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A study to compare the efficacy of neoadjuvant chemotherapy in locally advanced human epidermal growth factor receptor 2 overexpressing breast cancer

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ABSTRACT

Background: This prospective single institutional study was conducted to compare the efficacy of the two different neoadjuvant chemotherapy (NACT) regimens in human epidermal growth factor receptor 2 (Her2neu) overexpressing non metastatic breast cancer.

Materials and methods: Patients randomly assigned into two arms in a 1:1 ratio. Arm A received NACT containing docetaxel, doxorubicin, and cyclophosphamide (TAC) regimen. Arm B received NACT containing docetaxel, carboplatin, and trastuzumab (TCH) regimen. Patients underwent surgical intervention following completion of 6 cycles of NACT. Postoperative histopathological reports were compared in terms of pathological response.

Results: 122 patients (Arm A = 61; Arm B = 61) analysed. The mean breast tumor size was 7.724 cm and 7.896 cm in Arm A and Arm B, respectively, at diagnosis and clinical staging. After 6 cycles of NACT, the mean breast tumor size in Arm A and Arm B was 3.495 cm and 3.711 cm, respectively. The Arm A and Arm B exhibited 22.9% and 40.9% of pathological complete response (pCR), respectively, with statistically significant difference ($p = 0.033$). All patients experienced varying degrees of bone marrow suppression. Grade 2 or 3 chemotherapy induced nausea and vomiting was 37.7% and 23% in Arm A and Arm B, respectively, without statistically significant difference ($p = 0.076$). 14.8% and 4.9% of patients exhibited febrile neutropenia in Arm A and Arm B, respectively, without statistically significant differences ($p = 0.067$).

Conclusion: TCH exhibited greater pCR with tolerable adverse reactions in Her2neu overexpressing breast cancer compared to TAC regimen as NACT. Therefore, TCH regimen should be considered for node positive Her2neu overexpressing breast cancer.

Keywords: Her2neu overexpression; TCH; TAC; trastuzumab; neoadjuvant chemotherapy; breast cancer

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Introduction

Breast cancer is the most common cancer affecting females worldwide. It is one of the leading causes of cancer related death among females [1]. The incidence of breast cancer has increased but the death rate has decreased over the last several decades [2]. In India, breast cancer is the most frequently diag-

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nosed cancer and leading cause of cancer death [3]. Breast cancer is one of the most heterogenous diseases in terms of origin, pathology, tumor biology, molecular subtypes, therapeutic response, disease progression, and clinical outcome [4]. Previous studies have demonstrated that 20–25% of breast cancer patients exhibit human epidermal growth factor receptor-2 (Her2neu) overexpression [5, 6]. Her2neu is a transmembrane tyrosine kinase receptor related to cell differentiation, growth, and survival [7]. The overexpression of Her2neu gives rise to a malignant phenotype. Consequently, there is cell proliferation and more aggressive tumor phenotype [8]. Breast cancer overexpressing Her2neu predicts poor prognosis compared to Her2neu negative disease [9]. Her2neu overexpression has been reported to be an independent risk factor for the relapse of the disease [10]. Trastuzumab, a humanized monoclonal antibody which targets the extracellular domain of the Her2neu receptor, and its addition to adjuvant chemotherapy has been shown to improve disease-free survival (DFS) and overall survival (OS) [11–14]. Preoperative neoadjuvant chemotherapy (NACT) is an important treatment strategy for locally advanced breast carcinoma [15]. NACT is now an imperative part of the preoperative systemic treatment for breast cancer following the results of well-known large scale clinical trials National Surgical Adjuvant Breast and Bowel Project (NSABP) B18 and B27 [16]. The combination of chemotherapeutic drugs and trastuzumab may be used to enhance the pathological complete response (pCR). The pCR may be used to differentiate between patients with favourable and unfavourable outcomes in response to NACT [17]. pCR may be a suitable surrogate endpoint for patients with Her2neu overexpression (positive) [18]. In the present study, patients with Her2neu overexpressing breast carcinoma with axillary lymph node metastasis were administered trastuzumab containing NACT or non trastuzumab containing NACT regimens prior to surgical intervention. The outcomes were analysed in terms of pathological response in each treatment regimen.

Materials and methods

A prospective, single institutional randomized study was conducted at the All India Institute of Medical Sciences (AIIMS), Patna. The Institutional Ethics Committee of AIIMS, Patna (AIIMS/Pat/IEC/2020/435 dated 23rd March 2020) approved the study. This study included patients with biopsy proven locally advanced breast cancer overexpressing human epidermal growth factor receptor 2 (Her2neu) on immunohistochemistry (IHC) attending the Radiotherapy department at AIIMS, Patna from March 2020 to February 2022.

Primary objective

To compare the efficacy of two different neoadjuvant chemotherapy regimens in terms of pathological and radiological response.

Secondary objective

To compare the neoadjuvant chemotherapy related toxicity of both the chemotherapy regimens.

Randomization and sample size

Patients were randomly assigned to Arm A and Arm B with a 1:1 ratio by computer-generated random number. The differences in the rate of pCR ranged from 15–37% following neoadjuvant chemotherapy, assuming the difference of pCR between Arm A and Arm B of 20–25% with a type I error of 0.05 and power of 80%. Under these assumptions, the sample size amounts to 116. As the individual results for the primary objective are available within 2 weeks of surgery, the drop-out rate is expected to be small. This can be compensated by an additional 5% of patients being randomized, and therefore the total sample size required amounts to 116 + 6 = 122 patients (61 patients in each treatment arm).

Inclusion criteria: females aged between 20–60 years, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0–2 [19], histopathologically confirmed breast carcinoma (core needle biopsy from breast tumor), tumors overexpressing Her2neu on IHC (core needle biopsy sample from breast tumor), cytopathologically confirmed metastasis to axillary lymph nodes (fine needle aspiration cytology from axillary lymph nodes).

Exclusion criteria: patients with axillary lymph node negative for metastasis, distant metastasis, history of congestive cardiac failure, left ventricular ejection fraction (LVEF) < 50%, and previous history of chemotherapy and chest wall radiotherapy.

Histopathologically confirmed cases of breast carcinoma were subjected to a complete staging workup using mammogram, computed tomography (CT) scan thorax and abdomen, Tc99m whole body bone scan. Tumors with IHC of estrogen receptor (ER) and progesterone receptor (PR) having expression ≥ 1% were considered ER and PR positive, respectively. IHC for Her2neu was done on formalin fixed paraffin embedded sections by polymer horseradish peroxide technique. A score of +3 for Her2neu is considered positive or over expressed, a score of 0 or +1 was considered Her2neu negative. Her2neu score of +2 was considered as equivocal and samples were subjected to fluorescence in situ hybridization (FISH) study.

Biochemical parameters including complete blood count, liver function test, renal function test and echocardiography were done as diagnostic work-up investigations in all patients. All the patients were staged according to the American Joint Committee on Cancer (AJCC) tumor node metastasis 8th edition [20]. All patients were considered for ultra-sound guided metallic markers placement at the primary tumor site to facilitate localization during surgery. All patients in this study were subjected to neoadjuvant chemotherapy (NACT) with two different chemotherapy regimens. NACT regimens consist of intravenous injection of docetaxel 75 mg/m^2, injection of doxorubicin 50 mg/m^2 and injection of cyclophosphamide 500 mg/m^2 on day 1 (TAC) [21]. Intravenous injection of docetaxel 75 mg/m^2, injection carboplatin AUC 6, and trastuzumab 8 mg/kg loading dose followed by 6 mg/kg on subsequent cycles on day 1 (TCH) [22]. Both the NACT regimens were repeated every 21 days for 6 cycles. NACT of treatment Arm A and Arm B were TAC and TCH regimens, respectively. Prophylactic granulocyte colony stimulating factor (GCSF) was administered in both treatment arms. Patients underwent clinical examination and biochemical investigations before each NACT cycle to assess the clinical response and NACT related toxicities.

Cardiac function was monitored using echocardiography at baseline and every 3 months in both treatment arms. Two weeks after completion of NACT, a repeat CT scan thorax was done to evaluate radiological response using Response Evaluation Criteria in Solid Tumours (RECIST 1.1). Three weeks after completion of NACT, modified radical mastectomy (MRM) or breast conservative surgery (BCS) is performed. Adjuvant radiation, trastuzumab or hormonal therapy was considered in both treatment arms.

Treatment efficacy was assessed pathologically and radiologically in both treatment arms. Post-operative histopathological reports were reviewed and analysed in both treatment arms regarding pathological response of primary breast tumor and lymph nodes. The CT scan thorax was done prior to the start of NACT as a diagnostic workup and following the completion of NACT to determine breast primary tumor size and axillary lymph node size and to evaluate the efficacy of each chemotherapy regimen using RECIST 1.1.

Definition of outcome

pCR defined by the absence of invasive carcinoma in the breast and lymph nodes following neoadjuvant chemotherapy. The presence of in situ component after NACT in the absence of invasive disease, constitutes pCR. The presence of tumor within lymphatics or/and vascular spaces in the breast with or without other residual invasive cancer excludes pCR. Pathological partial response (pPR), a decrease in either or both T or N category compared to the pre-neoadjuvant chemotherapy or clinical assignment, and no increase in either T or N [23].

Radiological response assessment using RECIST 1.1 [24]: Complete response (CR), disappearance of all target lesions. Any pathological lymph nodes (target or non-target) must have a reduction in short axis to < 10 mm. Partial response (PR), at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive disease (PD), at least 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. The appearance of one or more new lesions is also considered PD. Stable disease (SD), neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

NACT related toxicities was compared in both treatment arms using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0 [25]. Treatment related to adverse events like nausea, vomiting, myelosuppression was managed accordingly. The consort flow diagram is given in Figure 1.

Statistical analysis

The Statistical Package for Social Sciences (IBM SPSS for Windows, version 25.0) is used for statisti-

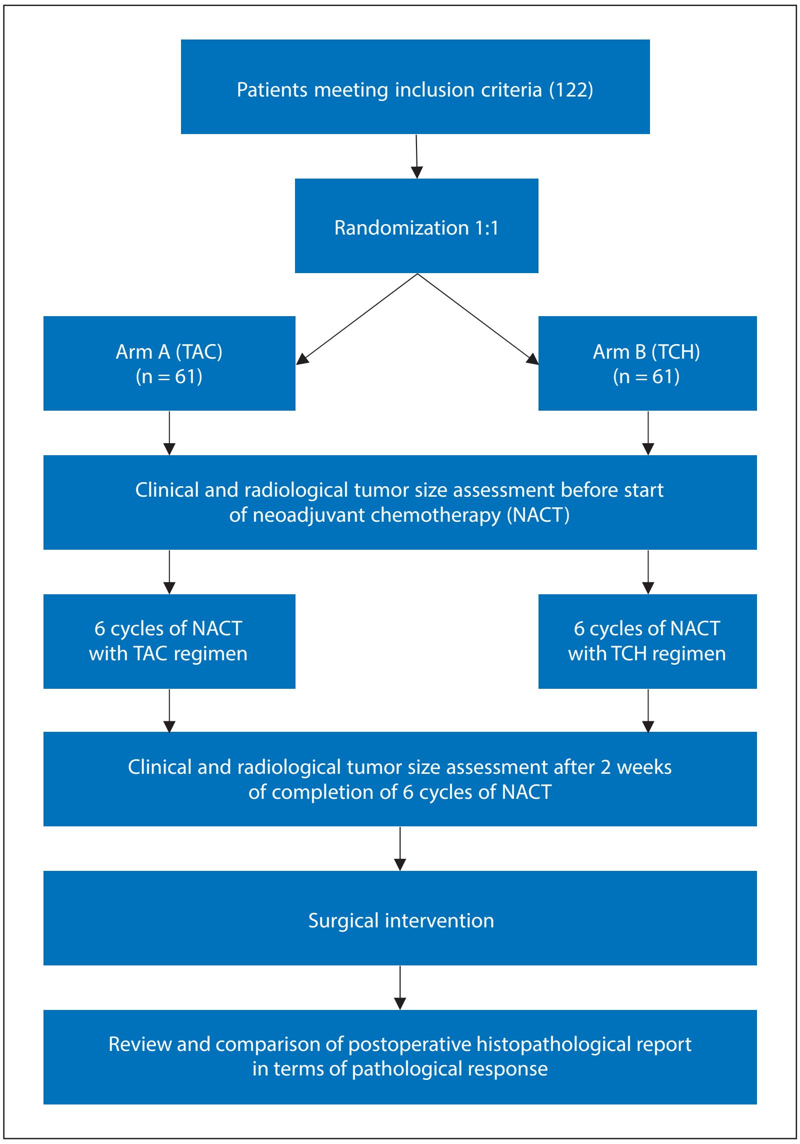

Figure 1. Consort flow chart. TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab; NACT — neoadjuvant chemotherapy

cal analysis. Descriptive statistics were used to characterize the study population using frequencies, mean, and median. The differences in the proportion regarding response to different neoadjuvant chemotherapy were assessed using the Chi-square test. Continuous variables regarding toxicity related to chemotherapy were compared using a student's t-test. A p-value < 0.05 was considered statistically significant in all performed analyses.

Results

Clinicopathological characteristics

A total of 122 patients (Arm A = 61; Arm B = 61) meeting inclusion criteria were included in the study and analysed. All patients of this study completed proposed 6 cycles of neoadjuvant chemotherapy followed by surgical intervention. The median age at diagnosis in the Arm A and Arm B was 46 years (20–60) and 47 years (25–60), respectively. 50.8% and 54.1% of patients were postmenopausal in Arm A and Arm B, respectively. The use of oral contraceptive pills was seen in 14.8% and 4.9% of patients in Arm A and Arm B, respectively. 6.6% of patients in Arm A showed first degree relative to breast cancer while 13.1% of patients in Arm B showed first degree relative to breast cancer. Arm A included 44.3% of patients in stage IIIA, while 47.5% of patients were in stage IIIB of Arm B. The median baseline LVEF was 60 in both treatment arms. ER were seen positive at 54.1% and 55.7% in Arm A and Arm B, respectively. PR was seen positive at 36.1% and 50.8 % in Arm A and Arm B, respectively. Other epidemiological characteristics are depicted in Table 1.

Efficacy of chemotherapy regimens

The mean breast tumor size was 7.724 cm and 7.896 cm in Arm A and Arm B, respectively, at diagnosis and clinical staging. After 6 cycles of neoadjuvant chemotherapy, the mean breast tumor size in Arm A and Arm B was 3.495 cm and 3.711 cm, respectively. There was no statistically significant reduction in tumor size difference while comparing the two treatment arms after neoadjuvant chemotherapy [95% confidence interval (CI): 0.456–0.889; p = 0.176], details given in Table 2.

Radiological response

There was no CR following the neoadjuvant chemotherapy in both the treatment arms compar-

Table 1. Clinicopathological characteristics

		Treatment arm				p-value
		Arm A (TAC)		Arm B (TCH)		
		Count (n = 61)	N %	Count (n = 61)	N %	
Side	Right	31	50.8%	25	41.0%	0.276
	Left	30	49.2%	36	59.0%	
Postmenopausal	Yes	31	50.8%	33	54.1%	0.717
	No	30	49.2%	28	45.9%	
HRT	Yes	0	0.0%	0	0.0%	
	No	61	100.0%	61	100.0%	
Family History	Yes	4	6.6%	8	13.1%	0.224
	No	57	93.4%	53	86.9%	
Use of OCP	Yes	9	14.8%	3	4.9%	0.068
	No	52	85.2%	58	95.1%	
cT	cT2	6	9.8%	9	14.8%	0.347
	cT3	27	44.3%	21	34.4%	
	cT4A	7	11.5%	5	8.2%	
	cT4B	19	31.1%	19	31.1%	
	cT4C	2	3.3%	7	11.5%	
cN	cN1	40	65.6%	36	59.0%	0.744
	cN2	19	31.1%	23	37.7%	
	cN3	2	3.3%	2	3.3%	
ER	Positive	33	54.1%	34	55.7%	0.856
	Negative	28	45.9%	27	44.3%	
PR	Positive	22	36.1%	31	50.8%	0.100
	Negative	39	63.9%	30	49.2%	
Pre operative stage	IIB	6	9.8%	9	14.8%	0.679
	IIIA	27	44.3%	21	34.4%	
	IIIB	26	42.6%	29	47.5%	
	IIIC	2	3.3%	2	3.3%	
Type of surgery	MRM	51	83.6%	45	73.8%	0.185
	BCS	10	16.4%	16	26.2%	
Margin status	Positive	2	3.3%	3	4.9%	0.648
	Negative	59	96.7%	58	95.1%	

Table 1. Clinicopathological characteristics

		Treatment arm				p-value
		Arm A (TAC)		Arm B (TCH)		
		Count (n = 61)	N %	Count (n = 61)	N %	
Pathological T	ypT0	14	23.0%	25	41.0%	0.233
	ypT1	12	19.7%	6	9.8%	
	ypT2	21	34.4%	18	29.5%	
	ypT3	11	18.0%	10	16.4%	
	ypT4	3	4.9%	2	3.3%	
Pathological N	ypN0	26	42.6%	27	44.3%	0.248
	ypN1	20	32.8%	16	26.2%	
	ypN2	7	11.5%	14	23.0%	
	ypN3	8	13.1%	4	6.6%	
Post operative stage	Stage 0	14	23.0%	25	41.0%	0.041
	Stage IA	4	6.6%	1	1.6%	
	Stage IIA	11	18.0%	3	4.9%	
	Stage IIB	13	21.3%	10	16.4%	
	Stage IIIA	9	14.8%	16	26.2%	
	Stage IIIB	2	3.3%	2	3.3%	
	Stage IIIC	8	13.1%	4	6.6%	

TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab; HRT — hormone replacement therapy; OCP — oral contraceptive pills; cT — clinical tumor stage; cN — clinical nodal stage; ER — estrogen receptor; PR — progesterone receptor; MRM — modified radical mastectomy; BCS — breast conservative surgery

Table 2. Tumor size and axillary lymph node size pre and post chemotherapy

	Arm A (TAC) (n = 61)		Arm B (TCH) (n = 61)		Mean difference	Std error difference	95% CI	p-value
	Mean	SD	Mean	SD				
Tumor size at diagnosis	7.724	2.238	7.896	2.613	0.172	0.440	0.700–1.044	0.206
Tumor size after 6 cycles of NACT	3.495	2.059	3.711	1.676	0.216	0.340	0.456–0.889	0.176
Lymph node size at diagnosis	2.491	0.708	2.363	0.749	0.127	0.132	0.133–0.389	0.411
Lymph node size after 6 cycles of NACT	0.950	0.437	0.904	0.380	0.045	0.074	0.101–0.192	0.468

TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab; SD — standard deviation; NACT — neoadjuvant chemotherapy; CI — confidence interval

ing the images before the start of NACT and after completion of 6 cycles of NACT using RECIST 1.1. Arm A showed 90.1% of PR and 9.9% of SD for breast primary. Arm B showed 91.8% of PR and 8.2% of SD for breast primary. The rate of PR of the breast primary was higher in Arm B but statistically this difference was not significant (p = 0.752). The RECIST 1.1 evaluation of the axillary lymph nodes revealed that there was 100% PR for axillary lymph nodes in Arm A, while 98.3% of PR with one patient having SD in axillary lymph nodes in Arm B. The rate of PR of the axillary lymph nodes was more in Arm A but statistically this difference was not significant (p = 0.315).

Pathological response

The Arm A and Arm B exhibited 22.9% and 40.9% of pCR, respectively. The difference in the rate of pCR was statistically significant in both treatment arms (p = 0.033). This indicates that the Arm B (TCH) chemotherapy regimen was more efficacious than Arm A (TAC) for Her2neu

Table 3. Comparison of pathological and radiological response

		Arm A (TAC)		Arm B (TCH)		Pearson Chi-square	p-value
		Count (n = 61)	N %	Count (n = 61)	N %		
Pathological response	pCR	14	22.9%	25	40.9%	4.560	0.033
	pPR	47	77.1%	36	59.1%		
RECIST primary	CR	0	0.0%	0	0.0%	0.100	0.752
	PR	55	90.1%	56	91.8%		
	SD	6	9.9%	5	8.2%		
RECIST axillary LNs	CR	0	0.0%	0	0.0%	1.008	0.315
	PR	61	100.0%	60	98.3%		
	SD	0	0.0%	1	1.7%		

TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab; RECIST — Response Evaluation Criteria in Solid Tumours; LN — lymph node; pCR — pathological complete response; pPR — pathological partial response; CR — complete response; PR — partial response; SD — stable disease

positive breast cancer in a neoadjuvant chemotherapy setting in achieving a pathological complete response as depicted in Table 3.

Neoadjuvant chemotherapy related adverse events

There was no treatment related mortality noted in this study. All patients experienced varying degrees of bone marrow suppression. Arm A exhibited 13.1% and 0.8% of patients with grade 1 and grade 2 anaemia, respectively. Similarly, Arm B exhibited 11.5% and 0.8% of patients with grade 1 and grade 2 anaemia, respectively, without any statistically significant difference in chemotherapy induced anaemia between the treatment arms. Arm A and Arm B showed 12.8% and 9.8% grade 1 thrombocytopenia, respectively, depicted in Figure 2.

All patients showed varying degrees of chemotherapy induced nausea and vomiting (CINV).

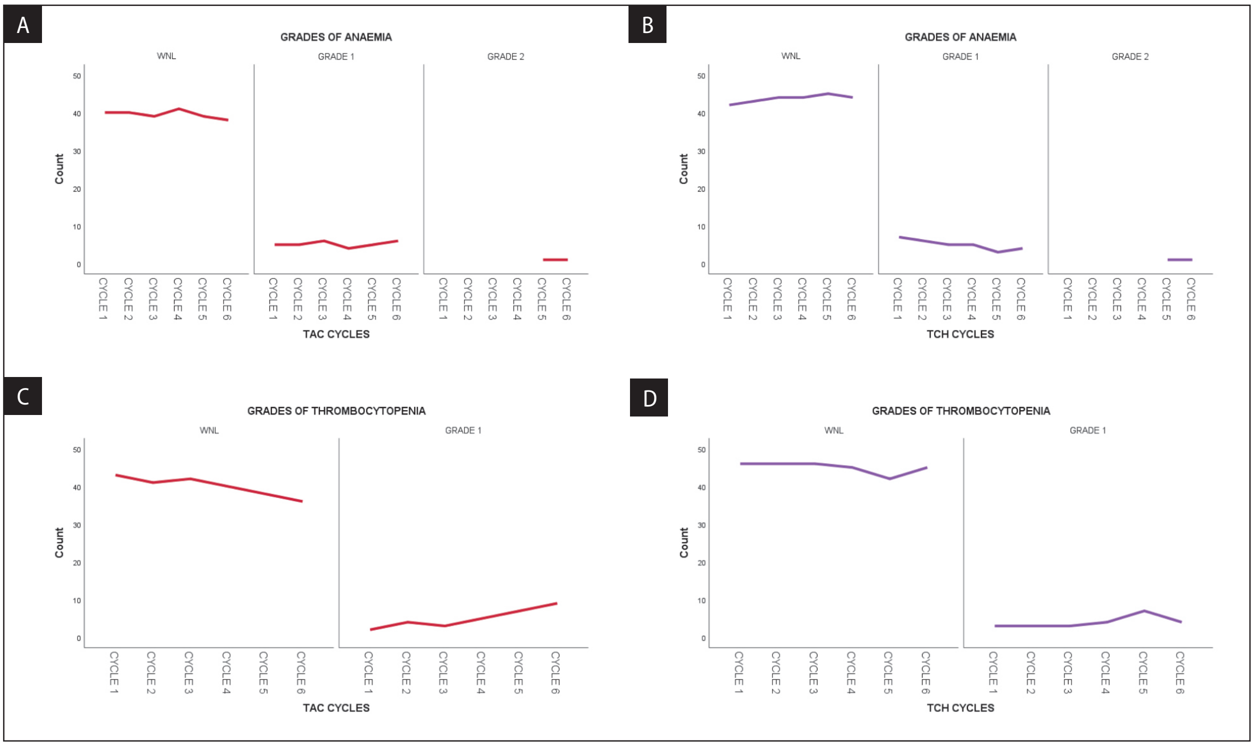

Figure 2. Grades of anaemia in docetaxel, doxorubicin, and cyclophosphamide (TAC) (**A**) and trastuzumab (TCH) (**B**) neoadjuvant chemotherapy; grades of thrombocytopenia in TAC (**C**) and TCH (**D**) neoadjuvant chemotherapy

Table 4. Comparison of chemotherapy related side-effects

		Arm A (TAC)		Arm B (TCH)		Pearson Chi-square	p-value
		Count (N = 61)	N %	Count (n = 61)	N %		
Febrile neutropenia	Yes	9	14.8%	3	4.9%	3.327	0.068
	No	52	85.2%	58	95.1%		
Alopecia (grade 2)	Yes	53	86.9%	45	73.8%	3.320	0.068
	No	8	13.1%	16	26.2%		
Chemo-induced nausea vomiting (grade 2 or 3)	Yes	23	37.7%	14	23.0%	3.142	0.076
	No	38	62.3%	47	77.0%		
Diarrhoea (grade 2 or 3)	Yes	19	31.1%	11	18.0%	2.829	0.093
	No	42	68.9%	50	82.0%		
Stomatitis (grade 2 or 3)	Yes	20	32.8%	13	21.3%	2.035	0.154
	No	41	67.2%	48	78.7%		

TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab

Table 5. Comparison of pre and post chemotherapy left ventricular ejection fraction (LVEF)

	Arm A (TAC) N = 61		Arm B (TCH) N = 61		Mean difference	Std error difference	95% CI	p-value
	Mean	SD	Mean	SD				
Baseline LVEF%	60.23	3.041	59.31	3.369	0.918	0.581	0.232–2.069	0.181
LVEF% after 6 cycles of NACT	59.95	3.232	55.31	3.744	1.639	0.633	0.385–2.893	0.846

TAC — docetaxel, doxorubicin, and cyclophosphamide; TCH — trastuzumab; CI — confidence interval; NACT — neoadjuvant chemotherapy

Grade 2 or 3 CINV was 37.7% and 23% in Arm A and Arm B, respectively. There was no statistically significant difference in CINV in treatment arms (p = 0.076). Chemotherapy induced alopecia (grade 2) was 86.9% and 73.8% in Arm A and Arm B, respectively, without statistically significant difference (p = 0.068). Arm A and Arm B exhibited 31.1% and 18% diarrhoea (grade 2 or 3), respectively. There was no statistically significant difference in incidence of chemotherapy induced diarrhoea in both treatment arms (p = 0.093). The rate of chemotherapy induced stomatitis (grade 2 or 3) was 32.8% and 21.3% in Arm A and Arm B, respectively. There was no statistically significant difference in the rate of chemotherapy induced stomatitis (p = 0.154) between Arm A and Arm B. There was increased incidence of febrile neutropenia in Arm A. 14.8% and 4.9% of patients exhibited febrile neutropenia in Arm A and Arm B, respectively, without statistically significant differences of febrile neutropenia between the treatment arms (p=0.068), given in Table 4. There was no chemotherapy related cardiac insufficiency and there was no statistically significant reduction in LVEF in both treatment arms (95% CI: 0.385–2.893; p = 0.846) as shown in Table 5.

Discussion

This study aims to assess the difference in the rate of pCR following NACT with two different chemotherapy regimens in node positive Her2neu overexpressing non metastatic breast cancer. Previous studies have demonstrated that breast carcinoma patients having Her2neu overexpression demonstrate a poor prognosis with malignant biological behaviour [26]. Trastuzumab, a humanised monoclonal antibody, was first used in Her2neu overexpressing metastatic breast cancer, but is presently combined with conventional chemotherapy in adjuvant or neoadjuvant settings. Many studies have shown that trastuzumab improves survival of Her2neu overexpressing breast cancer [27].

Trastuzumab has significantly improved disease-free survival and overall survival, but mostly in situations where trastuzumab is employed in adjuvant settings. Trastuzumab containing a chemotherapeutic regimen in neoadjuvant regimen, may enhance the rate of pCR in breast carcinoma patients with Her2neu overexpression [28]. Untch M et al. reported that the efficacy of NACT regimen containing trastuzumab was significantly greater than chemotherapy without trastuzumab containing NACT regimen in terms of pCR [29]. Salmon D et al. reported from the BCIRG006 trial that the efficacy of TCH regimen was similar to the regimen of doxorubicin and cyclophosphamide with sequential docetaxel and trastuzumab, but with fewer side effects [30]. Many studies have shown that trastuzumab enhances the anti-tumor activity of paclitaxel or docetaxel [31, 32]. Therefore, TCH regimen was compared to TAC regimen as neoadjuvant settings in this study. In this study, the median age was 46 and 47 years in Arm A and Arm B, respectively. Similar findings have also been reported by other Indian studies [33, 34]. The cumulative stage distribution of patients in this study was stage IIB, IIIA, IIIB, and IIIC 12.2%, 39.34%, 45.09%, and 3.37%, respectively. Doval et al. reported an almost similar distribution of patients in a study from India [35].

In our study, the cumulative rate of pCR was 31.96%. Arm A and Arm B showed pCR of 22.9% and 40.9%, respectively. Various studies reported the rate of pCR ranging from 25% to 69.2% in patients who received trastuzumab containing a chemotherapy regimen as NACT [36, 37, 38, 39, 40]. The pCR following NACT shows wide variations among the different studies. A study by Chen et al. reported 69.2% of pCR, which is more than any other study [41]. The result of the present study indicated that the efficacy of TCH regimen was more favourable than TAC regimen (40.9% *vs.* 22.9%; $p = 0.033$). Similarly, the superiority of the trastuzumab containing regimen in achieving pCR was demonstrated by many studies [42–44].

The adverse reactions caused by chemotherapy were mainly myelosuppression indicated by neutropenia. Other adverse reactions including diarrhoea, mucositis, alopecia, cardiac insufficiency are reported in many studies [45–47]. In the present study, 14.8% and 4.9% of the patients of Arm A and Arm B, respectively, experienced febrile neutropenia and none of the patients reported cardiac insufficiency. Other studies reported 24.7–33.87% of febrile neutropenia and 1.9–4.5% of febrile neutropenia in TAC and TCH chemotherapy regimens, respectively [48–51]. The underlying explanation may be the prophylactic use of granulocyte colony stimulation factor (GCSF) and patients with LVEF < 50% were not included in our study.

Limitations of the study include the fact of its being a single institutional study, and the fact that magnetic resonance imaging (MRI) of breast and axilla was not used to compare the radiological response, and survival outcome is not yet analysed. One of the important aspects, namely the correlation between pCR and survival outcome, is not analysed in this study. Future trials with a large number of samples need to answer these issues.

Conclusion

The neoadjuvant chemotherapy regimen containing docetaxel, carboplatin, and trastuzumab exhibited greater pCR with tolerable adverse reactions in Her2neu overexpressing breast cancer compared to TAC. The more effective TCH regimen is superior in eliminating detectable cancer cells, which is crucial for improving prognosis of breast cancer patients with Her2neu overexpression. Therefore, TCH regimen should be considered for node positive Her2neu overexpressing breast cancer to enhance clinical outcomes and increase the likelihood of achieving a pathological complete response.

Authors contribution

D.S.: Conceptualization, methodology, software, and original draft preparation; P.S.: Data curation; Amiy Arnav: Visualization, supervision; N.R.: Supervision, validation, reviewing and editing; A.R.: Writing reviewing and editing.

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Data availability

The datasets generated during current study are available from the corresponding author on reasonable request.

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

Ethical approval

The study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by Ethics Committee of All India Institute of Medical Sciences, Patna (AIIMS/Pat/IEC/2020/435 dated 23rd March 2020).

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