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Neoadjuvant TCHP for Stage II-III HER2-positive Breast Cancer: A Real-world Cohort

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ABSTRACT

Objective: The neoadjuvant combination regimen of taxane, carboplatin, trastuzumab, and pertuzumab (TCHP) is widely used for stage II-III human epidermal growth factor receptor 2 (HER2)-positive breast cancer; however, real-world pathologic complete response (pCR) rates and predictors vary. We evaluated pCR, response correlates, and treatment outcomes in a two-center cohort.

Material and Methods: Consecutive non-metastatic HER2-positive patients with clinical T2-4 and/or N1-3 who were treated with neoadjuvant TCHP at two centers from 2022 to 2025 were retrospectively analyzed. pCR was defined as ypT0/is ypN0. Groups were compared, and univariable logistic regression was used to assess factors associated with pCR.

Results: Among 43 patients (median age, 48 years), pCR occurred in 24 patients (55.8%). Hormone receptor (HR)-negative tumors were more frequent in the pCR group (66.7% vs. 31.6%; p=0.033). HR positivity predicted lower odds of pCR (odds ratio: 0.231; 95% confidence interval: 0.064-0.836; p=0.026), whereas age, baseline T/N stage, grade, and Ki-67 were not significant predictors. T- and N- downstaging occurred in 81.4% and 74.4%, respectively. Radiologic-pathologic agreement was limited (breast κ=0.272; axilla κ=0.081). Grade 3-4 toxicity was 11.6% (cardiotoxicity 4.7%). Breast-conserving surgery was performed in 72.1%; sentinel lymph node biopsy was performed in 79.1%. Median follow-up was 18 months, with one local recurrence and no deaths.

Conclusion: Real-world neoadjuvant TCHP achieved a 55.8% pCR rate with substantial downstaging. HR-negative disease was the key correlate, and imaging CR was an unreliable surrogate for pCR.

Keywords: Breast neoplasms; receptor, ErbB-2; neoadjuvant therapy; treatment outcome

INTRODUCTION

Breast cancer remains the leading malignancy among women globally, with more than 25,000 new diagnoses reported annually in Türkiye.[1] Human epidermal growth factor receptor 2 (HER2)-positive disease represents approximately 15-20% of breast cancers.[2] Despite major improvements in outcomes with HER2-directed therapies, stage II-III HER2-positive breast cancer continues to encompass a biologically and clinically heterogeneous population. In this setting, residual invasive disease after neoadjuvant therapy identifies patients who may benefit from post-neoadjuvant treatment escalation.[3] Neoadjuvant systemic therapy offers several clinical advantages, including downstaging of the breast tumor and axilla, facilitation of breast-conserving surgery (BCS), and direct assessment of treatment responsiveness in vivo.[3,4] Pathologic complete response (pCR) is associated with improved long-term outcomes, particularly in patients with HER2-positive, hormone receptor (HR)-negative tumors.[5] For patients with residual invasive disease, post-

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neoadjuvant escalation has become an established strategy; in the KATHERINE trial, adjuvant trastuzumab emtansine significantly improved invasive disease-free survival compared with continued trastuzumab.[6] Accordingly, pCR has become a clinically meaningful endpoint that also guides post-neoadjuvant management.

For stage II-III HER2-positive breast cancer, standard treatment combines chemotherapy with HER2-directed therapy, with dual HER2 blockade using trastuzumab and pertuzumab recommended for tumors >2 cm and/or node-positive disease.[3] The addition of pertuzumab improved pCR in the NeoSphere trial; the trastuzumab, docetaxel, and pertuzumab arm achieved a pCR rate of approximately 46%.[7] In clinical practice, the anthracycline-free taxane, carboplatin, trastuzumab, and pertuzumab (TCHP) regimen has since become widely used in routine practice, with pCR rates of approximately 66% in TRYPHAENA[8] and 55.7% in KRISTINE.[9] However, pCR rates are strongly influenced by tumor biology, with HR-negative tumors consistently showing a higher likelihood of pCR.[10]

The shift toward anthracycline-free strategies is driven by efforts to maintain efficacy while reducing toxicity. Anthracyclines are associated with cardiotoxicity when used alongside HER2-targeted therapy and, less commonly, with secondary hematologic malignancies.[11,12] In TRAIN-2, the addition of anthracyclines to dual HER2 blockade did not provide a clinically meaningful efficacy advantage, further supporting anthracycline-free strategies in appropriately selected patients.[13]

Against this background, we conducted a two-center retrospective study of patients with stage II-III HER2-positive breast cancer who were treated with neoadjuvant TCHP in routine clinical practice. In addition to evaluating real-world pCR rates and clinicopathologic correlates of response, we assessed the concordance of radiologic complete response with surgical pathology findings in the breast and axilla to inform interpretation of post-treatment imaging for surgical decision-making.

MATERIAL AND METHODS

Study Design and Population

This two-center retrospective cohort study evaluated patients with non-metastatic, HER2-positive breast cancer who were treated with neoadjuvant TCHP between 2022 and 2025. Patients were identified from institutional oncology records at the two participating centers. Eligible patients had clinical T2-4 and/or N1-3 disease and received neoadjuvant TCHP as part of routine care. Clinical, imaging, pathology, treatment, toxicity, and follow-up data were collected from electronic medical records.

Eligibility Criteria

Inclusion criteria were age ≥18 years, histologically confirmed HER2-positive breast carcinoma, absence of distant metastasis at baseline staging, and available post-neoadjuvant surgical pathology for response assessment. HER2 positivity was defined according to immunohistochemistry (IHC) and/or fluorescence *in situ* hybridization (FISH) results available in pathology reports. Patients were excluded if they had a synchronous malignancy, lacked key clinical or pathologic data required for response assessment, had unavailable radiologic or surgical pathology reports, or had incomplete follow-up information. During the study period, 242 patients with early-stage or locally advanced HER2-positive breast cancer who were receiving neoadjuvant treatment were screened. After excluding patients with missing key variables (n=18), those who received non-TCHP neoadjuvant regimens (n=172), and those with ongoing treatment, no surgery, or non-assessable pCR status (n=9), the final analytic cohort comprised 43 patients. Patient selection is summarized in Figure 1.

Definitions and Study Variables

The primary outcome was pCR. pCR was defined as the absence, on examination of the surgical specimen, of residual invasive carcinoma in the breast and axillary lymph nodes (ypT0/is ypN0). Patients were categorized into pCR and non-pCR groups based on final surgical pathology.

Prespecified covariates included patient-related characteristics (age, sex, performance status, comorbidities, menopausal status); tumor-related factors (HR status, histologic grade, Ki-67); HER2 category (IHC 3+; IHC 2+ with FISH amplification); and post-neoadjuvant/adjuvant treatment modalities (radiotherapy; anti-HER2 therapy; and endocrine therapy). HER2 expression categories were not included in comparative analyses because non-IHC 3+ cases were rare, and their inclusion would have produced unstable estimates. Treatment-related adverse events were captured from routine clinical documentation and analyzed only for grade 2-4 toxicities; grade 1 events were not systematically collected.

Radiologic Response Assessment

Systemic staging at diagnosis was performed according to routine institutional practice. Baseline local breast and axillary staging modalities were recorded; these included breast magnetic resonance imaging (MRI), breast and axillary ultrasonography (US), or both US and MRI. Radiologic response following neoadjuvant therapy was assessed using imaging modalities commonly used in routine clinical practice, including MRI, breast and axillary US, positron

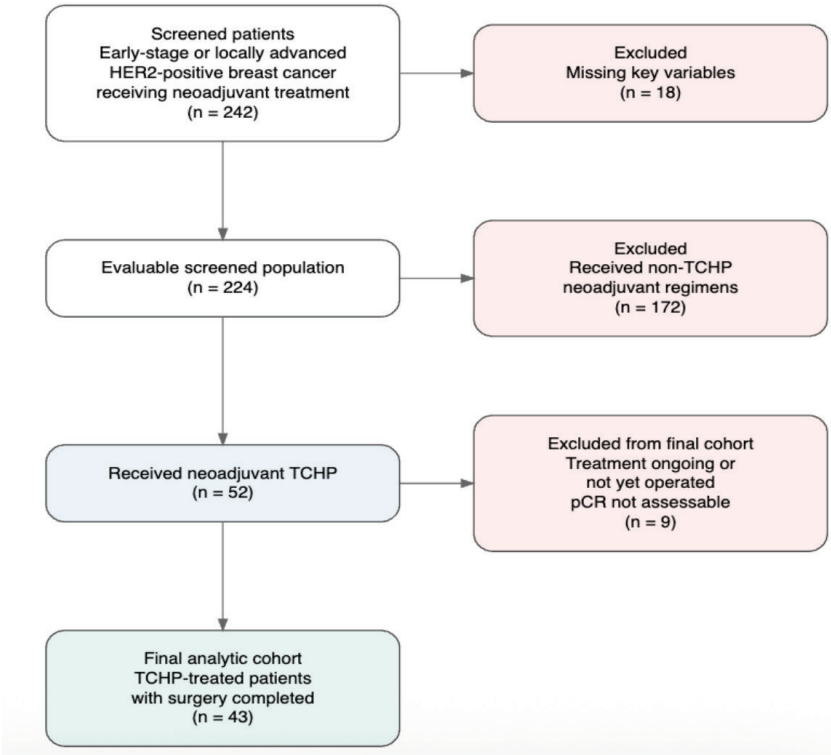

FIGURE 1: Flow diagram of patient selection.

HER2: Human epidermal growth factor receptor 2; TCHP: Docetaxel, carboplatin, trastuzumab, and pertuzumab; pCR: Pathologic complete response

emission tomography/computed tomography (PET/CT), or combined US and PET/CT. Imaging modality selection was based on institutional practice rather than a predefined study protocol.

Radiologic response was retrospectively abstracted from formal radiology reports. Central radiologic re-review was not performed. Standardized RECIST or PERCIST measurements were not uniformly available across all patients and imaging modalities; therefore, radiologic CR was defined pragmatically as the absence of a visible residual primary breast lesion on post-treatment imaging. Axillary radiologic CR was defined as the absence of suspicious residual axillary lymph nodes on post-treatment imaging, based on the reporting radiologist's assessment.

Statistical Analysis

All analyses were performed using IBM SPSS Statistics version 30.0 and R. Distributional assumptions for continuous variables were assessed using the Kolmogorov-Smirnov test. Continuous variables are presented as mean ± standard deviation when normally distributed and as median (range or interquartile range) when non-normally distributed; categorical variables are reported as frequencies and percentages. Baseline and treatment-related characteristics were compared between the pCR and non-pCR groups using the Student's t-test or the Mann-Whitney U test for continuous variables and the chi-square test or the Fisher's exact test for categorical variables, as appropriate. Univariable logistic regression was used to explore factors associated with pCR, and results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Because of the small sample size, multivariable modeling was not performed. A two-sided p-value of <0.05 was considered statistically significant. Survival outcomes were not formally analyzed because follow-up was not sufficiently mature, and the number of events was very low.

Ethical Approval

The study protocol was reviewed and approved by the Dokuz Eylül University Non-Interventional Clinical Research Ethics Committee (approval number: 2026/09-10, date: 02.03.2026). Given the retrospective design and the use of routinely collected clinical data, the requirement for written informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki, and all data were anonymized and de-identified prior to analysis to ensure patient confidentiality.

RESULTS

Among the 43 patients included in the study, the median age was 48 years (range, 28-78), and menopausal status was evenly distributed (51.2% premenopausal and 48.8% postmenopausal). Most patients (95.3%) underwent PET-based initial staging. Baseline local staging was performed using MRI alone in 21 patients (48.8%), US alone in 18 patients (41.9%), and combined US and MRI in 4 patients (9.3%). At presentation, the clinical T stage was most commonly T2 (53.5%), followed by T3 (20.9%), T1 (18.6%), and T4 (7.0). Multicentric or multifocal disease was present in 27.9% of cases. Clinical nodal stages were predominantly N1 (51.2%) and N2 (27.9%). HR status was balanced (51.2% HR-negative; 48.8% HR-positive); the median Ki-67 was 35% (range, 10-90); the grade distribution was similar (G2: 51.2%; G3: 48.8%) (Table 1).

pCR was achieved in 24 patients, corresponding to a pCR rate of 55.8% (24/43), while 19 patients (44.2%) had residual disease. Baseline characteristics were largely similar between the pCR and non-pCR groups; however, HR status differed

TABLE 1: Baseline clinicopathologic characteristics of the cohort according to pCR status.

Variable	All patients (n=43)	pCR (n=24)	Non-pCR (n=19)	p-value
Age, years	48 (28-78)	53 (29-78)	45 (28-69)	0.359
Menopausal status				
Premenopause	22 (51.2)	12 (50.0)	10 (52.6)	1.000
Postmenopause	21 (48.8)	12 (50.0)	9 (47.4)	
BMI (n=36)	27.14 (19.95-37.11)	26.48 (19.95-35.55)	27.49 (21.08-37.11)	0.824
Baseline systemic staging modality				
PET/CT	41 (95.3)	23 (95.8)	18 (94.7)	1.000
Conventional CT	2 (4.7)	1 (4.2)	1 (5.3)	
Baseline local staging modality				
MRI	21 (48.8)	14 (58.3)	7 (36.8)	0.158
US	18 (41.9)	7 (29.2)	11 (57.9)	
US + MRI	4 (9.3)	3 (12.5)	1 (5.3)	
Multicentric/multifocal tumor	12 (27.9)	5 (20.8)	7 (36.8)	0.314
Primary tumor size, mm	28 (12-70)	28 (12-70)	28 (12-52)	0.569
Clinical T stage				
T1	8 (18.6)	3 (12.5)	5 (26.3)	0.430
T2	23 (53.5)	12 (50.0)	11 (57.9)	
T3	9 (20.9)	7 (29.2)	2 (10.5)	
T4	3 (7.0)	2 (8.3)	1 (5.3)	
Clinical N stage				
N0	5 (11.6)	4 (16.7)	1 (5.3)	0.472
N1	22 (51.2)	12 (50.0)	10 (52.6)	
N2	12 (27.9)	7 (29.2)	5 (26.3)	
N3	4 (9.3)	1 (4.2)	3 (15.8)	
HR status				
HR negative	22 (51.2)	16 (66.7)	6 (31.6)	0.033
HR positive	21 (48.8)	8 (33.3)	13 (68.4)	
Ki-67, %	35 (10-90)	32.5 (15-90)	35 (10-80)	0.815
Grade				
G2	22 (51.2)	13 (54.2)	9 (47.4)	0.763
G3	21 (48.8)	11 (45.8)	10 (52.6)	
Baseline CA15-3 (n=35)	18.6 (6.0-64.6)	15.7 (6.9-24.4)	21.5 (6.0-64.6)	0.092

BMI: Body mass index; HR: Hormone receptor; MRI: Magnetic resonance imaging; pCR: Pathologic complete response; PET/CT: Positron emission tomography/computed tomography; US: Ultrasonography.

significantly: HR-negative tumors were more frequent among patients achieving pCR (66.7% vs. 31.6%; p=0.033) (Table 1 and Figure 2). Because of the small number of patients in some stage subgroups, this comparison was interpreted as exploratory.

Univariable logistic regression analyses for pCR are presented in Table 2. HR positivity was associated with significantly lower odds of achieving pCR compared with HR-negative disease (OR: 0.231; 95% CI: 0.064-0.836; p=0.026). In contrast, age, menopausal status, multicentric/multifocal disease, clinical T stage, clinical N stage, tumor grade, Ki-67, and body mass index were not significantly associated with pCR (all p>0.05).

Beyond pCR, neoadjuvant treatment led to clinically meaningful stage migration of both the primary tumor and the axilla, with T downstaging in 35/43 (81.4%) and N downstaging in 32/43 (74.4%), including transitions to ypT0 in 25/43 (58.1%), of whom 21 originated from cT≥2, and to ypN0 in 31/43 (72.1%), including 27 conversions from cN≥1 (Figure 3).

Post-treatment radiologic response was assessed in 35 patients (81.4%), most commonly by MRI (40.0%) or ultrasound (34.3%), with no difference in imaging modality distribution between groups (p=0.404). Primary breast radiologic CR was observed in 15/35 patients (42.9%) and was numerically more frequent among patients achieving pCR (57.9% vs. 25.0%),

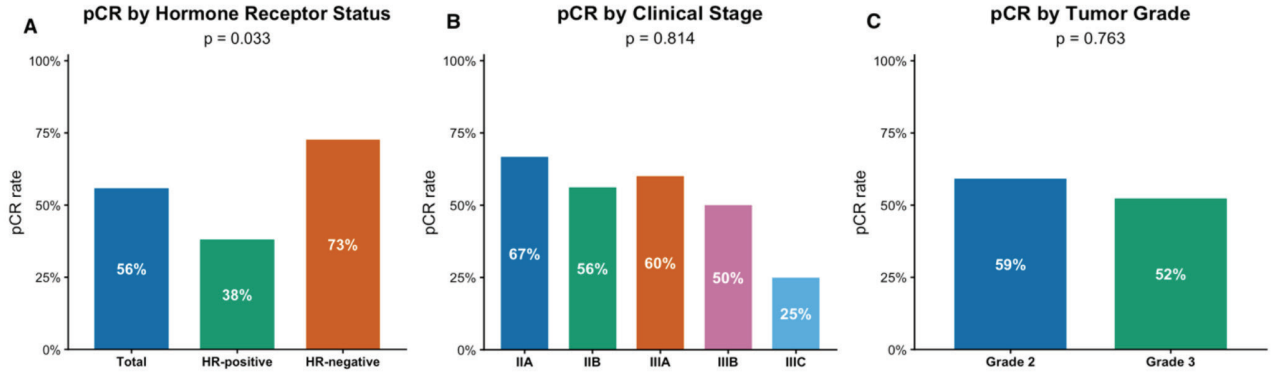

FIGURE 2: pCR rates stratified by **(A)** HR status, **(B)** clinical stage, and **(C)** tumor grade. The comparison across clinical-stage subgroups was considered exploratory because of the small numbers of patients in some stage categories.

HR: Hormone receptor; pCR: Pathologic complete response

TABLE 2: Univariate regression analyses for pCR.

Variable	Comparison/unit	OR (95% CI)	p-value
Age	Per 1 year increase	1.023 (0.967-1.081)	0.433
Menopausal status	Post- vs. pre- (ref)	1.111 (0.333-3.706)	0.864
Multicentric/multifocal tumor	Yes vs. no (ref)	0.451 (0.116-1.751)	0.250
Clinical T stage	Overall (ref=T1)	—	0.406
T2 vs. T1		1.818 (0.350-9.455)	0.477
T3 vs. T1		5.833 (0.696-48.873)	0.104
T4 vs. T1		3.333 (0.204-54.532)	0.398
Clinical N stage	Overall (ref=N0)	—	0.486
N1 vs. N0		0.300 (0.029-3.135)	0.315
N2 vs. N0		0.350 (0.029-4.153)	0.406
N3 vs. N0		0.083 (0.004-1.945)	0.122
HR status	HR+ vs HR- (ref)	0.231 (0.064-0.836)	0.026
Grade	G3 vs. G2 (ref)	0.762 (0.228-2.545)	0.658
Ki-67 (%)	per 1% increase	0.997 (0.971-1.025)	0.855
BMI	per 1 kg/m^2 increase	1.010 (0.864-1.180)	0.904

BMI: Body mass index; HR: Hormone receptor; OR: Odds ratio; CI: Confidence interval.

but the difference did not reach statistical significance (p=0.088; dichotomized p=0.087). Axillary radiologic CR was noted in 16/34 patients (47.1%) and was more common in the pCR group (57.9% vs. 33.3%); however, this difference was not statistically significant (p=0.372; dichotomized p=0.185) (Table 3).

Among patients with available post-treatment radiologic response assessment (n=35), baseline local staging was performed with MRI alone in 14 (40.0%), with US alone in 17 (48.6%), and with combined US and MRI in 4 (11.4%). The same imaging modality was used for both baseline local staging and post-treatment response assessment in 23 patients (65.7%): MRI-to-MRI in 14 (40.0%) and US-to-US in 9 (25.7%). When combined modalities that shared the same local imaging component were considered, an overlapping local modality was observed in 30 patients (85.7%). In the

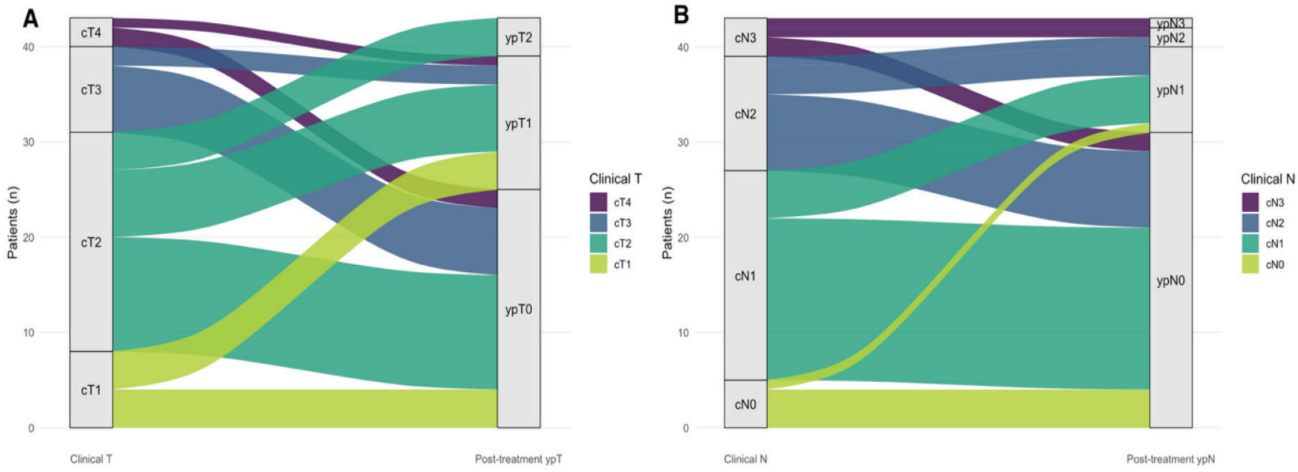

FIGURE 3: Sankey diagrams showing transitions from **(A)** clinical T to post-treatment pathologic ypT and **(B)** clinical N stage to post-treatment pathologic ypN stage after neoadjuvant TCHP.

TCHP: Docetaxel, carboplatin, trastuzumab, and pertuzumab

TABLE 3: Neoadjuvant treatment exposure, toxicity, and radiologic response assessment according to pCR status.

Variable	All patients	pCR	Non-pCR	p-value
Number of TCHP doses (n=42)	6 (3-6)	6 (3-6)	6 (6-6)	0.072
Grade 2 toxicity	12 (27.9)	5 (20.8)	7 (36.8)	0.626
Grade 3-4 toxicity	5 (11.6)	3 (12.5)	2 (10.5)	0.918
Radiologic response assessment	35 (81.4)	19 (79.2)	16 (84.2)	1.000
MRI	14 (40.0)	9 (47.4)	5 (31.3)	0.404
US	12 (34.3)	7 (36.8)	5 (31.3)	
PET/CT	5 (14.3)	1 (5.3)	4 (25.0)	
US + PET/CT	4 (11.4)	2 (10.5)	2 (12.5)	
Primary breast radiologic response (n=35)				
CR	15 (42.9)	11 (57.9)	4 (25.0)	0.088
PR	19 (54.3)	8 (42.1)	11 (68.8)	
PD	1 (2.9)	0 (0.0)	1 (6.3)	
Axillary radiologic response (n=34)				
CR	16 (47.1)	11 (57.9)	5 (33.3)	0.372
PR	12 (35.3)	6 (31.6)	6 (40.0)	
SD	5 (14.7)	2 (10.5)	3 (20.0)	
PD	1 (2.9)	0 (0.0)	1 (6.7)	

CR: Complete response; MRI: Magnetic resonance imaging; TCHP: Docetaxel, carboplatin, trastuzumab, and pertuzumab; pCR: Pathologic complete response; PET/CT: Positron emission tomography/computed tomography; PD: Progressive disease; PR: Partial response; SD: Stable disease; US: Ultrasonography.

remaining 5 patients (14.3%), post-treatment response assessment was based on PET/CT because the same baseline local imaging modality was not available.

Agreement between radiologic and pCRs was modest. For the primary breast tumors (n=35), radiologic CR showed an observed agreement of 62.9% with pathologic ypT0 status, corresponding to fair agreement (Cohen's κ=0.272). This concordance did not reach statistical significance (κ, p=0.094 by asymptotic testing; p=0.162 by Monte Carlo). For the axilla (n=34), agreement between radiologic axillary CR and pathologic ypN0 status was low (observed agreement, 52.9%) and negligible beyond chance (κ=0.081), with no evidence of statistically significant concordance (p=0.595).

Primary breast surgery favored breast-conserving approaches in the overall cohort: 31 of 43 patients (72.1%) underwent BCS, while 12 patients (27.9%) underwent mastectomy. Axillary management was predominantly de-escalated: 34 of 43 patients (79.1%) underwent sentinel lymph node biopsy, whereas only 9 (20.9%) required axillary lymph node dissection (ALND).

Adjuvant anti-HER2 treatment patterns diverged sharply by response status (p<0.001). Patients who achieved pCR almost uniformly received adjuvant trastuzumab (23/24; 95.8%), with one patient receiving trastuzumab plus pertuzumab (1/24; 4.2%); none received T-DM1. In contrast, among patients without pCR, adjuvant T-DM1 was the most common regimen (11/19; 57.9%), while trastuzumab alone was used less frequently (5/19; 26.3%), and trastuzumab plus pertuzumab was uncommon (1/19; 5.3%). Two non-pCR patients (2/19; 10.5%) did not receive adjuvant anti-HER2 therapy: one because of cardiotoxicity and the other because reassessment of the primary pathology and review of the surgical specimen demonstrated HER2 negativity. Surgical and adjuvant treatments are summarized in Table 4.

Neoadjuvant treatment exposure and toxicity were comparable between groups. Among patients with available cycle data (n=42), the median number of TCHP cycles was 6 (range, 3-6) both overall and in the pCR group; all non-pCR patients received 6 cycles, which represented a non-significant trend (p=0.072). Overall, grade 2 toxicity occurred in 12/43 patients (27.9%) and grade 3-4 toxicity occurred in 5/43 patients (11.6%). The most frequent grade 2 events were neutropenia (4/43; 9.3%) and diarrhea (3/43; 7.0%), followed by nausea (2/43; 4.7%) and isolated cases of hepatotoxicity, fatigue, and anemia-thrombocytopenia (each 1/43; 2.3%). Grade 3-4 toxicities were uncommon and included cardiotoxicity (2/43; 4.7%), neutropenia (1/43; 2.3%), fatigue (1/43; 2.3%), and neurologic toxicity (1/43; 2.3%). Only one patient discontinued treatment because of neurologic adverse events and proceeded directly to surgery after three cycles of treatment.

Median follow-up was 18 months, during which no deaths were observed. Only one patient experienced local disease recurrence; therefore, survival outcomes were considered immature and not formally analyzed.

TABLE 4: Surgical management and adjuvant treatments according to pCR status.

Variable	All patients	pCR	Non-pCR	p-value
Primary surgery				
BCS	31 (72.1)	17 (70.8)	14 (73.7)	1.000
Mastectomy	12 (27.9)	7 (29.2)	5 (26.3)	
Axillary surgery				
SLNB	34 (79.1)	21 (87.5)	13 (68.4)	0.127
ALND	9 (20.9)	3 (12.5)	6 (31.6)	
Adjuvant anti-HER2				
None	2 (4.7)	0 (0.0)	2 (10.5)	<0.001
Trastuzumab	28 (65.1)	23 (95.8)	5 (26.3)	
Trastuzumab + pertuzumab	2 (4.7)	1 (4.2)	1 (5.3)	
Trastuzumab emtansine	11 (25.6)	0 (0.0)	11 (57.9)	
Adjuvant radiotherapy	40 (93.0)	22 (91.7)	18 (94.7)	1.000
Adjuvant endocrine therapy (n=21)				
Aromatase inhibitor	10 (47.6)	3 (37.5)	7 (53.8)	0.010
Tamoxifen	4 (19.0)	0 (0.0)	4 (30.8)	
LHRH agonist + aromatase inhibitor/tamoxifen	7 (33.3)	5 (62.5)	2 (15.4)	

ALND: Axillary lymph node dissection; BCS: Breast-conserving surgery; HER2: Human epidermal growth factor receptor 2; LHRH: Luteinizing hormone-releasing hormone; SLNB: Sentinel lymph node biopsy.

DISCUSSION

In this two-center, retrospective, real-world cohort of patients with stage II-III HER2-positive breast cancer treated with neoadjuvant TCHP, the pCR rate was 55.8%. More than two-thirds of patients underwent BCS, and axillary management was frequently de-escalated, reflecting a substantial treatment effect in routine practice. Toxicity was generally manageable, with grade 3-4 events uncommon and cardiotoxicity observed in a small minority.

Although the overall pCR rate in our cohort (55.8%) supports the activity of neoadjuvant TCHP in routine practice, it was numerically lower than the 66.2% reported in the phase II TRYPHAENA study.[8] However, our finding is closely aligned with the 55.7% pCR rate observed in the standard TCHP arm of the Phase III KRISTINE trial.[9] This difference from TRYPHAENA should not be interpreted solely as a shortfall in real-world treatment delivery; it may also be partly explained by baseline disease burden and by the less-selected nature of our cohort. Specifically, 88.4% of our patients had clinically N+ disease at presentation. The nodal burden in our cohort was higher than that reported in KRISTINE and more similar to that observed in the high-risk population evaluated in TRAIN-2.[9,13] Furthermore, nearly half of our cohort (48.8%) had HR+ disease. Across real-world cohorts treated with TCHP, pCR rates have ranged between 48% and 64%, highlighting that pCR rates vary substantially across populations even under the same regimen.[14-17]

Tumor biology appeared to be the clearest factor associated with response in our cohort. HR status was the only factor that significantly differed between the pCR and non-pCR groups, with the pCR rate dropping from 72.7% in HR-negative patients to 38.1% in HR-positive patients. This pattern is consistent with large TCHP cohorts that demonstrate markedly higher pCR rates in ER-negative compared with ER-positive disease (77.9% vs. 47.5%), which emphasizes that endocrine signaling modulates responsiveness to dual HER2 blockade.[10,18] Prior biomarker studies suggest that response heterogeneity within ER-positive/HER2-positive disease may relate to HER2 expression intensity and immune contexture, such as tumor-infiltrating lymphocytes.[18] These factors were not available in our dataset, and therefore should be evaluated in larger cohorts.

From a surgical standpoint, our high breast-conservation rate and low ALND utilization are clinically meaningful because they reflect patient-centered benefits, including effective neoadjuvant therapy, less extensive breast and axillary surgery, and potential reductions in morbidity. This aligns with real-world TCHP cohorts, in which breast-conservation rates are approximately 70%, and outcomes differ by pCR status, favoring patients with pCR.[14] Moreover, our cohort reflects contemporary post-neoadjuvant management: adjuvant anti-HER2 strategies diverged substantially according to response status, with T-DM1 used exclusively in non-pCR patients, which is consistent with the availability of escalation approaches for residual disease in modern practice.[3]

Beyond the pCR rate itself, the most distinctive contribution of this cohort is the evaluation, in routine practice, of radiologic-pathologic concordance in both the breast and axilla after neoadjuvant TCHP. A key pragmatic finding was the limited agreement between radiologic and pathologic responses. In our cohort, post-treatment radiologic response assessment was available in 35 patients and was most commonly based on breast MRI or breast/axillary US, with PET/CT used in a smaller proportion of patients. Importantly, baseline and post-treatment imaging showed modality continuity in most patients: the same imaging modality was used in 23 of 35 patients, and an overlapping local imaging component was present in 30 of 35 patients when combined modalities were considered. Radiologic CR showed only fair concordance with ypT0 in the breast (κ=0.272) and negligible concordance with ypN0 in the axilla (κ=0.081), indicating that an imaging complete response should not be used as a surrogate for pCR and cannot reliably exclude microscopic residual disease.

In our routine institutional practice, post-neoadjuvant imaging is used as a complementary tool to guide breast surgical planning and axillary evaluation, rather than as a stand-alone determinant of response. For axillary management, decisions are generally based on baseline nodal status, clinical examination, and surgical/pathologic assessment; radiologic CR alone is not considered sufficient to omit pathologic evaluation. Although baseline and post-treatment imaging showed modality overlap in most patients, imaging was selected according to routine clinical practice rather than a predefined protocol. Therefore, the observed discordance should be interpreted as a pragmatic estimate of radiologic-pathologic agreement in routine practice rather than as a modality-specific assessment of imaging accuracy.

With respect to safety, neoadjuvant TCHP was generally well tolerated in our cohort, with grade 3-4 toxicity and cardiotoxicity observed in 11.6% and 4.7% of patients, respectively. The relatively low rate of grade 3-4 toxicity may partly reflect patient selection, as the cohort had a young median age and included patients who were considered suitable for neoadjuvant TCHP. However, detailed data on dose reductions, treatment delays, G-CSF use, and other supportive care interventions were not uniformly available, limiting our ability to determine their contribution to toxicity

outcomes. Compared with a large real-world Korean TCHP experience (n=447), in which adverse events, particularly anemia and non-hematologic toxicities such as diarrhea, were commonly documented,[14] our observed high-grade event rates appeared numerically lower; however, direct comparisons are limited by differences in toxicity capture, grading practices, and treatment modification strategies. Importantly, grade 1 adverse events were not systematically captured in the present study, and toxicity data were extracted from routine clinical documentation, which may have led to an underestimation of the toxicity burden. Nevertheless, the overall pattern supports the feasibility of anthracycline-free TCHP delivery in real-world settings with routine cardiac monitoring and proactive supportive care.

Study Limitations

This study has limitations inherent to its retrospective design. The modest sample size and two-center setting introduce potential selection bias, limit generalizability, reduce statistical power, and preclude robust multivariable modeling. Detailed data for patients receiving non-TCHP neoadjuvant regimens were not systematically available, precluding comparative assessment of selection bias. In addition, radiologic assessment was not standardized across centers, imaging modalities varied, and central radiologic review was not performed. Toxicity may have been underestimated because adverse events were collected from routine clinical documentation, and grade 1 events were not systematically captured. Finally, the follow-up was short, with only one recurrence and no deaths; therefore, survival outcomes remain immature. Despite these constraints, the real-world setting, the contemporary systemic and surgical management patterns, and the detailed characterization of pCR, surgical outcomes, and radiologic-pathologic concordance strengthen the clinical relevance of our findings.

CONCLUSION

Neoadjuvant TCHP achieved a pCR rate of 55.8% in a real-world cohort of stage II-III HER2-positive breast cancer. HR-negative disease was associated with higher pCR rates, underscoring biological heterogeneity in response to dual HER2 blockade. The regimen was generally well tolerated and associated with high rates of breast conservation and low ALND rates, supporting meaningful downstaging in routine practice. Given the limited radiologic-pathologic concordance, surgical pathology remains essential for definitive response assessment; larger cohorts with standardized biomarker assessment and longer follow-up are needed to refine predictors of long-term outcomes.

Ethics

Ethics Committee Approval: The study protocol was reviewed and approved by the Dokuz Eylül University Non-Interventional Clinical Research Ethics Committee (approval number: 2026/09-10, date: 02.03.2026).

Informed Consent: Retrospective study.

Footnotes

The single center results of this study have been submitted as an abstract to Turkish Medical Oncology Congress 2026.

Authorship Contributions

Surgical and Medical Practices: K.C., A.T., M.K., T.Y., Concept: K.C., M.K., T.Y., Design: K.C., T.Y., Data Collection or Processing: K.C., E.D., A.M.A., A.T., Analysis or Interpretation: K.C., E.D., M.K., Literature Search: K.C., E.D., A.M.A., A.T., M.K., T.Y., Writing: K.C., E.D., A.M.A., A.T., M.K., T.Y.

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