

RESEARCH ARTICLE

The Impact of adding platinum-base Regime for Neoadjuvant therapy in Patient with Triple- Negative Breast Cancer patients: A Retrospective Study

Rutaba Alam¹, Omema Saleem², Maryum Nouman³, Umm-e-Habiba Abdul Rauf⁴, Khadija Mobeen⁵, Faisal Ghani Siddiqui⁶

Abstract

Objective: To evaluate the impact of incorporating platinum-based agents into neoadjuvant chemotherapy regimens on achieving pathological complete response in patients with triple-negative breast cancer.

Method: The retrospective, cohort study was conducted in March 2025 at the Dow University Hospital, Karachi, and comprised data from January 2021 to January 2023 of female triple-negative breast cancer patients treated with neoadjuvant chemotherapy. Clinical characteristics, treatment regimens, response assessments and histopathological findings were noted and analysed. Pathological complete response was defined as the absence of invasive tumours in breast and lymph nodes post-surgery. Data was analysed using Stata 17.0.

Results: Of the 50 women whose data was screened, 38(76%) met the eligibility criteria. Of them, 17(44.7%) patients were aged ≤ 50 years, 21(55.3%) were aged > 50 years, 22(57.9%) received a combination of paclitaxel and carboplatin, constituting the platinum-based group, and 16(42.1%) received standard chemotherapy comprising anthracycline, cyclophosphamide and paclitaxel. Pathological complete response was achieved in 12(31.6%) patients: 8(36.4%) in the platinum-based group and 4(25%) in the standard chemotherapy group ($p=0.45$).

Conclusion: The addition of platinum-based agents to neoadjuvant chemotherapy NACT did not demonstrate a significant improvement in pathological complete response rates among triple-negative breast cancer TNBC patients.

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Introduction

Breast cancer (BC) is a global disease with 2.3 million new cases in 2020, accounting for one in every four cancer cases among women. Factors such as ageing population, genetic susceptibility, oestrogen exposure, radiation exposure, poor parity, high breast density and a history of atypical hyperplasia contribute to the increase in prevalence.^{1,2} Obesity and Western lifestyle, including alcohol consumption, also contribute to this increase. Over the last five years, 1,814,572 cases were diagnosed in Europe, resulting in 6,875,099 instances globally. BC makes up 23% of all cancer patients and 14% of cancer-related fatalities. Asia's largest prevalence is in Pakistan, where there are around 40,000 fatalities and 90,000 afflicted females annually.¹⁻⁴

BC prognosis is influenced by various factors, such as histological type, size, tumour necrosis, lymphovascular invasion, skin, nipple and chest wall invasion, oestrogen and progesterone receptor status, human epidermal

growth factor receptor 2 (HER2), cell proliferation marker Ki-67 (ki-67) and therapy type.^{1,2} Oestrogen and progesterone receptors are the most reliable indicators of prognosis. Triple-negative BC (TNBC) accounts for 12-17% of all BCs, and is more common in African-Americans with an early manifestation.³⁻⁶

Treatment options include primary surgery, neoadjuvant chemotherapy (NACT), hormone therapy and targeted radiation. TNBC has a poor prognosis for disease-free survival (DFS) and overall survival (OS), and no effective targeted therapies are available.^{4,5} In Pakistan, to our knowledge, there is limited research to determine the demographic characteristics and frequency of TNBC.

The current standard course of action for TNBC patients is the combination of taxanes and anthracycline. To obtain a pathological complete response (pCR) in the breast and axilla, studies have been done to assess the use of platinum-based chemotherapy in combination with anthracycline and taxanes.^{7,8} However, the lack of research on increased toxicity and enhanced long-term effects limits its use. An important first step towards making platinum-based chemotherapy the norm for treating TNBC patients is to ascertain how the drug's NACT affects the patients' pCR.⁸

NACT is a potential alternative for treating TNBC, which is an aggressive type with few therapeutic choices.⁹ TNBCs

^{1,2,4-6}Department of Surgery, Dow University Hospital, Ojha, Dow University of Health Sciences, Karachi, Pakistan; ³Department of Medical Oncology, Dow University Hospital, Ojha, Dow University of Health Sciences, Karachi, Pakistan.

Correspondence: U.H. Abdul Rauf. e-mail: drhabiba290@gmail.com

ORCID ID: 0009-0006-3035-5648

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have several molecular subtypes, including claudin-low tumours, interferon-rich subgroups, and normal-breast-like subgroups. These tumours have great genetic heterogeneity, with some exhibiting no triple-negative characteristic on immunohistochemistry (IHC). Platinum-based chemotherapy, including cisplatin and carboplatin, is cytotoxic, causing deoxyribonucleic acid (DNA) damage and cell death^{8,10,11}. Homologous recombination repair (HRR) deficits are common in TNBC, which increases their susceptibility to platinum drugs. TNBC instances frequently include genetic breast cancer (BRCA) 1/2 mutations that are critical for the HRR pathway. Cells with BRCA mutations lower the ability to repair platinum-induced DNA damage, leading to higher cell mortality.¹¹⁻¹³

Incorporating platinum drugs into neoadjuvant treatment for TNBC has shown increased pCR rates, better surgical outcomes, and possible response biomarkers.^{12,13} BRCA mutations or other signs of HRR insufficiency can be used as predictive biomarkers for platinum-based therapy response, allowing treatment regimens to be tailored, and individuals are most likely to benefit from this strategy. Platinum compounds work against cancer by inducing several molecular processes, such as DNA adduct creation, DNA damage response (DDR), apoptosis and cell death, and HRR.¹⁴ Cells without DNA repair mechanisms cannot properly repair damage, which leads to apoptosis and persistent DNA lesions. Platinum-based chemotherapy increases treatment efficacy in the neoadjuvant context for TNBC by generating DNA damage and exploiting TNBC-specific deficiencies in DNA repair systems.^{14,15}

The current study was planned to evaluate the effect of platinum chemotherapy on pCR as neoadjuvant treatment for TNBC.

Patients and Methods

The retrospective, cohort study was conducted in March 2025 at the Dow University Hospital, Karachi, and comprised data from January 2021 to January 2023. After exemption from the ethics review board of the Dow University of Health Sciences (DUHS), Karachi, data was extracted from the institutional electronic medical records and it was cross-verified with physical case files to ensure accuracy and completeness. Cases were identified based on histopathology-confirmed TNBC diagnosis using IHC criteria comprising oestrogen, progesterone and HER2 receptor-negative status.¹⁶ Those included were females aged 18 years or older with histologically confirmed TNBC, presenting with either early-stage or locally advanced disease. Those excluded were patients with pregnancy, prior chemotherapy for any malignancy, metastatic (stage IV) disease at diagnosis, presence of significant

haematological, renal or hepatic disorders, abnormal cardiac function as determined by echocardiography, and incomplete medical records.

The sample was raised using non-probability consecutive sampling technique.

Patient confidentiality and data anonymity were strictly maintained through all stages of data collection, analysis and publication.

The patients were assessed for age, tumour grade, tumour-node-metastasis (TNM) staging and stage of disease.

All the patients had received NACT, with treatment regimens determined based on clinical judgment and patient preference. Two primary chemotherapy protocols were utilised. One was the standard chemotherapy regimen consisting of four cycles of anthracycline (doxorubicin) and cyclophosphamide, followed by 12 weekly cycles of paclitaxel. The other was the platinum-based chemotherapy regimen incorporating concurrent carboplatin with the standard regimen.

Surgical interventions post-NACT included either modified radical mastectomy or breast-conserving surgery (BCS) with axillary lymph node (LN) dissection, and the decisions were influenced by tumour response and patient preference.

The patients were followed retrospectively from the start of NACT until surgery and the date of final histopathology report. The primary endpoint was pCR, defined as the absence of invasive carcinoma in breast tissue and axillary LNs, as assessed by histopathological examination of the surgical specimen post-surgery.

Chemotherapy regimens were not changed during treatment based on interim response. All patients who showed either complete or partial response proceeded to surgery. The type of surgery was decided after chemotherapy based on whether the tumour was operable, its location, the size of the residual tumour in relation to breast size, and the patient's preference.

Data was analysed using Stata 17.0. Continuous variables were summarised as mean±standard deviation (SD) and median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages. Comparisons between the two treatment groups were performed using the chi-square test or Fisher's exact test. Two-sided $p < 0.05$ was considered statistically significant.

Results

Of the 50 women whose data was screened, 38(76%) met the eligibility criteria. Of them, 17(44.7%) patients were

Table-1: Tumour characteristics of patients with TNBC.

Characteristics	[n (%)] (n= 38)	Standard Chemotherapy [n (%)] (n=16)	Concurrent paclitaxel & Carboplatin [n (%)] (n=22)	p-value
Age (years)				
<50	17 (44.7)	6 (37.5)	11 (50)	0.44
>50	21 (55.2)	10 (62.5)	11 (50)	
Tumour size				
T1	3 (8)	1 (6.3)	2 (9)	0.31*
T2	18 (47.4)	10 (62.5)	8 (36.4)	
T3	8 (21)	3 (19)	5 (22.7)	
T4	9 (23.7)	2 (13)	7 (31.8)	
Tumour grade				
II	21 (55.3)	8 (50)	13 (59.1)	0.57
III	17 (44.7)	8 (50)	9 (40.9)	
Lymph node status				
N0	13 (34.2)	6 (37.5)	7 (31.8)	0.18*
N1	17 (44.7)	9 (56.2)	8 (36.4)	
N2	8 (21.1)	1 (6.3)	7 (31.8)	
Surgical outcome After Chemotherapy				
Mastectomy + AC	24 (63.2)	8 (50)	16 (72.7)	0.51*
Mastectomy + Axilla Spared	3 (7.9)	2 (12.5)	1 (4.5)	
BCS + AC	3 (7.9)	2 (12.5)	1 (4.5)	
BCS + Axilla Spared	8 (21)	4 (25)	4 (18.1)	

* Fisher's exact test applied due to small, expected cell counts; TNBC: Triple-Negative Breast Cancer, BCS: Breast Conserving Surgery, AC: Axillary Clearance.

Table-2: Pathological complete response (pCR) of the patients.

Pathological Complete Response	[n (%)] (n= 38)	Standard Chemotherapy [n (%)] (n=16)	Concurrent paclitaxel & Carboplatin [n (%)] (n=22)	p-value
Yes	12 (31.6)	4 (33.3)	8 (66.7)	0.45
No	26 (68.4)	12 (46.2)	14 (53.8)	

aged ≤50 years, 21(55.3%) were aged >50 years, 22(57.9%) received a combination of paclitaxel and carboplatin, constituting the platinum-based group, and 16(42.1%) received standard chemotherapy comprising anthracycline, cyclophosphamide and paclitaxel. The mean follow-up duration was 32.1±1.2 weeks, with a median follow-up of 32 weeks (IQR: 31-33 weeks). Demographic, clinical and surgical data of the patients was noted in detail and no statistically significant differences between the two treatment groups was found ($p>0.05$) (Table 1).

Overall, pCR was achieved in 12(31.6%) patients: 8(36.4%) in the platinum-based group and 4(25%) in the standard chemotherapy group ($p=0.45$) (Table 2).

Discussion

The present study compared the response of platinum-based NACT and standard chemotherapy on TNBC patients with respect to pCR.

Numerous studies have been conducted worldwide to evaluate such effects, but none has examined the effects

of platinum-based NACT on patients with TNBC in the local community yet.^{8,13,14}

A BC's molecular subtype influences how the treatment responds to NACT. Compared to other molecular subtypes, studies have demonstrated that both TNBC and HER2-positive BC have excellent prognoses once pCR is reached following NACT.¹⁷

The advantages of converting more TNBC patients to pCR and adding platinum-based chemotherapy to routine chemotherapy regimens in the neoadjuvant setting are still being argued for.¹⁷ This method is founded on research^{18,19} showing higher rates of pCR in TNBC patients treated with platinum-based agents.

The current study showed, in contrast, that platinum-based systemic treatment was not significantly superior in achieving pCR in the study population of TNBC patients.

Recent phase-III trials have shown that adding pembrolizumab to NACT improves pCR and event-free survival in early-stage TNBC. However, none of the current patients received immunotherapy due to financial constraints in the study settings. This difference in available treatment may partly explain the lower pCR rates observed in the cohort compared to earlier trials.²⁰

Prospective trials are recommended to assess the toxicity profile of platinum-based chemotherapy.

The current study has several limitations. It was a retrospective, single-centre study with a relatively small sample size, which may limit the generalisability of the findings. Treatment allocation was based on clinical judgment rather than randomisation, so selection bias cannot be excluded. Due to the limited sample size, only univariate analysis was performed, and multivariable regression analysis was not conducted. Follow-up was restricted to the period from NACT initiation to surgery and receipt of the final histopathology report. Post-surgical adjuvant treatments and long-term outcomes, such as recurrence or survival, were not assessed. Toxicity and quality-of-life data was also not systematically recorded. In addition, immunotherapy was not included in treatment protocols during the study period due to financial constraints, which may have influenced pCR rates.

Conclusion

The addition of platinum-based chemotherapy to the standard neoadjuvant regimen did not result in a

statistically significant increase in pCR rates among TNBC patients.

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Author Contribution:

RA: Concept, design, data acquisition, analysis, interpretation, drafting, revision and final approval.

OS & MN: Revision and final approval.

UHAR: Revision and drafting.

KM: Data acquisition and interpretation.

FGS: Final approval.