Neoadjuvant Chemoimmunotherapy in Early-Stage TNBC: Real-World Predictors of pCR and Survival

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SAN ANTONIO BREAST CANCER SYMPOSIUM

Abstract

Neoadjuvant chemotherapy plus pembrolizumab (NACP) has emerged as a standard-of-care approach to increase pathological complete response (pCR) rates and improve long-term outcomes in triple-negative breast cancer (TNBC). In this multicenter retrospective study, 164 patients with early-stage TNBC treated with NACP followed by surgery were evaluated using real-world data. The primary endpoint was pCR, and secondary endpoints were event free survival (EFS) and overall survival (OS). pCR was achieved in 60.4% of patients, with 18.3% experiencing recurrence and 3.0% mortality over a median follow-up of 49.2 months. In multivariable Cox analysis, weekly carboplatin scheduling, younger age, and achieving pCR were significantly associated with longer EFS. With only five deaths, the multivariable association between pCR and OS did not reach statistical significance and should be interpreted as a directional trend rather than a definitive effect. Multivariable logistic regression confirmed weekly carboplatin as an independent predictor of pCR. Exploratorily, among patients who achieved pCR and received adjuvant pembrolizumab, no EFS or OS events were observed; however, given sparse events and potential confounding by indication, this observation remains hypothesis-generating. These real-world findings underscore the importance of achieving pCR and optimizing chemotherapy scheduling—particularly weekly carboplatin—in early-stage TNBC. The incremental role of adjuvant pembrolizumab requires confirmation in prospective, adequately powered, biomarker-integrated studies.

Introduction

Neoadjuvant chemotherapy (NAC) has become an essential component of treatment in TNBC.

Achieving pathological complete response (pCR) after NAC has been associated with significantly improved event-free survival (EFS) and overall survival (OS), making pCR a surrogate marker for long-term outcomes.

Recent advances combining immunotherapy with chemotherapy have transformed the treatment landscape of TNBC by significantly improving pCR and survival outcomes. In particular, the phase 3 KEYNOTE-522 trial demonstrated that adding pembrolizumab (a PD-1 inhibitor) to platinum-based neoadjuvant chemotherapy significantly improved both pCR (64.8% vs. 51.2%) and EFS.

The primary aim of this study is to evaluate the real-world effectiveness of NACP in a large cohort of early-stage TNBC patients in Türkiye.

We present detailed analyses of pCR rates, EFS, and OS outcomes, and investigate clinicopathological predictors of pCR to inform personalized treatment strategies.

While randomized trials such as KEYNOTE-522 have established the efficacy of NACP in early-stage TNBC, real-world data—particularly from underrepresented populations—remain limited.

This study aims to fill that gap by evaluating treatment outcomes and prognostic factors in a multicenter Turkish cohort, thereby providing population-specific insights that complement existing global evidence.

Methods and Materials

This multicenter retrospective cohort study utilized real-world data from various oncology centers in Türkiye.

It included 164 patients diagnosed with early-stage TNBC between 2021 and 2025 who received NACP. Eligible patients had non-metastatic, treatment-naive TNBC with clinical staging of T1 (N1-3) or T2-4 (N0-3) based on the 8th edition of the AJCC staging system

Three different pembrolizumab-based regimens were used in the neoadjuvant phase, depending on physician preference.

The primary endpoint was pCR, defined as the absence of residual invasive or in situ carcinoma in both breast and regional lymph nodes (ypT0/Tis N0).

Univariate and multivariate Cox proportional hazards regression analyses were conducted to examine associations between variables and survival outcomes.

In post-hoc, exploratory analyses, patients were stratified by pCR (yes/no) and receipt of adjuvant pembrolizumab (yes/no). Survival comparisons were displayed with unadjusted Kaplan–Meier curves and assessed using log-rank tests.

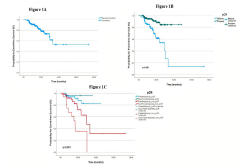


Figure 1. *(A) EFS in the overall study population; (B) EFS according to pCR status, demonstrating significantly longer EFS in patients who achieved pCR (log-rank p<0.001); (C) EFS stratified by adjuvant pembrolizumab and pathological complete response (pCR) status, showing significant differences among groups (p<0.001).*

Results

Weekly carboplatin was used in 73.8%. Anthracycline-first sequencing was observed in 61.6%. Following NACT, radiologic CR in the primary tumor and nodes occurred in 59.8% and 72.0%, respectively; the combined radiologic CR rate was 56.1%.

pCR was achieved in 60.4% of patients, with 18.3% experiencing recurrence and 3.0% mortality over a median follow-up of 49.2 months.

In the univariate analyses for EFS, the following variables were found to be statistically significant: Clinical T stage at diagnosis (p<0.001), carboplatin administration schedule (p<0.001), and pCR (p<0.001). Post-treatment radiologic response variables (exploratory) were also associated with EFS in univariable analyses. Notably, weekly carboplatin administration (median EFS not reached) was significantly associated with better EFS compared to administration every 2–3 weeks (median EFS: 19.4 months [95% CI: 15.7–23.08]; p<0.001). (Fig 1.)

In the univariate analyses for OS, ECOG PS (p=0.03), carboplatin administration schedule (p=0.043), radiological T response to treatment (p=0.003), and radiological N response (p=0.04) were found to be statistically significant. Notably, weekly carboplatin administration was associated with improved OS (median OS: 70.6 months) compared to administration every 2–3 weeks (median OS: 25.3 months) (Fig. 2).

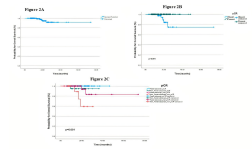


Figure 2. *(A) OS in the overall study population. Only 5 deaths (3.0%) were observed over a median follow-up of 49.2 months; (B) OS according to pCR status, demonstrating significantly better OS in patients who achieved pCR (p<0.001); (C) OS stratified by adjuvant pembrolizumab and pathological complete response (pCR) status, showing significant differences among groups (p<0.001).*

Patients were stratified into four groups based on pCR status following neoadjuvant therapy and whether they received adjuvant pembrolizumab: The most favorable EFS was observed in the pCR + adjuvant pembrolizumab group, with no events recorded (0/71, 100%), and the median EFS was not reached. Similarly, No deaths occurred in the pCR + adjuvant pembrolizumab group during the follow-up period (0/71), and the median OS was not reached (Fig. 1C and 2C)

To identify predictors of achieving pCR, a multivariate logistic regression analysis was performed. Only carboplatin dosing schedule was significantly associated with pCR (OR=0.308; 95% CI: 0.128–0.740; $p = 0.008$), with weekly dosing favoring higher pCR rates.

Discussion

Our real-world pCR rate (60.4%) is comparable to KEYNOTE-522 (64.8%), supporting translatability of NACP efficacy to routine practice(14). Furthermore, the recurrence rate of 18.3% and mortality rate of 3.0% suggest effective systemic disease control. However, the higher recurrence risk in patients who did not achieve pCR underscores the need for better-defined postoperative treatment strategies in this subgroup. The literature presents conflicting results regarding the impact of carboplatin on pCR(26-29). In contrast, our study showed that weekly carboplatin (AUC 1.5 mg/mL/min) was associated with higher pCR rates (66.7% vs. 40.0%) and improved EFS (HR = 5.137, p = 0.001). These findings support the hypothesis that lower, more frequent chemotherapy dosing may enhance antitumor immune responses without suppressing the immune system.

To identify independent predictors of pCR, a multivariate logistic regression was performed. Only the carboplatin dosing schedule remained significant, with weekly dosing increasing the likelihood of pCR. This supports the univariate findings and highlights dosing frequency as a potentially modifiable treatment factor. Traditional variables such as PD-L1 status and tumor burden (T/N stage) were not predictive after adjustment, suggesting their influence may be limited when treatment-related factors are considered. Consistent with prior evidence, pCR remains the most powerful prognostic indicator in early TNBC, strongly correlating with both EFS and OS. In our cohort, patients achieving pCR demonstrated durable survival with minimal recurrence, whereas non-pCR patients experienced early and steep declines in EFS. These findings underscore the critical role of achieving pCR as a surrogate for long-term benefit and the need to optimize systemic treatment strategies that maximize pCR rates.

Conclusions

In this multicenter real-world cohort of early-stage TNBC treated with neoadjuvant chemotherapy plus pembrolizumab, we observed a high pCR rate (60.4%) and a strong association between pCR and longer EFS, consistent with randomized evidence. Weekly carboplatin scheduling was independently linked to higher pCR and improved EFS versus 2–3-weekly dosing, suggesting that dose-density/frequency may be a modifiable lever to optimize outcomes in routine practice. Exploratory, unadjusted subgroup comparisons by pCR and adjuvant pembrolizumab suggested more favorable outcomes in pCR groups and numerically longer EFS among non-pCR patients who received adjuvant pembrolizumab, but these hypothesis-generating findings are susceptible to sparse events and potential confounding by indication.

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