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Comparison of Anthracycline-Containing and Anthracycline-Free Neoadjuvant Regimens in HER2-Positive Breast Cancer

Mahmut Kara

mkara@yyu.edu.tr

Van Yüzüncü Yıl University

Senar Ebinç

Van Yüzüncü Yıl University

Tuba Baydaş

Medeniyet Üniversitesi Göztepe Eğitim ve Araştırma Hastanesi

Hatice Ayyıldız Sevim

Ankara City Hospital

Murat Haskul

Turgut Özal Tıp Merkezi

Selahattin Çelik

Ankara City Hospital

Zekeriya Hannarici

Bursa Yuksek Ihtisas Egitim Ve Arastirma Hastanesi

Nadiye Akdeniz

Diyarbakır Gazi Yaşargil Eğitim ve Araştırma Hastanesi

Nurhan Kalkan

Batman University

Muslih Ürün

Van Yüzüncü Yıl University

Mehmet Naci Aldemir

Van Yüzüncü Yıl University

Yasin Sezgin

Van Yüzüncü Yıl University

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Abstract

Background

Concurrent administration of anti-HER2 therapies and chemotherapy has significantly improved response rates (43%–55%). However, the potential for cardiotoxicity when combining anti-HER2 agents with anthracyclines remains a concern. Consequently, anthracycline-free regimens are increasingly utilized, particularly for patients with cardiac history. This study aims to compare the efficacy and safety of anthracycline-containing chemotherapy versus anthracycline-free TCHP (Docetaxel, Carboplatin, Trastuzumab, and Pertuzumab) regimens in the neoadjuvant treatment of HER2-positive early-stage breast cancer.

Methods

This multicenter retrospective study analyzed patients diagnosed with HER2-positive breast cancer between 2015 and 2025 who received neoadjuvant anti-HER2 therapy followed by surgery. We evaluated the association between treatment regimens and outcomes, specifically pathological complete response (pCR)—defined as the absence of residual invasive tumor in the breast and axillary nodes—and event-free survival (EFS).

Results

A total of 358 patients were included, with a mean age of 50 years. Most presented with T2 tumors (74%) and N1 disease (60.9%). The most common regimens were Adriamycin, Cyclophosphamide, Docetaxel, Pertuzumab, Trastuzumab (AC + DPT) (35.2%) and TCHP (30.7%), with a 95.5% treatment completion rate. Pathological complete response rates were statistically comparable between the AC + DPT and TCHP regimens (p = 0.360). Conversely, significantly lower pCR rates were observed with other regimens (OR 0.35, 95% CI 0.17–0.73; p = 0.005). Advanced lymph node involvement (N3) was strongly associated with worse event-free survival (HR 8.43, p = 0.038), while ER and PR status showed no significant impact. Regarding safety, febrile neutropenia was more frequent in the TCHP group (8.2%) compared to the AC + DPT group (1.6%). Notably, no Grade 3–4 cardiac toxicity was detected in either cohort (Table 1, 2; Fig. 1).

Conclusions

The TCHP regimen demonstrates efficacy comparable to anthracycline-containing regimens without increased cardiac toxicity, despite a higher incidence of hematological adverse events. Therefore, anthracycline-free regimens may be the preferred option for patients with cardiac comorbidities, while advanced lymph node involvement remains a critical poor prognostic factor.

INTRODUCTION

Breast cancer is the most common cancer type worldwide (1). It is also the most common cause of cancer-related deaths in women (2). The most frequent subtype is invasive ductal carcinoma (IDC) (3). Analysis of subtypes reveals that the hormone receptor-positive (ER, PR) group is the most common (approximately 70%), while HER2 overexpression accounts for 23%, and the triple-negative group constitutes approximately 13% (4). HER2 positivity is determined by demonstrating HER2 overexpression immunohistochemically or a HER2/CEP17 ratio greater than 2.0 using fluorescence in situ hybridization (FISH) (5 Although breast cancer with HER2 overexpression is aggressive, chemotherapy responses are quite good (6).

Anti-HER2 targeted therapies administered concurrently with chemotherapy significantly increase response rates. Among these agents, trastuzumab inhibits the receptor by binding to subdomain IV of the HER2 receptor, whereas pertuzumab binds to subdomain II (7). Patients who are clinically lymph node positive or have large tumors are candidates for neoadjuvant therapy. Anthracycline, taxane, and platinum-based agents are preferred as chemotherapy alongside anti-HER2 therapies. In patients with tumors larger than 2 cm or positive lymph nodes, the addition of pertuzumab to trastuzumab and chemotherapy has been shown to be beneficial (8). Studies have reported response rates ranging from 43% to 55% when anti-HER2 therapies are added to chemotherapy (9, 10, 11). However, it is known that anti-HER2 targeted therapies and anthracycline-based drugs are cardiotoxic (12, 13).

Neoadjuvant treatment regimens without anthracyclines have also been used, especially in patients with a history of cardiac disease or who have previously received anthracycline-based treatment. The BCIRG-006 study compared anthracycline-free chemotherapy with anthracycline-containing regimens. Although a statistically significant increase in toxicity was observed in the anthracycline-containing regimen, survival differences favored trastuzumab-containing regimens. A higher incidence of hematological adverse events was observed in the anthracycline-free Docetaxel-Carboplatin-Trastuzumab arm (14). In another phase III study, the TRAIN-2 trial, patients receiving neoadjuvant chemotherapy with and without anthracyclines were compared. No significant differences were found between the two groups in terms of pathological complete response (pCR), event-free survival (EFS) and overall survival (OS) (15).

The TRYPHAENA study compared a group receiving anthracycline-free chemotherapy combined with trastuzumab and pertuzumab against an anthracycline-based group. The patients in the anthracycline-free group were administered trastuzumab, pertuzumab, carboplatin, and docetaxel (TCHP). While the pCR rate was approximately 55% in the anthracycline group, it was 64% in the TCHP arm. Hematological toxicity was similar in both groups, whereas cardiac toxicity was observed to be slightly lower in the TCHP arm (16). Completing one year of postoperative trastuzumab treatment was found to be more effective in patients who achieved a complete response after neoadjuvant therapy. For patients who did not achieve a complete response, the trastuzumab emtansine (T-DM1) regimen was found to be superior to trastuzumab (17, 18, 19).

Based on the existing uncertainties in the literature, the present study aims to compare the efficacy and safety of anthracycline-containing chemotherapy versus anthracycline-free (TCHP) chemotherapy in the neoadjuvant treatment of HER2-positive early-stage breast cancer.

MATERIAL AND METHODS

Patients diagnosed with HER2-positive breast cancer between January 2015 and December 2025 were analyzed in this study. The study was designed as a multicenter retrospective study. The patients' age, gender, tumour histology, receptor status, T, N, M stages, treatments received, treatment responses, recurrence status, and survival were obtained retrospectively from patient files and the hospital automation system. The study examined the clinicopathological characteristics of patients diagnosed with breast cancer who were HER2-positive, received neoadjuvant anti-HER2 therapy and subsequently underwent surgery. The objective was to investigate the relationship between the treatments received and both pathological complete response (pCR) and event-free survival (EFS).

Inclusion Criteria: Patients over 18 years of age, diagnosed with breast cancer, identified as HER2 2+/FISH+ or HER2 3+, received neoadjuvant therapy and had an ECOG performance status of 0-1 were included in the study.

Exclusion Criteria: Patients under 18 years of age, those with prior breast surgery, metastatic disease, those who had previously received chemotherapy, those with a history of breast radiotherapy and HER2-negative/HER2 1+ status were excluded.

Treatment protocols were determined according to ASCO, ESMO and NCCN guidelines. The study included patients receiving either an anthracycline-containing chemotherapy regimen with HER2-targeted therapy or an anthracycline-free regimen as neoadjuvant treatment. In patients who underwent surgery following neoadjuvant therapy, adjuvant anti-HER2 therapy was completed to one year. Pathological complete response (pCR) was defined as the absence of invasive tumor cells in the breast and axillary lymph nodes. Event-free survival (EFS) was calculated as the time from the initiation of neoadjuvant therapy to disease progression, recurrence, or death.

Statistical Analysis: Statistical analysis was performed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, USA). The patient characteristics and parameter frequencies were evaluated using descriptive statistical methods. The evaluation of parameter frequencies was conducted through the utilisation of descriptive statistics. Kaplan-Meier survival analysis was utilised for the purpose of conducting survival analyses. The Log Rank P value was utilised as the foundation for determining statistical significance. For survival analyses, the Cox regression "Enter" method was used for univariate analysis and the Cox regression "Backward LR" method was used for multivariate analysis. The confidence interval was set at 95% and a two-sided p-value of <0.05 was considered statistically significant.

Assessment of Treatment-Related Toxicity: The assessment of treatment-related toxicity was conducted in accordance with the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0 guidelines Cardiac toxicity was assessed by echocardiography at three-month intervals before and after treatment. The development of symptomatic heart failure was defined as a decrease in ejection fraction to below 50% or a decrease of more than 10%. Hematological toxicities were determined based on laboratory analyses performed before, during and after treatment. The lower limit for neutropenia was defined as a neutrophil count of 2000/mm³, for anemia as a hemoglobin level of 10.5 g/dl and for thrombocytopenia as a platelet count of 100,000/mm³.

Ethical approval: Approval was obtained from the Ethics Committee of Van Yuzuncu Yıl

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RESULTS

The study comprised 358 patients with HER2-positive (HER+2/FISH+ or HER+3) breast cancer who received neoadjuvant chemotherapy. The mean age at diagnosis was 50 years and the majority of histopathological subtypes were invasive ductal carcinoma (IDC). Regarding clinical staging, most patients were in stage T2 (74%) and N1 (60.9%). In terms of hormone receptor status, 67.3% were estrogen receptor (ER) positive, and 56.4% were progesterone receptor (PR) positive. Regarding HER2 expression levels, 85.2% of patients were HER2 3+, while 14.8% were HER2 2+/FISH+. The administered treatment protocols were ddAC + DPT (Dose-dense Adriamycin-Cyclophosphamide + Docetaxel-Pertuzumab-Trastuzumab) in 35.2%, TCHP (Docetaxel-Carboplatin-Herceptin-Pertuzumab) in 30.7%, Taxane + ddAC + Herceptin in 22.9%, and other regimens in 11.2% of patients. Overall, 95.5% of the patients completed the planned treatment regimen (Table 1).

Table 1 Clinical characteristics of the patients

Variables	N 358 (%)
Median Age	50.36 (25.0–81.0)
Pathological subtype	
IDC	274 (76.5)
ILC	13 (3.6)
NOS	59 (16.5)
Diğer	12 (3.4)
Grade	
Grade 1	10 (3.2)
Grade 2	207 (66.1)
Grade 3	96 (30.7)
Clinical T Stage	
cT1	56 (15.6)
cT2	265 (74.0)
cT3	21 (5.9)
cT4	16 (4.5)
Clinical N Stage	
cN0	40 (11.2)
cN1	218 (60.9)
cN2	69 (19.3)
cN3	31 (8.7)
Hormone receptors	
ER Positive	241 (67.3)
PR Positive	202 (56.4)
HER2 expression	
HER2 (+++)	305 (85.2)

HER2 (++)	53 (14.8)
Mediastinal lymph nodes	
Yes	21 (5.9)
No	337 (94.1)
Treatment regimen	
ddAC + DPT	126 (35.2)
TCHP	110 (30.7)
Taksan+ ddAC+Herceptin	82 (22.9)
Diğer	40 (11.2)
Completed treatment (Yes)	342 (95.5)
Radiotherapy (Received)	271 (75.7)

Abbreviations: n: Number of patients, IDC: Invasive Ductal Carcinoma, ILC: Invasive Lobular Carcinoma, ddAC: Dose-dense Adriamycin-Cyclophosphamide, DPT: Docetaxel-Pertuzumab-Trastuzumab, TCHP: Docetaxel-Carboplatin-Herceptin-Pertuzumab.

In the pCR subgroup analysis, a statistical contribution was observed in the invasive lobular carcinoma (ILC) group, despite the comparatively low number of patients. Regarding clinical lymph node subgroups, the N2 group benefited most from treatment in univariate analysis, whereas the N3 group showed greater benefit in multivariate analysis. However, no statistically significant difference was observed among lymph node groups. Although T2 and T4 subgroups, as well as Grade 2 and 3 groups, appeared more significant in terms of p-values, no statistically significant difference was found in terms of odds ratio (OR). Compared to the reference arm (AC+DPT), the probability of achieving pCR was significantly lower in the group receiving "other" treatment regimens (OR: 0.35, 95% CI: 0.17-0.73, p=0.005). No statistically significant difference in pCR was observed between the TCHP and AC+DPT regimens (p=0.360). In the HER2 3+ group, although pCR rates were numerically higher in univariate analysis, there was no statistical difference in multivariate analysis (Table 2).

Table 2 Univariate and multivariate analysis of parameters predicting pCR						
		Univariate analysis			Multivariate analysis	
Variables	**P value**	**OR**	**95% CI**	**P value**	**OR**	**95% CI**
Age	0.45	0.99	0.98-1.01	0.09	0.98	0.96-1.01
Pathological subtype						
IDC	0.16	1.00				
ILC	0.02	0.17	0.03-0.81			
Others	0.74	0.81	0.24-2.73			
NOS	0.86	1.05	0.59-1.86			
Clinical N stage						
N0	0.21	1.00				
N1	0.88	0.95	0.48-1.88			
N2	0.15	0.56	0.26-1.25			
N3	0.31	0.61	0.23-1.60			
Clinical T stage						
T1	0.67	1.00				
T2	0.33	0.75	0.41-1.35			
T3	0.80	0.88	0.32-2.42			
T4	0.29	0.53	0.17-1.71			
Histological grade						
Grade 1	0.53	1.00				
Grade 2	0.26	2.20	0.55-8.74			
Grade 3	0.31	2.06	0.50-8.44			
Treatment protocol						
AC+DPT	0.19	1.00		0.023	1.00	
TCHP	0.98	1.00	0.59-1.67	0.65	0.86	0.46-1.62

Others	0.11	0.66	0.40-1.10	0.009	0.40	0.20-0.79
ER status						
Negative (-)		1.00				
Positive (+)	0.85	0.96	0.61-1.50			
HER2 score (+2*/+3)	0.16	1.53	0.84-2.78	0.05	2.13	0.97-4.69

PCR: Pathological Complete Response, OR: Odds Ratio, CI: Confidence Interval, IDC: Invasive Ductal Carcinoma, ILC: Invasive Lobular Carcinoma, NOS: Not Otherwise Specified, AC: Doxorubicin (Adriamycin) and Cyclophosphamide, DPT: Docetaxel, Pertuzumab and Trastuzumab, TCHP: Docetaxel, Carboplatin, Herceptin and Pertuzumab, ER: Estrogen Receptor, HER2: Human Epidermal Growth Factor Receptor 2

When the event-free survival (EFS) analysis was examined, it was determined that ER and PR positivity had no effect on survival. HER2 3+ status was identified as a risk-increasing factor for EFS compared to HER2 2+/FISH+ patients. Regarding clinical lymph node status, advanced lymph node involvement (N3) was evaluated as a risk factor for EFS (HR: 8.43, p=0.038) (Table 3), (Figure 1,2).

With regard to adverse effects, febrile neutropenia was observed in 8.2% of patients in the TCHP arm and 1.6% of patients in the AC+DPT arm. Grade 1-2 anemia occurred in 42.7% of the TCHP arm versus 19.1% in the AC+DPT arm. With regard to adverse effects, febrile neutropenia was observed in 8.2% of patients in the TCHP arm and 1.6% of patients in the AC+DPT arm. No severe (Grade 3-4) cardiac events were observed (Table 4).

Table 3. Results of univariate and multivariate analyses of parameters affecting event-free survival

	Univariate analysis			Multivariate analysis		
Variables	**P value**	**HR**	**95% CI**	**P value**	**HR**	**95% CI**
Grade						
Grade 1*	0.81					
Grade 2	0.58	0.67	0.15-2.83			
Grade 3	0.52	0.6	0.13-2.80			
ER % (linear)	0.02	0.99	0.98-0.99	0.083	0.994	0.986-1.001
PR % (linear)	0.63	0.99	0.99-1.00			
HER-2 status (+2*/+3)	0.02	9.03	1.24-65.3	0.038	8.436	1.12-63.43
Pathological subtype						
İDC*	0.65					
İLC	0.97	0.00	0.00-6.43			
Others	0.63	0.61	0.08-4.49			
NOS	0.23	0.53	0.19-1.49			
Treatment protocol						
ddAC + DPT*	0.016					
TCHP	0.13	0.32	0.07-1.43			
Other	0.017	2.4	1.17-5.18			
ddAC+ taxan +herceptin	0.41	1.32	0.66-2.64			
T stage						
T1*	0.04					
T2	0.48	0.75	0.34-1.64			
T3	0.18	1.97	0.71-5.46			
T4	0.2	2.17	0.65-7.25			
N stage						
N0*	0			0.11		

N1	0.12	4.8	0.65-35.3	0.078	6.11	0.81-45.63
N2	0.1	5.4	0.69-42.3	0.163	4.38	0.54-34.97
N3	0.004	20.4	2.65-157.4	0.010	15.33	1.90-123.78

EFS: Event-Free Survival, HR: Hazard Ratio, CI: Confidence Interval, ER: Estrogen Receptor, PR: Progesterone Receptor, HER-2: Human Epidermal Growth Factor Receptor 2, IDC: Invasive Ductal Carcinoma, ILC: Invasive Lobular Carcinoma, NOS: Not Otherwise Specified, ddAC: Dose-dense Doxorubicin and Cyclophosphamide, DPT: Docetaxel, Pertuzumab and Trastuzumab, TCHP: Docetaxel, Carboplatin, Herceptin and Pertuzumab

Table-4: Distribution of Adverse Events (Toxicity) by Treatment Groups

Adverse Events and Grade	AC + DPT (n=126)	TCHP (n=110)	Others (n=122)	Total (n=358)
Febrile neutropenia, n (%)	2 (%1.6)	9 (%8.2)	2 (%1.6)	13 (%3.6)
Neutropenia, n (%)				
No	86 (%68.3)	67 (%60.9)	92 (%75.4)	245 (%68.4)
Grade 1-2	20 (%15.8)	27 (%24.5)	19 (%15.5)	66 (%18.5)
Grade 3-4	20 (%15.9)	16 (%14.6)	11 (%9.0)	47 (%13.1)
Anemia, n (%)				
No	102 (%81.0)	60 (%54.5)	95 (%77.9)	257 (%71.8)
Grade 1-2	24 (%19.1)	47 (%42.7)	25 (%20.5)	96 (%26.8)
Grade 3-4	0 (%0.0)	3 (%2.7)	2 (%1.6)	5 (%1.4)
Thrombocytopenia, n (%)				
No	120 (%95.2)	93 (%84.5)	114 (%93.4)	327 (%91.3)
Grade 1-2	5 (%4.0)	14 (%12.7)	5 (%4.1)	24 (%6.7)
Grade 3-4	1 (%0.8)	3 (%2.7)	3 (%2.4)	7 (%1.9)
Hepatotoxicity, n (%)				
No	103 (%81.7)	97 (%88.2)	102 (%83.6)	302 (%84.4)
Grade 1-2	22 (%17.5)	13 (%11.8)	19 (%15.6)	54 (%15.1)
Grade 3-4	1 (%0.8)	0 (%0.0)	1 (%0.8)	2 (%0.6)
Nephrotoxicity, n (%)				
No	126 (%100)	104 (%94.5)	119 (%97.5)	349 (%97.5)
Grade 1-2	0 (%0.0)	5 (%4.5)	3 (%2.5)	8 (%2.3)
Grade 4	0 (%0.0)	1 (%0.9)	0 (%0.0)	1 (%0.3)
Cardiotoxicity, n (%)				
No	126 (%100)	106 (%96.4)	121 (%99.2)	353 (%98.6)
Grade 1-2	0 (%0.0)	4 (%3.6)	1 (%0.8)	5 (%1.4)

DISCUSSION

A previous meta-analysis found that patients in stages T3 and T4 had worse pCR, EFS, and OS. Patients who achieved a complete response were found to have a longer survival time In the present study, although a numerical difference was observed between stages T2 and T4, this difference was not statistically significant. The observation of comparable pCR rates in the TCHP arm indicates that it may be as beneficial as anthracycline-containing regimens for long-term survival. While meta-analyses have shown better pCR results in hormone receptor-negative groups, our study observed no statistically significant difference in pCR between hormone receptor-positive and negative groups. Our study included a high rate of ER+ patients (67%). İt is thought that the gap may have been closed by new-generation anti-HER2 therapies (20).

Although it is generally believed that patients achieving pCR with neoadjuvant therapy will have better survival, some studies do not support this. A different meta-analysis found a weak correlation between pCR and long-term survival. This result suggests that if pCR does not affect survival, anthracycline-based regimens, which are more toxic particularly to the heart, could be avoided. The present study indicated that the biological aggressiveness of the tumour may be a factor in the observed difference in survival rates between pCR and non-pCR. The fact that the HER2 3+ group in our study had worse EFS supports the notion that survival may differ in biologically aggressive diseases (21).

Studies by Symmans et al. indicate that lymph node involvement is the most critical factor affecting prognosis. Metastatic lymph node involvement dramatically negatively impacts the prognosis of the disease. The high recurrence risk observed in N3 patients in our study is consistent with the literature. While the Symmans study noted that the risk of recurrence in the hormone receptor-positive group could occur in later years, it stated that the hormone receptor-negative group typically recurs within the first 5 years. In our study, hormonal status did not affect EFS. This may be explained by the insufficient maturation of our follow-up period and patient sample size (22).

The Phase 3 Z1041 study demonstrated no difference between concurrent and sequential administration of trastuzumab with anthracycline-based chemotherapy. The study found no additional benefit from dose intensification. Our study goes a step further, identifying that omitting anthracyclines does not alter pCR rates. In the Z1041 study, the pCR rate was distinctly better in the hormone-negative subgroup compared to the hormone-positive subgroup. The absence of such a difference in our study may be related to the development of new anti-HER2 targeted therapies, as mentioned above (9).

In the previously conducted TRAIN-2 study, an anthracycline-containing regimen was compared with an anthracycline-free regimen, and pCR rates were found to be similar. which aligns with our findings. However, while febrile neutropenia was more common in the anthracycline-containing regimen arm in the TRAIN-2 study, the opposite was true in our study. This could be due to the use of paclitaxel with carboplatin in the anthracycline-free regimen of that study, whereas our study utilized docetaxel, which is hematologically more toxic. Consistent with our study, cardiac events were found to be rare and similar between groups (15).

In the GETN(A)-1 study, only docetaxel with carboplatin and trastuzumab were used as the anthracycline-free regimen. The response rate in this study was around 40%. Our study demonstrated a higher pCR rate We thought that this could be due to the use of dual anti-HER2 (trastuzumab+pertuzumab) therapy. The lower incidence of neutropenia in the GETN(A)-1 study compared to ours may be due to the inclusion of more selected patients. No cardiac adverse events were reported in that study. In our study, no additional cardiac events were observed with the addition of pertuzumab (22).

In a Phase 2 study conducted by Chen and colleagues in a breast cancer patient population with HER2 +3, a pCR rate of approximately 33% was achieved with weekly paclitaxel + carboplatin. Although anti-HER2 therapy was not added in that study, it demonstrated the potential benefit of this chemotherapy group The higher pCR rate in our study demonstrates the synergistic effect of the taxane-platinum combination and anti-HER2 therapy (23).

A small-sample study by Sikov et al. also used weekly carboplatin + paclitaxel, finding a response rate of 76% when trastuzumab was added. Although the sample size was small, it supports the synergistic benefit of the drugs used similarly in our study (24).

In the TRYPHAENA study, the anthracycline-free TCHP regimen demonstrated sufficient efficacy in terms of pCR. In this respect, our study shows similar results, indicating that removing anthracyclines from the regimen does not negatively affect treatment. In a study by Schneeweiss et al., no cardiac events were observed in the TCHP arm, serving as a reference that omitting anthracyclines could reduce cardiac events. However, no significant difference in cardiac events was observed between regimens in our study The neutropenia rate in our study is consistent with the TCHP data in the TRYPHAENA study. This emphasizes the need for close monitoring for myelosuppression in the TCHP regimen (16).

The multicenter nature of our study is limited due to patient heterogeneity. Other limiting factors include the time frame of 2015-2025, the use of different regimens, and changes in supportive care. However, the fact that anthracycline-free regimens show similar effects in real-world data is instructive.

CONCLUSION

In conclusion, our study demonstrates that the TCHP regimen has similar efficacy when compared to the standard anthracycline-containing regimen. While no difference was observed between the regimens in terms of cardiac toxicity, greater caution is required regarding hematological toxicity in the TCHP regimen. It should not be overlooked that patients with advanced lymph node involvement may have a worse clinical course. It is concluded that in clinical practice, anthracycline-free regimens can be used, particularly in patients with cardiac disease and sufficient hematological reserve.

Abbreviations

TCHP: Docetaxel, Carboplatin, Trastuzumab, Pertuzumab

pCR: Pathological complete response

EFS: Event-free survival

AC+DPT: Adriamycin , Cyclophosphamide, Docetaxel, Pertuzumab, Trastuzumab

HR: Hazard Ratio

ER: Estrogen Receptor

PR: Progesterone Receptor

HER2: Human Epidermal Growth Factor Receptor 2

IDC: İnvasive ductal carcinoma

FISH: Fluorescence in situ hybridization

T-DM1: Trastuzumab emtansine

ECOG: Eastern Cooperative Oncology Group

Declarations

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None

Authors' contributions

M.K and S.E conceived and designed the study, performed the statistical analysis, drafted the manuscript, and critically revised it for important intellectual content. T.B, H.A.Y, M.H, S.Ç, and Z.H collected and organized the clinical data. N.A, N.K, M.Ü, M.N.A and Y.S critically reviewed the manuscript, performed additional statistical analyses, obtained funding, and provided administrative, technical, and material support. All authors read and approved the final manuscript.

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Availability of data and materials

The database of the study is available in the corresponding author and will be sent when requested by e-mail

Ethics approval and consent to participate

This study approved by Ethical Committee of Van Yüzüncü Yıl University Faculty of Medicine. Due to retrospective nature of the study, Van Yüzüncü Yıl University Faculty of Medicine waived off the informed consent in our study. All methods/ protocols were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1*2] [10] [11][12] Department of Medical Oncology, Faculty of Medicine, Van Yüzüncü Yıl University, Van, Turkiye [3]Department of Medical Oncology, Goztepe Suleyman Yalcin City Hospital, Istanbul, Turkiye [4][6]Department of Medical Oncology, Etlik City Hospital, Ankara, Turkiye [5]Department of Medical Oncology, Faculty of Medicine , Turgut Ozal Medical Center, Malatya, Turkiye,[7] Department of Medical Oncology, Bursa City Hospital, Bursa, Türkiye, [8] Department of Medical Oncology, Diyarbakır Gazi Yaşargil Training and Research Hospital, Diyarbakır, Türkiye [9] Department of Medical Oncology, Batman Training and Research Hospital, Batman, Türkiye

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Figures

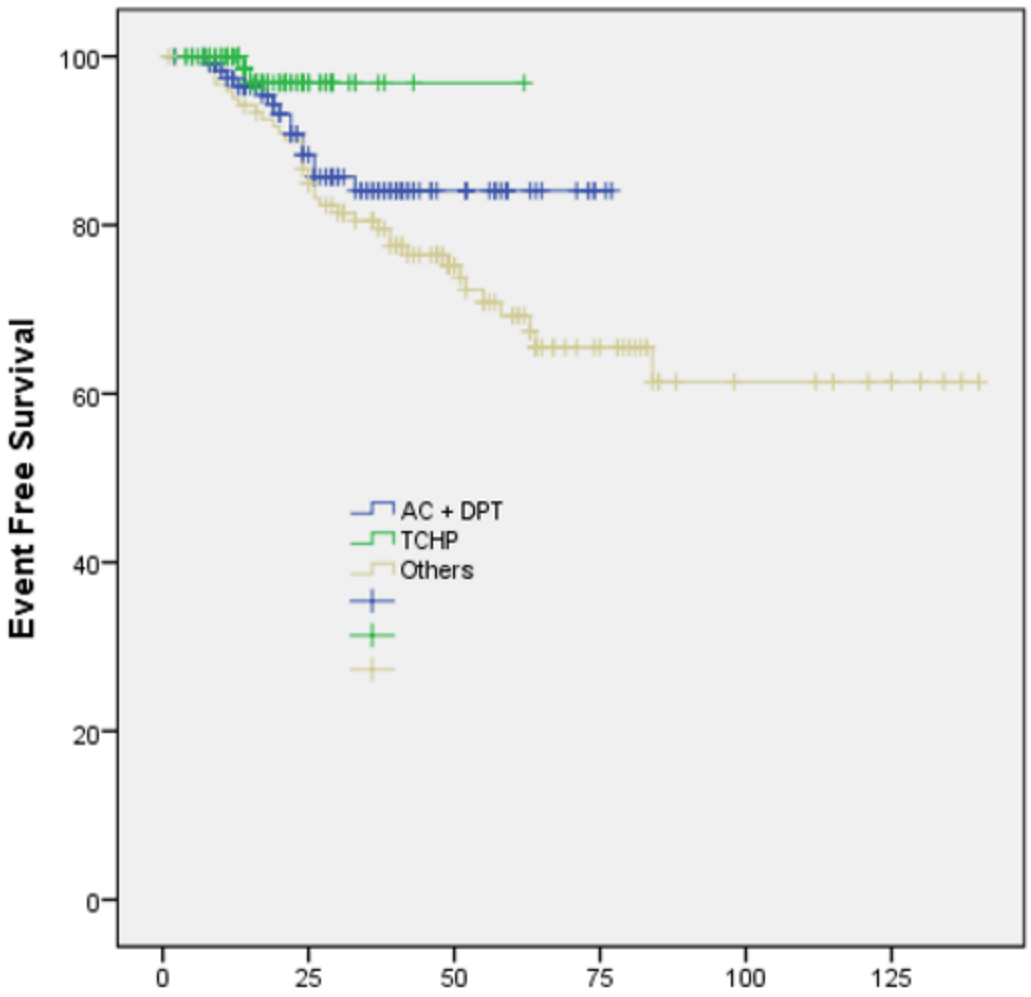


Figure 1

Kaplan-Meier analysis comparing treatment options for event-free survival

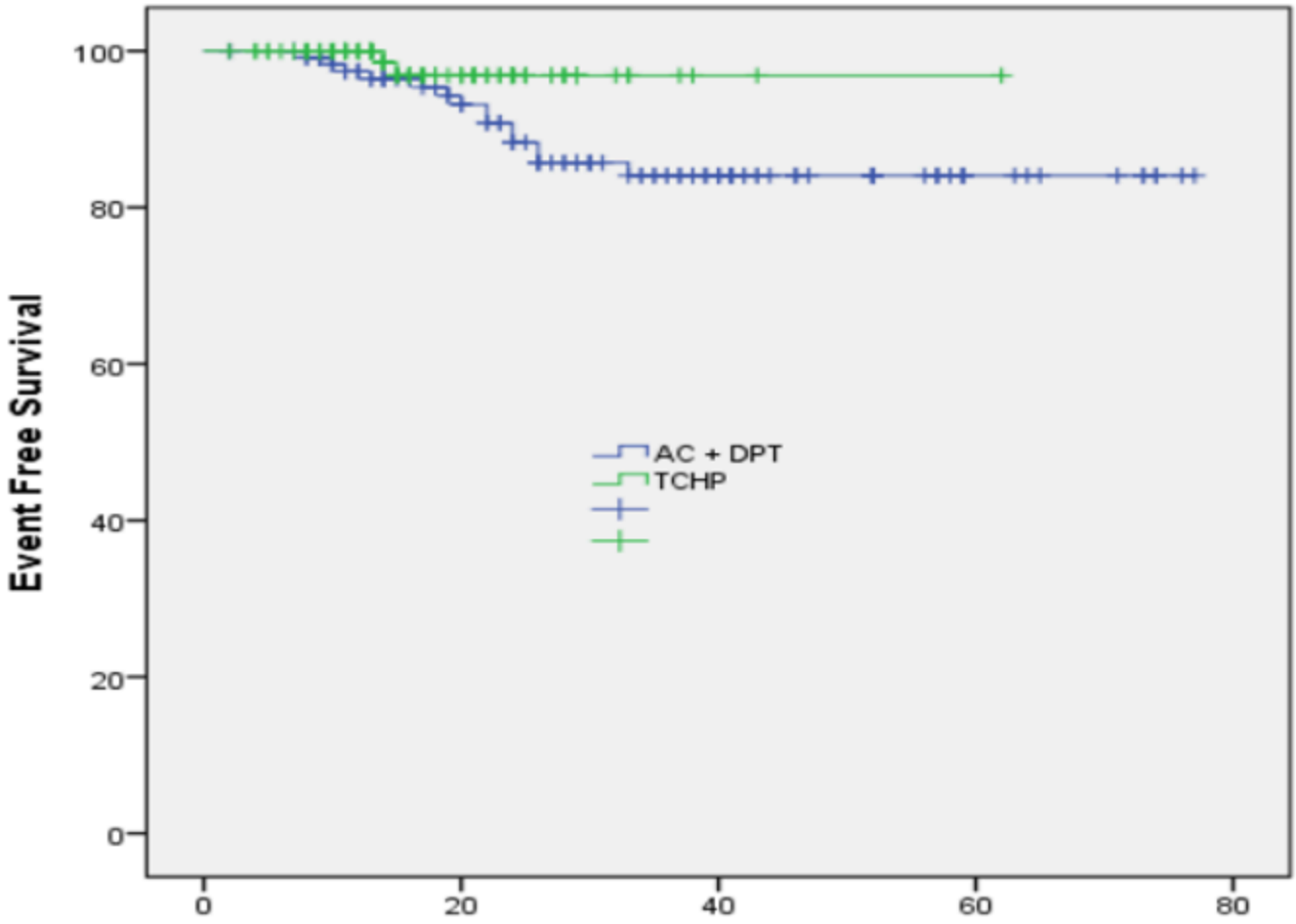


Figure 2

Kaplan-Meier analysis comparing AC+DPT and TCHP treatment regimens for event-free survival