Impact of Adjuvant Capecitabine in TNBC Patients Undergoing Perioperative Pembrolizumab: A Real-World Brazilian Cohort.

Marcela de O. Sá, MD[1]; Enaldo M. Lima, MD[1]; Renata V. Guedes, MD[1]; Virgínia A. Silva MD[1]; Ianca E. Mendes, MD[1]; Caroline C. Avelar, MD[1]; Paulo H. C. Diniz, MD[1], PhD[2]
[1]Hospital Materdei; [2]Universidade Federal de Minas Gerais

Introduction

Triple-negative breast cancer (TNBC) is a heterogeneous and aggressive disease with limited effective treatment strategies. The addition of pembrolizumab to neoadjuvant chemotherapy (NACT) has reshaped standard care, as demonstrated in the KEYNOTE-522 trial. However, adjuvant capecitabine—previously shown to benefit patients with residual disease in the CREATE-X trial—was not permitted in KEYNOTE-522. This study aimed to evaluate the real-world impact of adjuvant capecitabine in TNBC patients receiving perioperative pembrolizumab in a resource-limited setting.

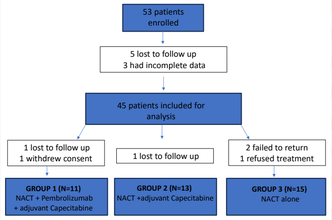


Figure 1. PRIMA diagram

Methods

We conducted a retrospective observational study using electronic medical records from a referral cancer center in Brazil. Eligible patients had non-metastatic triple-negative breast cancer (TNBC) with T≥2 cm tumors and/or axillary involvement, treated with neoadjuvant chemotherapy (NACT) between 2016 and 2024. Patients were grouped as follows: (1) NACT + pembrolizumab + adjuvant capecitabine (28.2%), (2) NACT + adjuvant capecitabine (33.3%), and (3) NACT alone (38.5%).

The primary endpoint was event-free survival (EFS), defined as the time from diagnosis to recurrence or death. Cox regression was used for multivariable analysis. Intergroup comparisons were performed using appropriate statistical tests, and the Bonferroni correction was applied to adjust for multiple comparisons and reduce the risk of false-positive findings.

Variable Comparison Analysis

Variable	Group 1 NACT + P + C (N=11)	Group 2 NACT + C (N=13)	Group 3 NACT (N=15)	p-value
Menopausal status –no.(%)				**0.620**
Premenopausal	9(81.8)	8(61.5)	10(66.7)	
Posmenopausal	2(18.2)	5(38.5)	5(33.3)	
Smoking – no.(%)				**0.585**
Yes	1(9.1)	2(15.4)	4(26.9)	
No	10(90.9)	11(84.6)	11(73.3)	
Alcohol intake – no.(%)				**1.000**
Yes	4(36.4)	5(38.5)	6(40.0)	
No	7(63.6)	8(61.5)	9(60.0)	
ECOG performance status – no.(%)				**0.103**
0-1	7(63.6)	12(92.3)	14(93.3)	
2	4(36.4)	1(7.7)	1(6.7)	
Body Mass Index – no.(%)				**0.070**
18.5-24.9	8(72.7)	4(30.7)	5(33.3)	
>25	3(27.3)	9(69.3)	10(66.7)	
Histologic type– no.(%)				**0.032**
DIC	10(90.9)	11(84.6)	15 (100)	
others	1(9.1)	2(15.4)	0(0)	
Axillary procedure –no.(%)				**0.003**
SNLB	8(88.9)	4(30.8)	13(86.7)	
Axillary Surgery	1(11.1)	9(69.2)	2(13.3)	

Table 1. Variables comparison analysis.

Results

In this cohort (n=39), the mean age was 46.6 years; 69.2% were premenopausal, and 92.3% had stage II–III disease. Invasive ductal carcinoma was the predominant histology. The most frequent regimen was dose-dense doxorubicin/cyclophosphamide followed by weekly paclitaxel and carboplatin (53.8%) regardless of treatment group. Clinical characteristics were well balanced.

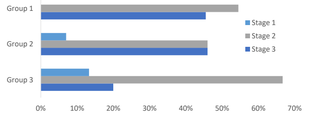


Chart 1. Clinical Stage between the three groups

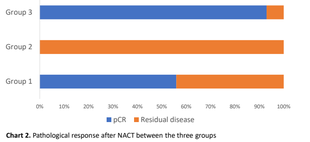


Chart 2. Pathological response after NACT between the three groups

Results

After a median follow-up of 58.6 months, pathologic complete response (pCR) was achieved in 51.4% of the cohort. Across all patients, no significant difference in EFS was observed between groups (p=0.316). However, among patients without pCR (Group 1: 44.4%, Group 2: 100%, Group 3: 6.7%) median EFS was notably higher in group 2 than group 1 (p=0.026).

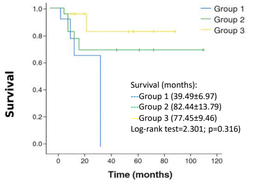


Figure 2. Overall survival curve among groups. The average survival time did not differ significantly, showing curves that overlap over time.

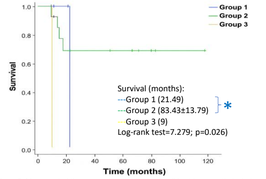


Figure 3. Mean survival time among those patients who did not have a pathological complete response.

Discussion and Conclusion

These real-world findings suggest that in TNBC patients with residual disease the benefit of perioperative immunotherapy may be mitigated by concurrent use of adjuvant capecitabine. This underscores the need for individualized post-neoadjuvant strategies, particularly in low-resource settings, where access to immunotherapy remains limited.

MaterDei Rede de Saúde

Contact
Marcela de Oliveira Sá
Rede Materdei de Saúde, Belo Horizonte, MG, Brasil
Email: marcela.osa1@gmail.com
X account: MarcelaOncology
Phone: +55 31 99634-3065

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