Real-world efficacy of a non-anthracycline neoadjuvant chemo-immunotherapy in early-stage triple negative breast cancer: a retrospective two site cohort study

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Abstract

- Prior studies have found that cT1c TNBC patients do benefit from chemotherapy. However, the optimal treatment strategy for patients with smaller node-negative tumors who do not meet K522 eligibility criteria is not known.
- We conducted a retrospective cohort study comparing pCR rates in patients with lower risk early TNBC who received full K522 versus only the anthracycline-free arm of K522.
- We further investigated the role of the presence of Tumor Infiltrating Lymphocytes (TILs) and response to neoadjuvant chemoimmunotherapy between treatment groups, given earlier studies which have indicated their potential use as a predictive biomarker of treatment response.

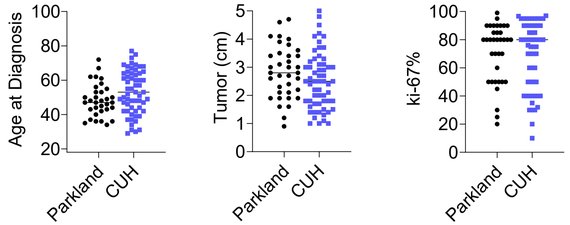
Introduction

- About $^{1}/_{3}$ of newly diagnosed cases of TNBC are stage I, which were excluded from the practice-changing Keynote-522 clinical trial[1].
- A SEER database analysis of 8,601 women with stage 1 TNBC found that patients with T1c cancers derived a significant benefit with chemotherapy, experiencing an improvement in 5 year cancer survival rate from 89.9% to 94.5%[2].
- The landmark CTNeoBC pooled analysis identified a clear association between pCR and OS in TNBC patients. A later study of 1033 T1c cancers found failure to achieve a pCR after neoadjuvant chemotherapy was associated with worse cancer specific and overall survival (HR 2.207%, 95% CI 1.431-3.405)[3,4].
- There is strong clinical interest in identifying prognostic biomarkers able to improve the ability to predict which early TNBC will benefit from chemotherapy and improve survival. There is interest in stromal tumor infiltrating lymphocytes (TILs) representing such a biomarker, with a pooled analysis of 2,148 patients finding that each 10% increase in TILs was associated with further improvements in OS[5].

Methods and Materials

- From institutional databases, we reviewed 271 cases of TNBC and identified 83 diagnosed with clinical T1-T2 N0 TNBC between June 2021 and December 2024 at two academic sites—UT Southwestern Medical Center (UTSW) and Parkland Memorial Hospital (PH).
- Imaging and pathology reports at diagnosis and at time of surgery were evaluated for all cases, as well as chemoimmunotherapy records. All cases had ER positive staining of ≤ 1%, PR staining of ≤5%, and HER2 staining of 0-2 with negative FISH results in those cases with 2+ staining.
- Presence of TILs within the tumor biopsy pathology report was considered positive, and its association with pCR was assessed. Standard statistical analyses were performed via univariate logistic regression and simple linear regression in Graphpad Prism.

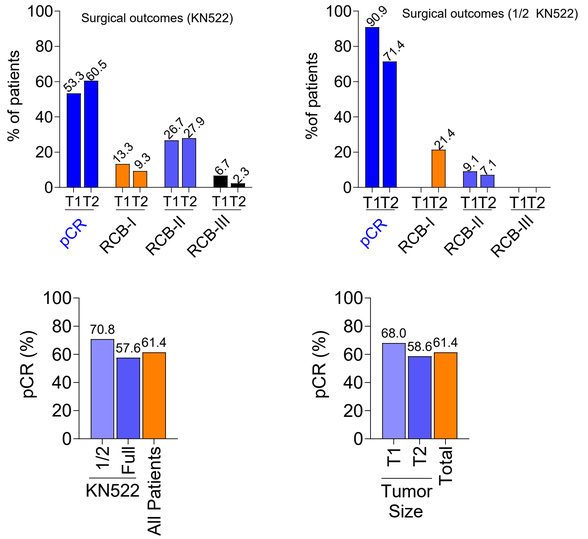
Site	#Cases	T1-T2 N0	Evaluated	#pCR
Parkland	176	47	25	16
CUH	198	101	53	35
Total	**374**	**148**	**83**	**51**



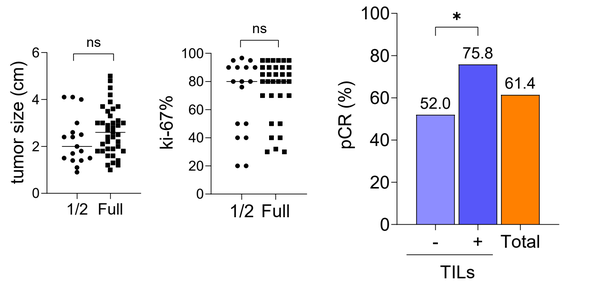
Regimen	T1	T2	Total
½	11	14	**25**
Full KN 522	15	43	**58**
	26	**57**	**83**

Results

- Among the 83 patients evaluated, 51 (61.4%) achieved a pathologic complete response. 34 (57.6%) patients who received the K522 regimen achieved pCR, while 17 (70.8%) patients who received the non-anthracycline regimen achieved a pCR (p = 0.45).
- TILs were reported in 33 patients (39.8%), of whom 25 received the entire K522 regimen (42.4% of this treatment group) and 8 received the non-anthracycline regimen (33.3% of this group). Presence of TILs was significantly associated with pCR (p = .032) with 75.8% of cases achieving pCR while only 52% achieved pCR in the negative TIL cases. This was not due to differences in grade (p=.54), tumor size (p=.98), or ki-67 (p=.34).



Characteristics of patients who achieved pCR:



Discussion

- Our findings suggest that in selected patients with early-stage TNBC (T1–T2, N0), a neoadjuvant non-anthracycline regimen combining carboplatin, paclitaxel, and pembrolizumab can achieve pCR rates comparable to the full K522 regimen.
- These results are consistent with prior prospective studies, including NeoPACT and CALGB40603, that demonstrate comparable pCR rates with platinum- and taxane-based regimens in early TNBC[6,7].
- Furthermore, TILs continue to show promise as a predictive biomarker of treatment response and may play an important role in tailoring treatment recommendations for select patients.
- The Neo-N Trial (BCT1902/IBCSG 61-20) is investigating neoadjuvant nivolumab alongside carboplatin and paclitaxel in early TNBC (cT1c-cT3N0 or cT1c-T2N1) and reported an overall pCR rate of 53%, with TILs being a significant prognostic indicator: patients with high TILs (>30%) had a pCR rate of 67% versus 46% in patients with low TILs[8].
- The SCARLET (SWOG S2212) trial is investigating outcomes in patients with early TNBC who receive KN522 versus docetaxel, carboplatin, and pembrolizumab and will help to further define the appropriate chemotherapy regimen for patients with early TNBC.

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