Safety and efficacy of neoadjuvant cyclophosphamide, methotrexate, fluorouracil (CMF) and pembrolizumab in older adults with early triple negative breast cancer (TNBC)

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BACKGROUND

- The current treatment of early-stage, locally advanced TNBC consists of neoadjuvant pembrolizumab, and a four-drug chemotherapy backbone, including paclitaxel, carboplatin, doxorubicin and cyclophosphamide, based on the KEYNOTE-522 trial.[1]
- Many older adults are unable to receive this regimen due to comorbidities or performance status that increase their risk of toxicities.[2]
- CMF is a chemotherapy regimen that is used in TNBC and safe with little long-term toxicity even in older patients.[3] However, it has not been studied in combination with pembrolizumab, which was approved for early-stage TNBC in 2021.

OBJECTIVES

- To assess the safety and efficacy of neoadjuvant CMF and pembrolizumab in patients with early TNBC who are not eligible for the KEYNOTE-522 regimen.

METHODS

- Retrospective chart review of patients with following inclusion criteria:
  - Diagnosed with clinical Stage II-III TNBC between 2021-2024 at our institution's health system
  - Treated with neoadjuvant CMF and pembrolizumab for at least 1 cycle
- Demographics, tumor characteristics and treatment information were extracted from the electronic medical record.
- Toxicity of the regimen was measured by rates of:
  - Early discontinuation of one or more drugs
  - Dose reductions and delays
  - Hospitalizations, and/or emergency department (ED) visits due to treatment-related adverse events (TRAEs)
- Efficacy of the regimen was measured by:
  - Rates of pathologic complete response (pCR), defined as the absence of invasive disease in the breast and axilla at time of definitive surgery

REFERENCES

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The combination of neoadjuvant CMF and pembrolizumab was found to be well tolerated and effective in older patients with early TNBC who were ineligible to receive the KEYNOTE-522 regimen.

- Of 10 patients, only 1 required a dose reduction in CMF due to neutropenic fever, discontinuation of pembrolizumab due to Grade 3 colitis, and hospitalization for these TRAEs. Twenty percent (N=2) had treatment delays due to Grade 2 adverse events but did not require dose reductions.
- The pCR rate with neoadjuvant CMF and pembrolizumab was 55.6% in 9 patients.
- While the findings are limited by their retrospective nature and small patient cohort, the preliminary safety and efficacy in a predominantly older population with comorbidities are promising and warrant further evaluation.
- A prospective phase II trial evaluating the combination of CMF and pembrolizumab is currently being planned.

RESULTS

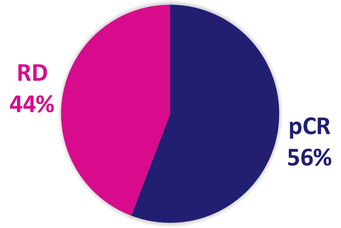
Table 2. Tolerability of Neoadjuvant CMF and Pembrolizumab

Treatment Characteristic	Overall Population (N=10)
Number of Neoadjuvant Cycles, Median	
CMF	8
Pembrolizumab	7
Dose Reductions with CMF, % (N)	10% (1)
Drug Discontinuations, % (N)	
CMF	0
Pembrolizumab	10% (1)
Treatment Delays, % (N)	20% (2)
Hospitalizations/ED Visits due to TRAEs, % (N)	10% (1)

RESULTS

Table 1. Baseline Patient Characteristics

Patient Characteristics	Overall Population (N=10)
Median Age, years (range)	81 (62-92)
Race, % (N)	
White	40% (4)
Black	40% (4)
Asian or Pacific Islander	10% (1)
Other/Unknown	10% (1)
Tumor Size, % (N)	
T1	10% (1)
T2	50% (5)
T3	20% (2)
T4	10% (1)
TX	10% (1)
Lymph Node Status, % (N)	
N0	40% (4)
N1	60% (6)
Anatomic Clinical Stage, % (N)	
Stage II	60% (6)
Stage III	40% (4)
≥ 1 Comorbidities, % (N)	60% (6)
ECOG Performance Status, Median (range)	1 (0-2)



Of the 10 patients, 1 patient has not undergone surgery yet due to comorbidities but clinically had a treatment response based on exam. Of the remaining 9 patients with surgical information available, the pCR rate was 55.6%.

Figure 1. pCR Rates with CMF and Pembrolizumab (N=9)