Analysis of Adverse Events and Outcomes of Adjuvant Therapies in TNBC as Monotherapy and Combination: Pembrolizumab, Capecitabine, and Olaparib

Rodolfo Garza-Morales[1], Farah Raheem[1], Drake Alton[2], Somanshu Sharma[2], Bruno Murad[3], Whitney Harris[4], Emma Terwilliger[2], Felipe Batalini[1]

[1]Division of Hematology and Oncology, Mayo Clinic, Phoenix, AZ, [2]Mayo Clinic Alix School of Medicine, Phoenix, AZ, [3]Faculdade de Medicina de Barbacena, MG, Brazil, [4]Department of Internal Medicine, Mayo Clinic, Phoenix, AZ.

INTRODUCTION

- Triple-Negative Breast Cancer (TNBC) is an aggressive subtype of breast cancer lacking ER, PR, and HER2 expression, accounting for ~15% of BC. It is more common in Black women, younger patients, and those with germline *BRCA1* pathogenic variants.
- For high-risk patients, adjuvant therapies include capecitabine, pembrolizumab, and/or olaparib (*BRCA* carriers).
- In KEYNOTE-522, chemoimmunotherapy improved pCR, EFS, and OS. 5-year OS was 86.6%. While pts with pCR had excellent outcomes, those with residual disease remained high risk, supporting additional therapy.
- Before pembrolizumab approval, capecitabine was SOC for TNBC with residual disease (CREATE-X; OS HR 0.52). Common AEs included HFS and fatigue. Notably, **K522 did not allow capecitabine.**
- Adjuvant olaparib was approved in 2022 for high-risk *BRCA*-related TNBC based on OlympiA which improved IDFS and OS. Grade ≥3 AE included anemia, neutropenia, and fatigue. **OlympiA did not include pembrolizumab or capecitabine.**

RATIONALE AND OBJECTIVES

While NCCN allows combined/sequential use in high-risk patients, real-world safety and outcome data are limited. This study evaluates the **safety** and **outcomes** of adjuvant capecitabine, olaparib, pembrolizumab, and their combinations (pembrolizumab and capecitabine, pembrolizumab and olaparib) in early TNBC.

©2025 Mayo Foundation for Medical Education and Research

METHODS

- Retrospective study
- All Mayo Clinic sites
- Eligible patients: ≥18 years with early-stage TNBC who started adjuvant capecitabine, pembrolizumab, olaparib, or
- combinations from Oct 2018-Sep 2024
- Patients with metastatic disease, other active malignancies, or investigational therapies were excluded

RESULTS

2201 patients were screened; 364 met eligibility criteria and were included in the final analysis **(Table 1).** The 5-year cumulative incidence of AEs in all patients was 54.9% (50.7-61.7%). There were 194 AEs among 364 patients who developed an AE. The median time to AE was 12 days (95% CI 4-66). Patients receiving combination of capecitabine and pembrolizumab experienced the highest AE rates (58/76, 76.3%), the most common AE were HFS (50.6%), diarrhea (23.4%), and stomatitis (9.1%) **(Figure 1, Table 2)**.

Both pembrolizumab and olaparib monotherapy were very well tolerated with < 50% reporting AEs; Olaparib monotherapy with AE rate 41.6% (5/12, most commonly fatigue and diarrhea 16.7% each, elevated LFTs (8.3%). Pembrolizumab-only patients had an AE rate of 27% (38/137, most common irAEs were endocrinopathy 12.7%, MSK 5.1% and colitis 4.4%).

The overall 5-year EFS was 77.5% (56/364), but EFS differed across subgroups (p=0.0068) **(Figure 2).**

TABLE 1

	Total (N=364)
Age at Adjuvant Initiation	
Median (IQR)	55.0 (46.5, 65.0)
Range	24.0, 92.0
Sex, n (%)	
Female	363 (99.7%)
Male	1 (0.3%)
Race, n (%)	
White or Caucasian	303/363 (83.5%)
Black or African American	27/363 (7.4%)
Asian American	16/363 (4.4%)
Hispanic	5/363 (1.4%)
Native American	4/363 (1.1%)
Other	8/363 (2.2%)
BMI at time of adjuvant therapy initiation	
Median (IQR)	27.9 (23.9, 33.5)
Range	16.9, 404040.4
Stage at diagnosis, n (%)	
Stage I	47/341 (13.8%)
Stage II	177/341 (51.9%)
Stage III	117/341 (34.3%)
Adjuvant agent or combination, n(%)	
Capecitabine	130 (35.7%)
Olaparib	12 (3.3%)
Pembrolizumab	137 (37.6%)
Pembrolizumab + capecitabine	77 (21.2%)
Pembrolizumab + olaparib	7 (1.9%)
Other	1 (0.3%)
Neoadjuvant chemotherapy, n(%)	364 (100%)
ECOG performance status at time of adjuvant therapy initiation, n(%)	
Grade 0	292/359 (81.3%)
Grade 1	56/359 (15.6%)
Grade 2	4/359 (1.1%)
Grade 3	1/359 (0.3%)
Grade 4	1/359 (0.3%)
Not recorded	5/359 (1.4%)

Capecitabine alone had the lowest 5-year EFS rate (69.9%), reflecting a higher-risk pts w/o pCR. Pembrolizumab alone and in combination showed very low event rates.

RESULTS

FIGURE 1

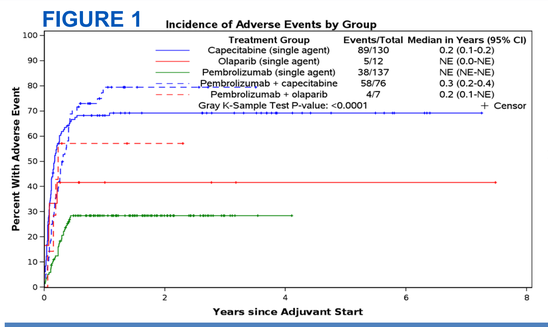


FIGURE 2

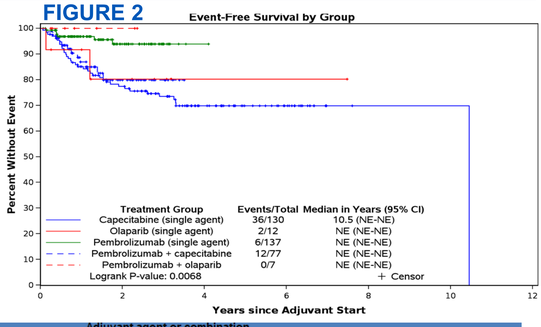


TABLE 2

	Adjuvant agent or combination				
	Capecitabine (single agent) (N=130)	Olaparib (single agent) (N=12)	Pembrolizumab (single agent) (N=137)	Pembrolizumab + capecitabine (N=76)	Pembrolizumab + olaparib (N=7)
Diarrhea, n (%)	29 (22.3%)	2 (16.7%)	6 (4.4%)	18 (23.4%)	0 (0.0%)
Colitis, n (%)	0 (0.0%)	0 (0.0%)	6 (4.4%)	4 (5.2%)	0 (0.0%)
Stomatitis, n (%)	4 (3.1%)	0 (0.0%)	1 (0.7%)	7 (9.1%)	1 (14.3%)
Elevated LFTs (grade 3 or higher), n (%)	0 (0.0%)	1 (8.3%)	3 (2.2%)	1 (1.3%)	1 (14.3%)
Immunotherapy related hepatitis,n (%)	0 (0.0%)	0 (0.0%)	4 (2.9%)	4 (5.2%)	1 (14.3%)
Bilirubin elevation, n (%)	3 (2.3%)	0 (0.0%)	1 (0.7%)	2 (2.6%)	0 (0.0%)
Dermatologic toxicity, n (%)	12 (9.2%)	0 (0.0%)	1 (0.7%)	7 (9.1%)	1 (14.3%)
Hand foot skin syndrome from capecitabine, n (%)	71 (54.6%)	0 (0.0%)	0 (0.0%)	39 (50.6%)	0 (0.0%)
Neutropenia (grade 4), n (%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (1.3%)	0 (0.0%)
Thrombocytopenia (grade 3), n(%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	1 (1.3%)	0 (0.0%)
Anemia (grade 3), n (%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (14.3%)
Fatigue (grade 3 or higher), n (%)	5 (3.8%)	2 (16.7%)	2 (1.5%)	5 (6.5%)	2 (28.6%)
ILD/pneumonitis, n (%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
Cardiovascular adverse events, n(%)	1 (0.8%)	0 (0.0%)	1 (0.7%)	3 (3.9%)	0 (0.0%)
Endocrinopathy from pembrolizumab, n (%)	0 (0.0%)	0 (0.0%)	17 (12.4%)	8 (10.4%)	0 (0.0%)
Ocular adverse events, n (%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	0 (0.0%)
MSK, n (%)	0 (0.0%)	0 (0.0%)	7 (5.1%)	2 (2.6%)	1 (14.3%)
Neurologic event, n (%)	0 (0.0%)	0 (0.0%)	3 (2.2%)	1 (1.3%)	0 (0.0%)
Renal adverse events, n (%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other side effect, n (%)	12 (9.2%)	2 (16.7%)	2 (1.5%)	4 (5.2%)	0 (0.0%)

CONCLUSIONS

- In this real-world cohort of 364 patients with early TNBC treated with adjuvant capecitabine, olaparib, pembrolizumab or their combinations, AE occurred in 54.9% of pts.
- Among all the treatment options, AE rates were lowest with pembrolizumab (27%) and olaparib (41%), higher with capecitabine (68%), olaparib+pembro (57%), and highest with capecitabine+pembro (76.3%).
- These data provide real world evidence on the safety profile of adjuvant therapies for early TNBC. Larger sample size and longer follow up will be needed to refine comparative safety and efficacy.

Schmid et al. NEJM 2020;382;810-821, Masuda et al. NEJM 2017; 376:2147-2159, Tutt et al. NEJM 2021; 384:2394-2405

"Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without person from SABCS and the author"