Abstract 122: Olaparib in patients with colorectal cancer with *ATM* mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

D Behl[1], M Rothe[2], PK Mangat[2], E Garrett-Mayer[2], LC Farrington[3], OV Crysler[4], EG Dib[5], HL Duvivier[6], MJ Hall[7], JS Salmon[8], OB Alese[9], AS Marr[10], I Ngirailemesang[11], L Polavaram[12], R Thota[13], ES Yang[14], GN Grantham[2], A Gregory[2], S Halabi[15], RL Schilsky[2]

[1]Sutter Sacramento Medical Center, Sacramento, CA; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Cancer Treatment Centers of America - Chicago, part of the City of Hope, Zion, IL; [4]University of Michigan Rogel Comprehensive Cancer Center, Ann Arbor, MI; [5]Michigan Cancer Research Consortium, Ypsilanti, MI; [6]Cancer Treatment Centers of America - Atlanta, part of City of Hope, Newnan, GA; [7]Fox Chase Cancer Center, Philadelphia, PA; [8]Levine Cancer Institute, Atrium Health, Charlotte NC; [9]Winship Cancer Institute of Emory University, Atlanta, GA; [10]University of Nebraska Medical Center, Omaha, NE; [11]Providence Cancer Institute, Portland, OR; [12]Cancer Research Consortium of West Michigan, Grand Rapids, MI; [13]Intermountain Healthcare, Murray, UT; [14]Department of Radiation Oncology, O'Neal Comprehensive Cancer Center at the University of Alabama at Birmingham School of Medicine, Birmingham, AL; [15]Duke University Medical Center, Durham, NC

Background:

- TAPUR is a phase II basket study that evaluates antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- **Results of a cohort of pts with colorectal cancer (CRC) with *ATM* mutation (mut) treated with olaparib (O) are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced CRC, no standard treatment (tx) options, ECOG performance status (PS) 0-2, adequate organ function, measurable disease. Tx assigned according to pre-specified matching rules based on genomic tests selected by sites. 17/30 pts had an FMI test performed on tissue.
- Dosing was O orally twice daily for total daily dose of 600 mg (tablets, n=20) or 800 mg (capsules, n=10), depending on formulation provided, until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) defined as objective response (OR) or stable disease (SD) of at least 16+ weeks (wks) duration per RECIST v1.1.
- **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, duration of SD, and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to O are reported.

Statistical Methods:

- Simon's optimal two-stage design used to test null hypothesis of 15% DC rate vs. alternative of 35%. Power = 85%; 1-sided α = 10%.
- At least 7 of 28 pts must achieve DC to reject null hypothesis and consider tx worthy of further study.

Results:

- 30 pts were enrolled between September 2016 to August 2019. 2 pts were not evaluable for efficacy (1 pt left study early due to an unrelated grade 3 SAE and 1 pt chose to discontinue participation in the study); 1 pt was found ineligible after receiving 1 dose.
- **Demographics**: Median age 59.5 y (range 32-84); 53% female; 25 pts (83%) self-identified as White, 3 pts (10%) as Black/African American, 1 pt (3%) as Asian/Asian American and 1 (3%) as Other; 26 pts (87%) as not Hispanic or Latino, 3 pts (10%) self-identified as Hispanic or Latino and 1 pt (3%) preferred not to answer.

Conclusion: Olaparib does not show antitumor activity in this population of heavily pre-treated patients with colorectal cancer with *ATM* mutations.

Future Direction: Other treatments should be considered for these patients, including treatments offered in clinical trials.

- **Clinical characteristics:** 40% PS 0, 57% PS 1, 3% PS 2; 83% received ≥3 prior systemic regimens.
- **Alterations:** All pts had *ATM* mut, but germline vs. somatic status was not reported. 6/30 pts had a *BRCA2* co-alteration, no pts had a *BRCA1* co-alteration.
- **Outcomes**: 1 pt had PR and 3 pts had SD16+ for a DC rate of 23% (95% CI: 6, 39) (Table 1, Table 2 and Figure 1). The null hypothesis was not rejected (p=0.38). Time on tx among pts with PR or SD16+ is shown in Figure 2.
- **Safety:** 7 pts (23%) had ≥1 SAE or grade 3 AE at least possibly related to O, including: urinary tract infection, white blood cell decreased, febrile neutropenia (SAE), anemia (1 SAE), lung infection (SAE), fatigue (SAE), and nausea (SAE).

Table 1. Tumor Sidedness and Mut of Pts With PR or SD16+ (n=4)

Response	Tumor Sidedness	*ATM* Mut and HRR co-mut
PR	Right	*ATM* P938fs*11; *RAD50* V89I[a]
SD16+	Not specified	*ATM* E522*
SD16+	Left	*ATM* R1875*; *ATR* R433H[a]
SD16+	Right	*ATM* splice site 4237-11_4241del16

[a] Variant of unknown significance

Funding supported by AstraZeneca and Merck Sharp & Dohme Corp. The authors would like to acknowledge the patients who participated in this cohort, the clinical centers and staff, as well as Josefa Briceno, MD, clinical lead of AstraZeneca, and Eric Rubin, MD, clinical lead of Merck Sharp & Dohme Corp, both of which are TAPUR supporting pharmaceutical companies.

Contact: TAPURPublications@asco.org

Table 2: Efficacy Outcomes (n=27)

DC rate, % (95% CI)	23 (6, 39), p=0.38
OR rate, % (95% CI)	4 (0.1, 19)
Median PFS, wks (95% CI)	8 (8, 16)
Median OS, wks (95% CI)	34 (22, 50)
Duration of PR, wks (n=1)	19
Duration of SD in pts with SD16+, wks (n=3)	20, 21, 27

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=27)

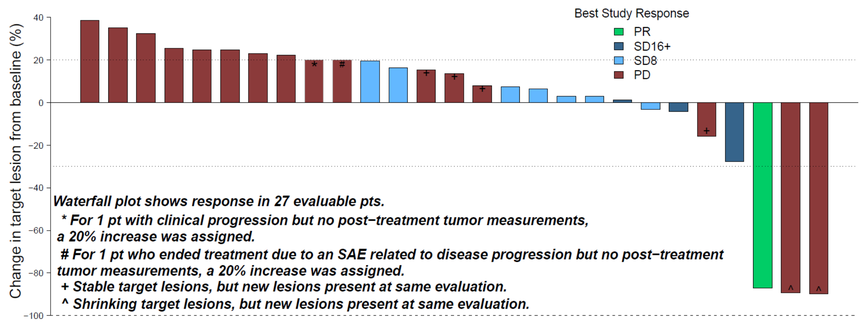

Figure 2: Time on Tx in Pts with PR or SD16+ (n=4)