Evaluating the tolerability of the combination of adjuvant pembrolizumab and capecitabine in a diverse real-world cohort of patients with early-stage TNBC

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BACKGROUND

- Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer characterized by a high risk of recurrence.[1]
- The KEYNOTE-522 trial established neoadjuvant chemoimmunotherapy with pembrolizumab and carboplatin, paclitaxel, anthracycline, and cyclophosphamide as the new standard of care for early TNBC. The combination resulted in improved pathologic complete response (pCR) rates, event free survival, and overall survival compared to chemotherapy alone. All patients received adjuvant pembrolizumab for 9 cycles[2].
- Despite novel therapy, 35.2% of patients receiving chemoimmunotherapy had residual disease - a finding associated with a poorer prognosis. The CREATE-X trial previously demonstrated improved overall survival with adjuvant capecitabine in patients with residual disease after neoadjuvant chemotherapy[3] .
- KEYNOTE-522 did not incorporate CREATE-X findings into trial design, despite common usage there is a paucity of data on the tolerability of the combination of capecitabine and pembrolizumab.

OBJECTIVE

- Examine the tolerability of the adjuvant combination in a real-world, diverse, urban population at a large tertiary referral center.

METHODS

- We performed a retrospective chart review of patients diagnosed with TNBC within Mount Sinai Health system between August 2021 to February2025.
- Patient population:
  - Triple negative stage II-III breast cancer
  - Received the Keynote-522 regimen
  - Received at least 1 cycle of adjuvant pembrolizumab
- Patients were stratified based on adjuvant pembrolizumab alone compared to combination of pembrolizumab and capecitabine.
- Demographics, adjuvant toxicity data including rates of treatment delays, dose holds, and treatment discontinuations were extracted from the medical record.
- Descriptive statistics were used to describe patient data, and non-parametric tests were utilized in the stratified analyses

CONCLUSIONS

The adjuvant combination of capecitabine and pembrolizumab was well tolerated in this real-world cohort of patients with early-stage TNBC and residual disease after neoadjuvant chemoimmunotherapy.

- While treatment interruptions, dose reductions, or discontinuations occurred, these were predominantly due to known toxicities associated with each individual agent—rather than from cumulative toxicity of the combination itself.
- Overall, the combination of capecitabine and pembrolizumab warrants further study for patients with residual disease after neoadjuvant therapy per KEYNOTE-522.

RESULTS

Table 1: Tolerability of Pembrolizumab and Capecitabine

Toxicity Measure	N=30
Pembrolizumab	
Dose hold	3.3% (1)
Early discontinuation(prior to 9 cycles)	13% (4)
Capecitabine	
Dose reduction	47% (14)
Dose hold	27% (8)
Early discontinuation (prior to 6 cycles)	30% (9)

- The early discontinuation rate (prior to 9 cycles) of adjuvant pembrolizumab in the pembrolizumab cohort and combination cohort was 17% (N=9) and 13% (N=4), respectively (p=0.761). In the combination cohort, 47% (N=14) required a capecitabine dose reduction, 27%(N=8) required a dose hold, and 30% (N=9) discontinued capecitabine prior to 6 cycles.
- Pembrolizumab was discontinued most frequently due to irAEs including thyroiditis, colitis, pneumonitis and myocarditis. Capecitabine was dose reduced or held most frequently for non-hematologic reasons including hand-foot syndrome, GI toxicity, and mucositis.

RESULTS

Table 2: Patient Population and Treatment Distribution

Characteristic	N (%)
Total patients	83 (100%)
Lymph node involvement	37(45%)
Disease stage	
Stage II	69 (83%)
Stage III	14 (17%)
Adjuvant treatment	
Pembrolizumab alone	53 (64%)
Pembrolizumab + Capecitabine	30 (36%)

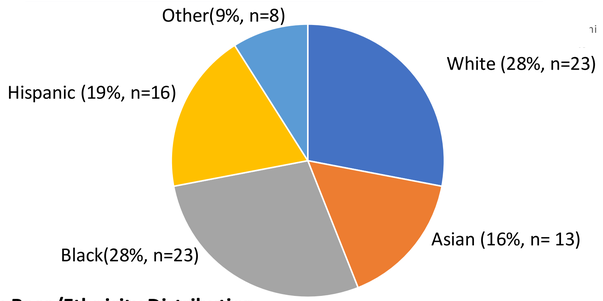


Figure 1: Race/Ethnicity Distribution

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