with ER 1-9%, 11 patients (5.2%) with ER 10-40%, and 200 (92.5%) patients with ER over 40%. PR was negative in 28 (12.9%) patients.

Table 2. Clinicopathological characteristics and oncological outcome with respect to pathologic complete response achievement

			pCR achievement		
		Total (n=216)	Yes (n=30)	No (n=186)	P value
Diagnosis age (year)	<50 years	113	18 (15.9)	95 (84.1)	0.433
	≥50 years	103	12 (11.7)	91 (88.3)	
Menopausal status, n (%)	Premenopausal	112	17 (15.2)	95 (84.8)	0.694
	Postmenopausal	104	13 (12.5)	91 (87.5)	
N stage, n (%)	NX and N0	18	1 (5.6)	17 (94.4)	0.478
	N1-N2-N3	189	27 (14.4)	162 (85.7)	
T stage, n (%)	TX and T1	62	6 (9.7)	56 (90.3)	0.377
	T2-T3-T4	146	22 (15.1)	124 (84.9)	
Clinical stage, n (%)	I	4	0 (0)	4 (100)	0.651
	II	125	18 (18.4)	107 (85.6)	
	III	75	9 (12.0)	66 (88.0)	
Grade (n=189), n (%)	Grade 1 and 2	154	16 (10.4)	138 (89.6)	**0.029**
	Grade 3	47	11 (23.4)	36 (76.6)	
ER positivity, n (%)	1-9%	5	3 (60)	2 (40)	**0.001**
	10-40%	11	4 (36.4)	7 (63.6)	
	>40%	200	23 (11.5)	177 (88.5)	
PR status	Positive	186	27 (14.5)	159 (85.5)	0.385
	Negative	28	2 (7.1)	26 (92.9)	
HER2 score	HER2-0	63	8 (12.7)	55 (87.3)	0.831
	HER2-Low	153	22 (14.4)	131 (85.6)	
Ki-67 (n=212), n (%)	<20 %	79	5 (6.3)	74 (93.7)	**0.047**
	≥20 %	120	20 (16.7)	100 (83.3)	
Surgery type, n (%)	Mastectomy	136	19 (14.0)	117 (86.0)	0.99
	Breast conserving	80	11 (13.8)	69 (86.2)	
Relaps	Yes	34	2 (5.9)	32 (94.1)	0.182
	No	182	28 (15.4)	154 (84.6)	
DFS (months), median (SE, 95%CI)			NR	91.9 (81.81-101.95)	**0.045**

ER=estrogen receptor, PR=progesterone receptor, HER2=human epidermal growth factor receptor 2, pCR=pathologic complete response

One hundred and twenty patients (55.5%) had Ki67 ≥ 20% (Table 1).

Regarding the type of surgery performed, 136 (62.9%) patients underwent mastectomy and 80 (37.1%) patients underwent breast-conserving surgery. While 30 (13.9%) patients had pathological complete response, 186 (86.1%) patients did not achieve pCR.

When we looked at the distribution of clinical and pathological characteristics of HER2-0 and HER2-Low groups, only the number of premenopausal patients was not normally distributed (P=0.004). The rate of premenopausal patients was higher in the HER2-low group (58.2%).

According to the results of univariate analysis, tumour grade, ER and Ki67 percentages were seen to be the elements affecting pCR (P=0.029, P=0.001 and P=0.047, respectively). According to the results of multivariate analysis, only low ER receptor percentage was found to be a factor affecting pCR (P=0.005). Patients with ER receptor percentage less than 10% had 3.7 times more pCR (Table 2).

When analysing DFS according to pCR, the median DFS of pCR participants was not reached, whereas the median DFS of non-pCR patients was

Table 3. Variables influencing pathologic complete response

		Univariate		Multivariate	
		OR, 95%CI	P value	OR, 95% CI	P value
Diagnosis age (year)	<50 years	0.69 (0.31-1.52)	0.365		
	≥50 years				
Menopausal status	Premenopausal	0.79 (0.36-1.739	0.573		
	Postmenopausal				
N stage	NX and N0	2.83 (0.36-22.17)	0.321		
	N1-N2-N3				
T stage	TX and T1	1.65 (0.63-4.30)	0.30		
	T2-T3-T4				
Clinical stage	I	0.93 (0.42-2.06)	0.87		
	II				
	III				
Grade (n=189)	Grade 1 and 2	2.63 (1-12-6.17)	**0.02**	0.98 (0.32-2.99)	0.97
	Grade 3				
ER positivity	1-9%	0.27 (0.12-0.60)	**<0.001**	0.27 (0.11-1.67)	**0.005**
	10-40%				
	>40%				
PR Status	Positive	0.45 (0.10-2.02)	0.29		
	Negative				
HER2 score	Her2-0	0.86 (0.36-2.06)	0.74		
	Her2-Low				
Ki-67 (n=212)	≥20 %	2.96 (1.06-8.25)	**0.03**	2.48 (0.74-8.33)	0.13
	<20 %				
Surgery type	Mastectomy	0.98 (0.44-2.18)	0.96		
	Breast conserving				

ER=estrogen receptor, PR=progesterone receptor, HER2=human epidermal growth factor receptor 2, pCR=pathologic complete response, OR=odds ratio, CI=confidence interval

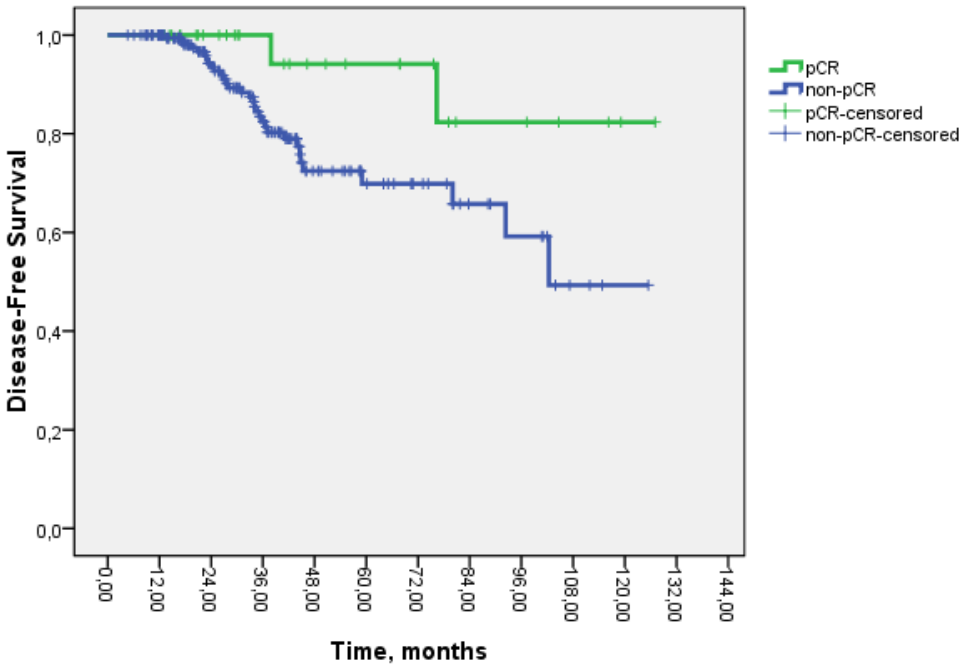

Fig. 1. **Associations between pathological complete response and disease-free survival.**

91.9 (81.81-101.95) months, which was statistically significant (P=0.045, Table 3 and Fig. 1).

There was no variation in pCR (P=0.83) or DFS (P=0.12) between the HER2-0 and HER2-low groups (Fig. 2). However, the 3 and 5-year DFS was numerically better in the HER2-0 group. The 3-year and 5-year DFS of HER2-0 patients were 88.7% and 86%, respectively, while those of HER2-Low patients were 83.2% and 69.6% (Table 4).

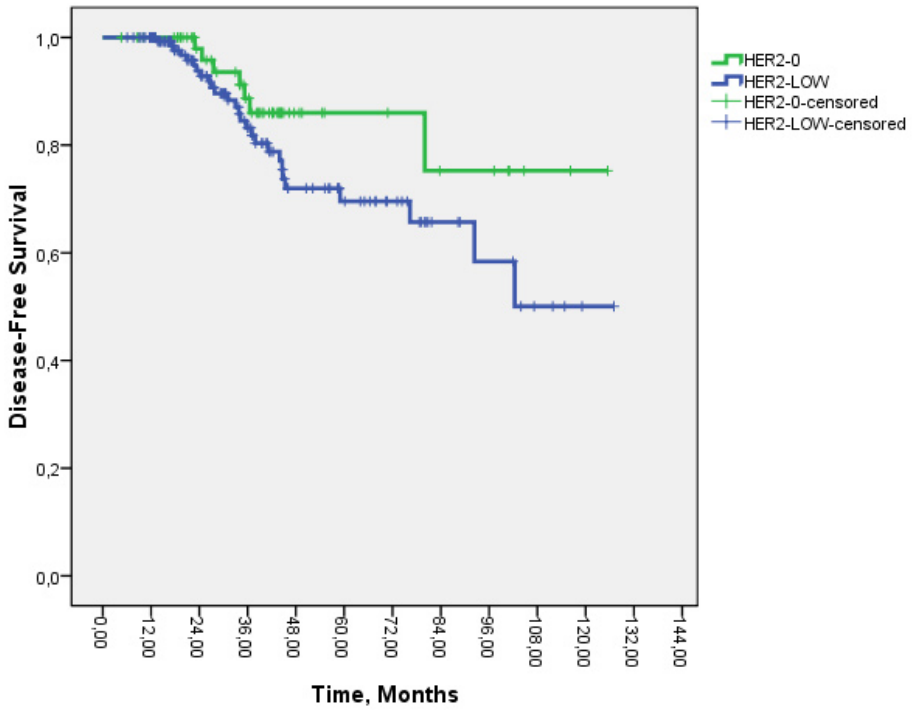

Fig. 2. **Associations between HER2 status and disease-free survival.**

DISCUSSION

HER2 low BC is a popular topic. Concern in HER2 low subgroups has grown after trastuzumab-deruxtecan's effectiveness in the HER2 low and extreme low subgroups was demonstrated [10]. We shared this interest and investigated the status influence of HER2 on complete response in HR (+) BC patients receiving NACT. It was shown that there was no varitation among HER2-0 and low subgroups regarding pCR and DFS. The DFS was longer for individuals who attained pCR than for those who could not. When the factors influencing pCR were analysed, low ER was found to be the factor influencing pCR.

pCR rates with neoadjuvant chemotherapy are lower in HR(+) tumours compared to HER2(+) and TNBC tumours [12, 13]. Complete response rates do not exceed 20% in the literature [12]. In our study, there was a pCR rate of 13% in accordance with the literature.

Zhou *et al*. [14] showed that HER2-0 and HER2-low groups had similar pCR values in a study of 325 patients receiving NACT. Similar results were found in another study of 855 patients conducted in Brazil [15]. In the meta-analysis of 2310 patients by Denkert *et al*. [16], the relationship between HER2-0 and HER2-low pCR in individuals with HR(+) and TNBC was analysed. It was seen that individuals with HER2-low in the general population and HR(+) had lower pCR rates. Baez-Navarro *et al*. [17] showed the same results in a study of 11721 individuals. de Moraes *et al*. [18] performed one of the largest meta-analyses on this topic. In this study, which included 70104 patients, it was shown that HER2-0 patients had a better pCR than HER2-low individuals. This was also true in the HR(+) subgroup. Although there are investigations in the literature showing no variation in pCR among HER2-0 and HER2-low patients [19, 20], large meta-analyses suggest that HER2-0 patients have better pCR rates. The fact that there was no difference in pCR among the two groups in our study may be explained by the relatively small size of our patient population.

It is known that HR (+) BC has a lower response rate to neoadjuvant treatment compared to TNBC [21, 22]. Dieci *et al*. [23] showed that ER-negative (<1%) and ER-low (1-9%) TNBC patients had similar pCR rates and emphasised that the ER-low group should be classified as TNBC. Similarly, another study showed that patients with ER-low and ER(-) TNBC had similar pCR rates [24]. Fuji *et al*. [25] showed in a study of 3055 patients that the pCR probability of patients with ER <10% tumours was notably greater than that of patients with ER≥10% tumours. In the study of PAM50 testing to predict NACT response, it was found that individuals with ER-low had TNBC like behaviour and should be treated with chemotherapy. It was shown that pCR rates were greater in individuals with ER-low [26]. Similarly, in our study, pCR scores were significantly greater in the ER-low group.

There are many studies in the literature that have investigated the relation among Ki67 levels and pCR. Rapoport *et al*. [27] showed in a research of 208 individuals that pCR rates were notably better in individuals with Ki67>40. A similar result was observed in a research of 522 patients by Fasching *et al*. [28]. The findings of the research by Akdag *et al*. [5] were consistent with those documented in the available research. Although the pCR rates of patients with Ki67 ≥ 20% were better in our study, they lost significance in multivariate analysis.

Tumour grade is another parameter for predicting pCR. Fisher *et al*. [29] showed that higher tumour grade was linked with greater pCR in a study of 1523 patients. Similar outcomes were seen in the Jones *et*

Table 4. Disease-free survival outcomes

		Whole cohort	Subgroup analysis		
			HER2-0	HERE2-Low	P value
Disease free survival	Median (months)	Not reached	Not Reached	Not reached	
	3 years (%)	85	88.7	83.2	0.12
	5 years (%)	74	86	69.6	
mFU (months)			37		

HER2= human epidermal growth factor receptor, FU=follow-up

al. [22]. Similarly, the study of Ring *et al*. [21] confirmed this. Although the pCR rates of patients with tumour grade 3 were better in our study, it lost its significance in multivariate analysis. The small number of patients may have reduced the statistical power of the study and may have caused this.

There are studies within the source material showing that individuals having HR (+) who had pCR got better survival outcomes than those who could not achieve pCR [13, 28]. A meta-analysis of 27895 patients by Spring *et al*. [30] also showed that the DFS was noticeably longer for those who attained pCR. In this current research, the median DFS of those who attained pCR was not reached, whereas the median DFS of those who attained pCR was 92 months, which was statistically significant.

Although there are mixed outcomes in the source material about the relationship among HER2-0 and HER2-low status and pCR, large meta-analyses suggest that the HER2-0 group has better pCR rates [20]. However, the similar pCR rates of both groups in our study and the existence of studies with similar results emphasise the requirement for more study to clarify the intricate relationship between HER2-low status and HER2-0 and other tumor features in determining prognosis and responsiveness to therapy. Based on the current clinical and pathological data, our study offers insightful information; nevertheless, more research will clarify the many biological traits and prognostic consequences linked to the HER2-0 and HER2-low subgroups.

Limitations

When evaluating the findings, it is important to take into account the many limitations of our study. First, our findings may not be as generalizable to broader populations due to its retrospective nature and single-center methodology. Second, the relatively small sample size is a limitation that may affect the statistical power of multivariate analyses and requires careful interpretation. Notwithstanding these drawbacks, we think that our research offers useful empirical information that will further knowledge of HER2-0 and HER2-low early BC.

CONCLUSION

Our study concludes that NACT-treated individuals who had early HR (+) HER2-low and HER2-0 BC had comparable DFS and pCR rates. In line with previous research, we found that those who attained pCR had longer DFS. More significantly, our multivariate analysis revealed that low ER % was linked to pCR on its own. To validate these findings, explore the underlying biological processes, and facilitate the creation of more individualized treatment plans for individuals in these categories, further extensive prospective investigations are required.

Ethics Approval and Consent to Participate

This study was approved by the Tokat Gaziosmanpasa University Faculty of Medicine Non-Interventional Scientific Research Ethics Committee (Decision no: 25-MOBAEK-043 and date: 04.02.2025), and it was realized in compliance with the Declaration of Helsinki's enets.

Data Availability

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

Authors' Contribution

Study Conception: AT; Study Design: AT; Supervision: MB; Funding: AT; Materials: AT, MB; Data Collection and/or Processing: AT, MB; Statistical Analysis and/or Data Interpretation: AT; Literature Review: AT; Manuscript Preparation: AT and Critical Review: AT, MB.

Conflict of Interest

The author(s) disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during the conduction or writing of this study.

Acknowledgments

We would like to express our sincere gratitude to Prof. Dr. Banu Öztürk and Prof. Dr. Özge Gümüşay for their valuable contributions in establishing the oncology clinic at Tokat Gaziosmanpaşa University and for their dedicated care of the patients included in this study.

Generative Artificial Intelligence Statement

The author(s) declare that no artificial intelligence-based tools or applications were used during the preparation process of this manuscript. The all content of the study was produced by the author(s) in accordance with scientific research methods and academic ethical principles.

Editor's Note

All statements made in this article are solely those of the authors and do not represent the views of their affiliates or the publisher, editors, or reviewers. Any claims made by any product or manufacturer that may be evaluated in this article are not guaranteed or endorsed by the publisher.

REFERENCES

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;75(1):10-45. Epub 20250116. doi: 10.3322/caac.21871.
2. Trapani D, Ginsburg O, Fadelu T, et al. Global challenges and policy solutions in breast cancer control. Cancer Treat Rev. 2022;104:102339. doi: 10.1016/j.ctrv.2022.102339.
3. Schettini F, Martínez-Sáez O, Falato C, et al. Prognostic value of intrinsic subtypes in hormone-receptor-positive metastatic breast cancer: systematic review and meta-analysis. ESMO Open. 2023;8(3):101214. doi: 10.1016/j.esmoop.2023.101214.
4. Cejalvo JM, Martínez de Dueñas E, Galván P, et al. Intrinsic Subtypes and Gene Expression Profiles in Primary and Metastatic Breast Cancer. Cancer Res. 2017;77(9):2213-2221. doi: 10.1158/0008-5472.CAN-16-2717.
5. Akdag G, Yildirim S, Dogan A, et alNeoadjuvant Chemotherapy and Pathologic Complete Response in HR+/HER2- Breast Cancer: Impact of Tumor Ki67 and ER Status. Chemotherapy. 2024;69(3):141-149. doi: 10.1159/000537874.
6. Yau C, Osdoit M, van der Noordaa M, et al. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. Lancet Oncol. 2022;23(1):149-160. doi: 10.1016/s1470-2045(21)00589-1.
7. Boughey JC, Ballman KV, McCall LM, et al. Tumor Biology and Response to Chemotherapy Impact Breast Cancer-specific Survival in Node-positive Breast Cancer Patients Treated With Neoadjuvant Chemotherapy: Long-term Follow-up From ACOSOG Z1071 (Alliance). Ann Surg. 2017;266(4):667-676. doi: 10.1097/sla.0000000000002373.
8. Tarantino P, Viale G, Press MF, et al. ESMO expert consensus statements (ECS) on the definition, diagnosis, and management of HER2-low breast cancer. Ann Oncol. 2023;34(8):645-59. doi: 10.1016/j.annonc.2023.05.008.
9. Modi S, Jacot W, Yamashita T, et al.; DESTINY-Breast04 Trial Investigators. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. N Engl J Med. 2022;387(1):9-20. doi: 10.1056/NEJMoa2203690.
10. Corti C, Giugliano F, Nicolò E, Tarantino P, Criscitiello C, Curigliano G. HER2-Low Breast Cancer: a New Subtype? Curr Treat Options Oncol. 2023;24(5):468-478. doi: 10.1007/s11864-023-01068-1.
11. Zhang H, Katerji H, Turner BM, Hicks DG. HER2-Low Breast Cancers. Am J Clin Pathol. 2022;157(3):328-336. doi: 10.1093/ajcp/aqab117.
12. Ogston KN, Miller ID, Payne S, et al. A new histological grading system to assess response of breast cancers to primary chemotherapy: prognostic significance and survival. Breast. 2003;12(5):320-327. doi: 10.1016/s0960-9776(03)00106-1.
13. Guarneri V, Broglio K, Kau SW, et al. Prognostic value of pathologic complete response after primary chemotherapy in relation to hormone receptor status and other factors. J Clin Oncol. 2006;24(7):1037-1044. doi: 10.1200/jco.2005.02.6914.
14. Zhou S, Liu T, Kuang X, et al. Comparison of clinicopathological characteristics and response to neoadjuvant chemotherapy between HER2-low and HER2-zero breast cancer. Breast. 2023;67:1-7. doi: 10.1016/j.breast.2022.12.006.
15. de Moura Leite L, Cesca MG, Tavares MC, et al. HER2-low status and response to neoadjuvant chemotherapy in HER2 negative early breast cancer. Breast Cancer Res Treat. 2021;190(1):155-163. doi: 10.1007/s10549-021-06365-7.
16. Denkert C, Seither F, Schneeweiss A, et al. Clinical and molecular characteristics of HER2-low-positive breast cancer: pooled analysis of individual patient data from four prospective, neoadjuvant clinical trials. Lancet Oncol. 2021;22(8):1151-1161. doi: 10.1016/S1470-2045(21)00301-6.
17. Baez-Navarro X, van Bockstal MR, Jager A, van Deurzen CHM. HER2-low breast cancer and response to neoadjuvant chemotherapy: a population-based cohort study. Pathology. 2024;56(3):334-342. doi: 10.1016/j.pathol.2023.10.022.
18. de Moraes FCA, de Castro Ribeiro CHD, Pessôa FDDL, et al. Pathologic response rates in HER2-low versus HER2-zero early breast cancer patients receiving neoadjuvant therapy: a systematic review and meta-analysis. Breast Cancer Res. 2025;27(1):39. doi: 10.1186/s13058-025-01989-9.
19. Yang M, Sun J, Liu L, et al. Clinicopathological characteristics of HER2-low breast cancer: a retrospective study. Sci Rep. 2023;13(1):12382. doi: 10.1038/s41598-023-39372-3.
20. Ilie SM, Briot N, Constantin G, et al. Pathologic complete response and survival in HER2-low and HER2-zero early breast cancer treated with neoadjuvant chemotherapy. Breast Cancer. 2023;30(6):997-1007. doi: 10.1007/s12282-023-01490-1.
21. Ring AE, Smith IE, Ashley S, Fulford LG, Lakhani SR. Oestrogen receptor status, pathological complete response and prognosis in patients receiving neoadjuvant chemotherapy for early breast cancer. Br J Cancer. 2004;91(12):2012-2017. doi: 10.1038/sj.bjc.6602235.
22. Jones RL, Salter J, A'Hern R, et al. Relationship between oestrogen receptor status and proliferation in predicting response and long-term outcome to neoadjuvant chemotherapy for breast cancer. Breast Cancer Res Treat. 2010;119(2):315-323. doi: 10.1007/s10549-009-0329-x.

23. Dieci MV, Griguolo G, Bottosso M, et al. Impact of estrogen receptor levels on outcome in non-metastatic triple negative breast cancer patients treated with neoadjuvant/adjuvant chemotherapy. NPJ Breast Cancer. 2021;7(1):101. doi: 10.1038/s41523-021-00308-7.
24. Gloyeske NC, Dabbs DJ, Bhargava R. Low ER+ breast cancer: Is this a distinct group? Am J Clin Pathol. 2014;141(5):697-701. doi: 10.1309/AJCP34CYSATWFDPQ.
25. Fujii T, Kogawa T, Dong W, et al. Revisiting the definition of estrogen receptor positivity in HER2-negative primary breast cancer. Ann Oncol. 2017;28(10):2420-2428. doi: 10.1093/annonc/mdx397.
26. Ohara AM, Naoi Y, Shimazu K, et al. PAM50 for prediction of response to neoadjuvant chemotherapy for ER-positive breast cancer. Breast Cancer Res Treat. 2019;173(3):533-543. doi: 10.1007/s10549-018-5020-7.
27. Rapoport BL, Barnard-Tidy J, Van Eeden RI, Smit T, Nayler S, Benn C. Pathological complete response in early breast cancer patients undergoing neoadjuvant chemotherapy: Focus on Ki-67 and molecular subtypes. Ann Oncol. 2019;30(Supplement 3):iii37. doi: 10.1093/annonc/mdz097.012.
28. Fasching PA, Heusinger K, Haeberle L, et al. Ki67, chemotherapy response, and prognosis in breast cancer patients receiving neoadjuvant treatment. BMC Cancer. 2011;11:486. doi: 10.1186/1471-2407-11-486.
29. Fisher ER, Wang J, Bryant J, Fisher B, Mamounas E, Wolmark N. Pathobiology of preoperative chemotherapy: findings from the National Surgical Adjuvant Breast and Bowel (NSABP) protocol B-18. Cancer. 2002;95(4):681-695. doi: 10.1002/cncr.10741.
30. Spring LM, Fell G, Arfe A, et al. Pathologic Complete Response after Neoadjuvant Chemotherapy and Impact on Breast Cancer Recurrence and Survival: A Comprehensive Meta-analysis. Clin Cancer Res. 2020;26(12):2838-2848. doi: 10.1158/1078-0432.CCR-19-3492.