Talazoparib in patients with solid tumors with *ATM* alterations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

ASCO TAPUR Targeted Agent and Profiling Utilization Registry Study

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Abstract #: CT228

Background

- The TAPUR Study is a phase II basket study that evaluates the antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- ATM plays a critical role in DNA damage repair, and evidence suggests that PARP inhibitors may be effective in tumors with ATM dysfunction [1-2].
- Results in a cohort of pts with solid tumors with *ATM* mutation (mut) or deletion (del) treated with the oral PARP inhibitor, talazoparib (Tala), are reported.

Methods

Study Design:

- **Eligible pts:** Advanced solid tumors, Eastern Cooperative Oncology Group performance status (ECOG PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options available. Tx was assigned according to prespecified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.
- Pts received 1 mg of Tala orally daily, until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) determined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16 weeks (wks) duration (SD16+) per RECIST v1.1. Radiographic confirmation of response was not required.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response (DOR), duration of SD are reported. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) per CTCAE v4.0 at least possibly related to tx are reported.
- DOR is defined as time from pt's first documented OR to progressive disease (PD). Duration of SD is defined as time from tx start to PD.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.
- For most patients, the genomic test performed did not distinguish between germline and somatic mutations; therefore, germline status is not reported unless explicitly identified on test reports.

Statistical Methods:

- Inferences are based on a one-sided exact binomial test with a null hypothesis of DC rate ≤15%; power and alpha were 82% and 0.10, respectively. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- 29 pts with *ATM* mut (n=28) or del (n=1) were enrolled from June 2020 to July 2023.
- Baseline demographics and clinical characteristics are summarized in **Table 1.**
- 1 pt was not evaluable for efficacy; pt withdrew consent prior to any follow-up visits.
- 2 pts had PR (**Table 2**). 1 pt with PR and thyroid cancer had a DOR of 38 wks. 1 pt with PR and NSCLC is still on tx and has exceeded 88 wks on study as of February 2025.
- 10 pts had SD16+ (**Table 2**). Median duration of SD was 29 wks (range, 23-64) for pts with SD16+.
- The DC rate was 41% (1-sided 90% CI, 29% to 100%); the null DC rate was rejected (p=0.0005). The OR rate was 7% (95% CI, 1 to 23; **Table 3**).

Safety:

- 8 pts (28%) experienced 4 tx-related grade 3-4 AEs. All events were consistent with the drug label. No SAEs were reported.

Table 1. Baseline Characteristics (N=29)

Characteristic		No. (%)[a]
Median Age	Years (range)	65 (31-81)
Sex	Female	10 (35)
Race	Asian/Asian American	2 (7)
	Black/African American	3 (10)
	White	23 (79)
	Prefer not to answer	1 (3)
Ethnicity	Not Hispanic or Latino	27 (93)
	Prefer not to answer	2 (7)
ECOG Performance Status	0	10 (35)
	1	17 (59)
	2	2 (7)
Prior systemic regimens	1-2	11 (38)
	≥3	18 (62)
Primary Tumor Origin	Pancreas	9 (31)
	Breast	4 (14)
	NSCLC	4 (14)
	Stomach	3 (10)
	Kidney, RCC	2 (7)
	Prostate	2 (7)
	Thyroid	2 (7)
	Colon	1 (3)
	Peritoneum	1 (3)
	Rectum	1 (3)

[a] Percentages may not sum to 100% due to rounding.

Table 2. Tumor Origin and Alteration in Pts with DC (n=12)

Pt	Response	Tumor Origin	*ATM* Alteration	Co-alterations[a]
A	PR	NSCLC	pQ127*[b]	--
B	PR	Thyroid	L186*[b], D639_Q684del[c]	--
C	SD16+	Prostate[d]	splice site 1066-2A>G	--
D	SD16+	Thyroid	K3016*[b]	--
E	SD16+	Breast	V1841fs*7[b]	*BRCA2* K3326*[c]
F	SD16+	RCC	splice site 4236+1G>A[e], R2719C[c], I2752F[c], F2799fs[b], H1082L[c], R3008H[b]	--
G	SD16+	Pancreas	R2993*[bf]	--
H	SD16+	Pancreas	D1237fs[b]	--
I	SD16+	Pancreas	W1933*[b]	--
J	SD16+	Stomach	splice site SNV, C2488Y[c], A1089P[c]	--
K	SD16+	Colon	R3047*[b]	*BRCA2* I3224T[c]
L	SD16+	Rectum	T2113fs*7[b]	--

Abbreviation: NSCLC, non-small cell lung cancer; PR, partial response; RCC, renal cell carcinoma
[a] The following comutations were examined: *BRCA1, BRCA2, FANCA, PALB2, RAD51D, ARID1A, ATR, ATRX, BARD1, CDK12, CHEK1, CHEK2, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MLH1, MRE11, NBN, BRIP1, RAD51, RAD51B, RAD54L.*
[b] Alteration is likely loss of function and oncogenic
[c] Variant of unknown significance
[d] PD-L1 negative
[e] Suspected germline
[f] Germline
Note: Unless otherwise noted all *ATM* alterations were somatic or status not reported.

Table 3. Efficacy Outcomes (n=28)

DC rate, % (1-sided, 90% CI), p-value	41 (29, 100), p=0.0005
OR rate, % (95% CI)	7 (1, 23)
Median PFS, wks (95% CI)	16 (8, 24)
Median OS, wks (95% CI)	63 (22, 88)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=28)

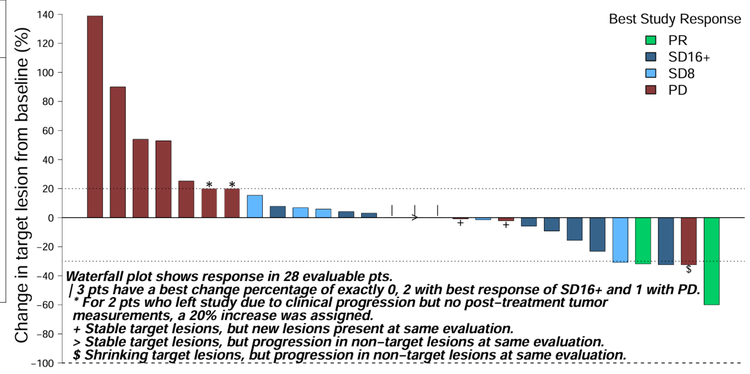
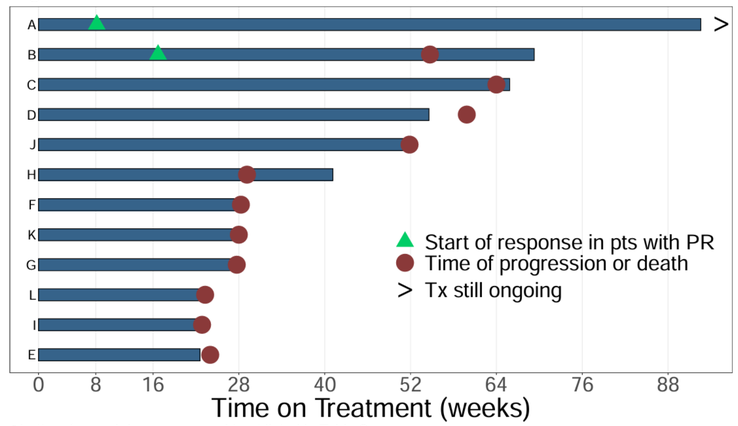
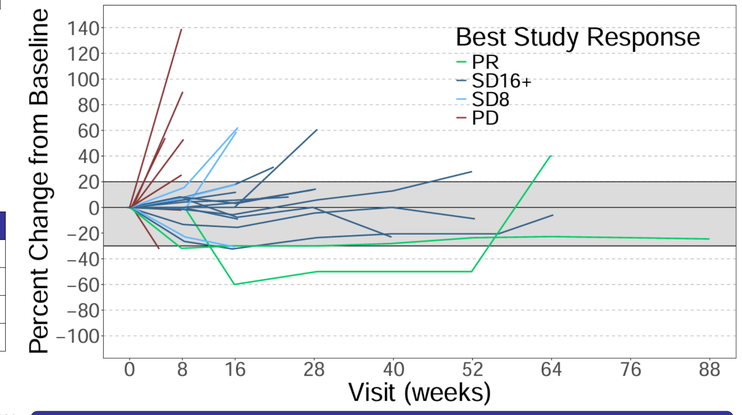


Figure 2: Time on Tx in Pts with SD16+ or OR (n=12)[a]



[a] Letters for each bar correspond to pt listed in Table 2.

Figure 3: Percent Change from Baseline of Tumor Burden During Tx of Tala in Pts with Advanced Solid Tumors with *ATM* Alterations (n=28)



Conclusions

Talazoparib met prespecified criteria to declare clinical activity in patients with solid tumors with *ATM* mutation or deletion. Additional study is warranted to confirm the efficacy of talazoparib in this patient population.

Acknowledgements and References

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1. Mateo J, Porta N, Bianchini D, et al. Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. *Lancet Oncol*. 2020;21(1):162.
2. Bang YJ, Im SA, Lee KW, et al. Randomized, double-blind phase II trial with prospective classification by ATM protein level to evaluate the efficacy and tolerability of olaparib plus paclitaxel in patients with recurrent or metastatic gastric cancer. *Journal of Clinical Oncology*. 2015;33(33):3858-3865