POLY (ADP-RIBOSE) POLYMERASE INHIBITOR (PARPI) THERAPY: RETROSPECTIVE ANALYSIS OF ADVERSE EVENTS AND TREATMENT MODIFICATIONS DURING THE FIRST 90 DAYS OF THERAPY

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BACKGROUND

Poly (ADP-ribose) polymerase inhibitor (PARPi) therapy is used to treat various cancers, but patients often encounter frequent and challenging adverse events (AEs) in the first several months after initiating therapy that may lead to treatment modifications.

OBJECTIVES

PRIMARY	Identify the type and frequency of AEs and the corresponding rate of treatment modifications (holds, dose reductions, discontinuations) related to AEs in patients initiating PARPi therapy
SECONDARY	Measure adherence to PARPi therapy

METHODS

DESIGN	Single-center retrospective cohort analysis. Patients were followed for 90 days from medication initiation.
INCLUSION	Patients initiating olaparib, rucaparib, niraparib or talazoparib therapy for an FDA-approved indication from November 2017 through October 2019.
EXCLUSION	Clinical trial participation

RESULTS

TABLE 1. COHORT CHARACTERISTICS (N=28)

	n (%)
Age, years-median (IQR)	62 (53-72)
Gender, female	27 (96)
Race	
White	23 (82)
Black or African American	4 (14)
Asian	1 (4)
Body mass index-median (IQR)	30 (25-35)
Insurance	
Commercial	13 (46)
Medicare	12 (43)
Medicaid	1 (4)
Tricare	1 (4)
None	1 (4)
Disease duration, years-median (IQR)	1.8 (1.4-3.6)
Total previous chemotherapies	
1	5 (18)
2	12 (43)
3	4 (14)
4	4 (14)
5	1 (4)
6	2 (7)

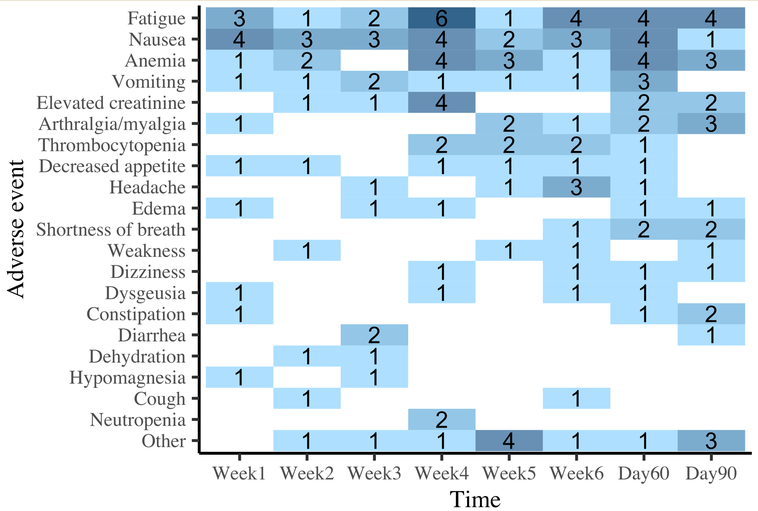
IQR = interquartile range

Table 2. MEDICATION BY CANCER TYPE (N=28)

	olaparib % (n) N=25	rucaparib % (n) N=2	talazoparib % (n) N=1
Cancer Type			
Breast cancer	8 (2)	--	100 (1)
Ovarian cancer	84 (21)	100 (2)	--
* 1st line maintenance tx, BRCA+	29 (6)	--	--
* Maintenance tx, recurrent	57 (12)	--	--
* Tx refractory, BRCA+	14 (3)	100 (2)	--
Pancreatic cancer	4 (1)	--	--
Prostate cancer	4 (1)	--	--

* % based on N=21 for olaparib and N=2 for rucaparib

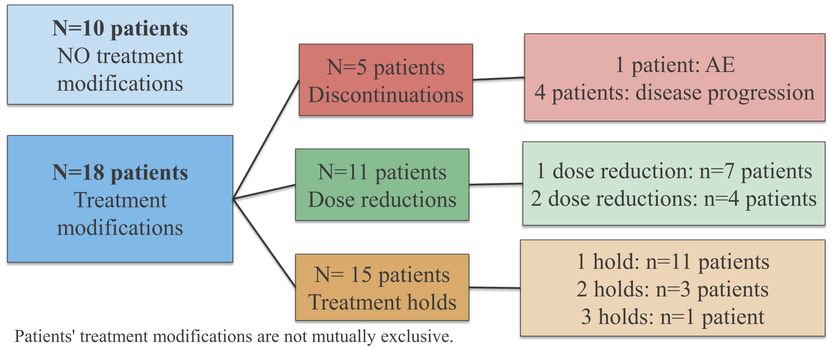
FIGURE 1. FREQUENCY OF ADVERSE EVENTS



- Most common AEs reported were fatigue, nausea, anemia and vomiting, which occurred throughout the first 90 days
- All patients experienced at least one AE during the first 90 days

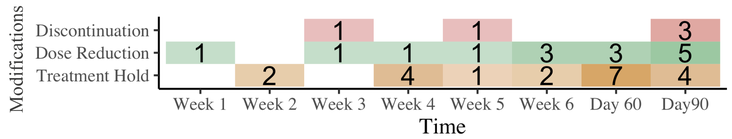
RESULTS

FIGURE 2. TREATMENT MODIFICATION



Patients' treatment modifications are not mutually exclusive.

FIGURE 3. FREQUENCY OF TREATMENT MODIFICATION



- Treatment modifications commonly occurred between week 6 and day 90 of therapy

FIGURE 4. TIME TO DISCONTINUATION

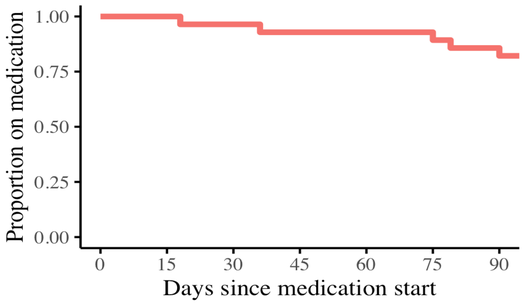


TABLE 3. ADHERENCE (N=24)

PDC	97% (IQR 92-100)
Hold Adjusted PDC	100% (IQR 96-100)

PDC = proportion of days covered

Hold adjusted PDC: removed medically-advised treatment hold days from PDC denominator

Four records were excluded from PDC analysis (filled externally).

- High patient-level adherence (≥ 97%-) was seen in patients that remained on therapy, despite treatment modifications

CONCLUSIONS

- In patients initiating PARPi therapy, rates of AE were similar to previous literature.[1]
- Though treatment modifications were common in the first 90 days of therapy, patients achieved high medication adherence rates.
- The subsequent prospective phase will evaluate the integrated specialty pharmacist role in AE mitigation including patient education & providing supportive therapy.

1. LaFargue CJ, Dal Molin GZ, Sood AK, Coleman RL. Exploring and comparing adverse events between PARP inhibitors. Lancet Oncol. 2019 Jan;20(1):e15-e28. doi: 10.1016/S1470-2045(18)30786-1. PMID: 30614472; PMCID: PMC7292736. This study was supported by AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, who are codeveloping olaparib.