Olaparib in Patients with Solid Tumors with *ATM* mutations or deletion: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Abstract #: CT110

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Background

- The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results of a cohort of pts with solid tumors with *ATM* mutations (mut) or deletion (del) treated with olaparib (O) are reported.

Methods

Study Design:

- **Eligible pts**: Advanced solid tumors, no standard treatment (tx) options, ECOG PS 0-2, adequate organ function, and measurable disease. Tx was assigned according to pre-specified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.
- Pts received O orally twice daily for a total daily dose of 600 mg (tablets) or 800 mg (capsules) until disease progression, unacceptable toxicity, or pt preference.
- **Primary endpoint**: Disease control (DC) defined as objective response (OR) or stable disease of at least 16 weeks (wks) duration (SD16+) per RECIST v1.1. **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to O are reported.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.

Statistical Methods:

- For histology-pooled cohorts with sample size >28, inferences are based on an exact 90% confidence interval (CI). If the lower limit of a one-sided 90% CI is >15%, the null hypothesis of a DC rate of 15% is rejected. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- 39 pts with *ATM* mut (n=36) or del (n=3) were enrolled from June 2016 to January 2019. 2 pts were not evaluable due to lack of post-baseline tumor evaluation or absence of target lesions and excluded from efficacy analysis. Baseline demographics and clinical characteristics are shown in Table 1.

Table 1: Baseline Characteristics (N=39)

Characteristic		N (%)
Median Age	Years (range)	65 (35, 77)
Sex	Female	18 (46)
Race	White	33 (85)
	Black/African American	5 (13)
	Asian/Asian American	1 (3)
ECOG Performance Status	0	13 (33)
	1	23 (59)
	2	3 (8)
Prior systemic regimens	0	1 (3)
	1	3 (8)
	2	6 (15)
	≥3	29 (74)
Primary Tumor Origin	Prostate	6 (15)
	Breast	5 (13)
	Bladder	4 (10)
	Uterine	4 (10)
	Gallbladder and bile ducts	4 (10)
	Esophagus	2 (5)
	Head and Neck	2 (5)
	Liver	2 (5)
	Melanoma	2 (5)
	Brain[a]	1 (3)
	Small intestine	1 (3)
	Kidney	1 (3)
	Stomach	1 (3)
	Malignant neoplasm[b]	1 (3)
	Peritoneum	1 (3)
	Urothelial carcinoma	1 (3)
	Malignant carcinoid tumor[b]	1 (3)

[a] Pt was eligible at time of enrollment
[b] Site unspecified

Clinical Outcomes:

- 1 pt had CR (prostate; duration of CR was 24.4 wks; *ATM* mut, *BRCA1* M1775R co-mut, ≥3 prior therapies).
- 2 pts had PR (peritoneum and malignant neoplasm without specification of site; duration of PR was 4.3 and 18.9 wks, respectively; both *ATM* mut).
- 7 pts had SD16+ [brain, breast, prostate, uterine, bladder, liver, gallbladder and bile ducts; median duration of SD was 28.0 wks (range, 19.4 to 40.7 wks), all *ATM* mut, all had ≥3 prior therapies] (Figure 1).
- DC and OR were observed in 10 (27%) and 3 (8%) pts, respectively (Table 2) all with *ATM* mut. The 90% CI for the DC rate excludes 15% so the null DC rate was rejected. Time on tx among pts with SD16+ and OR is shown in Figure 2. Median PFS and OS are reported in Table 2 and Figure 3.
- 9 pts (23%) experienced ≥1 Grade 3 AE or SAE at least possibly related to O including, anemia, anorexia, colitis (SAE), dehydration, dizziness (SAE), fatigue, hypokalemia, lung infection (SAE), nausea, proteinuria (SAE), urinary tract infection (SAE), urinary tract obstruction (SAE).

Table 2: Efficacy Outcomes (N=37)

DC rate, % (1-sided 90% CI)	27 (18, 100)
OR rate, % (95% CI)	8 (2, 22)
Median PFS, wks (95% CI)	8.6 (8.0, 16.0)
Median OS, wks (95% CI)	40.9 (30.3, 52.4)

Conclusions

Olaparib monotherapy showed evidence of anti-tumor activity in patients with various solid tumors with *ATM* mutation. Additional study is warranted to confirm the efficacy of olaparib in this patient population.

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Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=33)

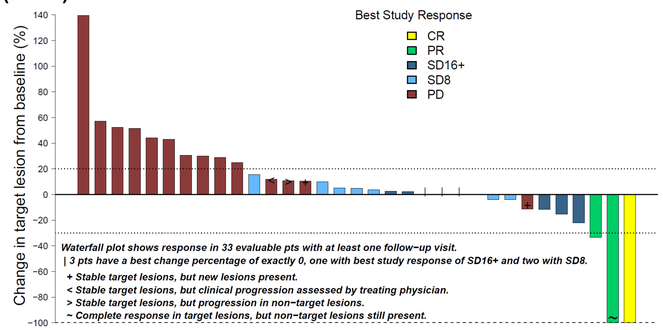

Figure 2: Time on Tx in Pts with SD16+ or OR (N=10)

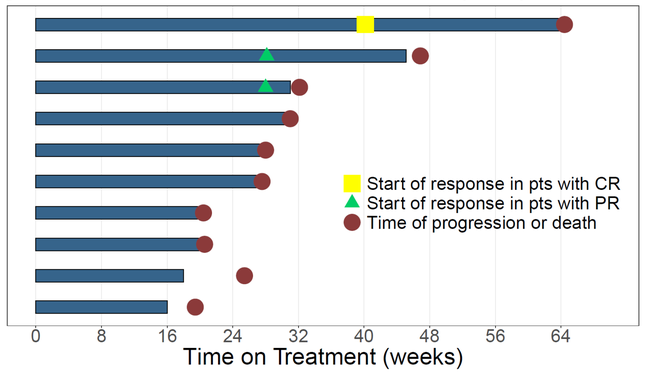

Figure 3: OS and PFS in Pts with Solid Tumors with *ATM* mut or del Treated with O (N=37)