Abstract 3115: Talazoparib in Patients with Solid Tumors with *BRCA1/2* Mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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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 various solid tumors with *BRCA1/2* mutations (mut) treated with talazoparib (Tala) are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced solid tumors, ECOG performance status (PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options. 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 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. Confirmation of response was not required.
- **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, duration of SD, and toxicity per CTCAE v4.0. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to tx are reported.

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:

- 28 pts enrolled from December 2019 to September 2021. All pts were evaluable and included in efficacy analysis.
- **Demographics**: Median age 66 (range, 32-80); 50% female; 93% self-identified as White, 4% as Black/African American, 4% as prefer not to answer; 93% as not Hispanic or Latino, and 7% preferred not to answer.
- **Clinical characteristics:** 96% PS 0-1, 4% PS 2; 61% received ≥3 prior systemic regimens. Primary tumor type (# pt): NSCLC (5), breast (3), pancreas (2), uterus (2), anus (1), biliary tract (1), cervix (1), cholangiocarcinoma (1), esophagus (1), GE junction (1), HCC (1), leiomyosarcoma (1), melanoma (1), mesothelioma/peritoneal (1), non-melanoma skin (1), ovary (1), prostate (1), SCLC (1), stomach (1), vagina (1).
- **Outcomes**: 16 pts had CR (1), PR (9), or SD16+ (6) for a DC rate of 57% (90% CI: 43 to 100) (**Tables 1 and 2**). The null DC rate of 15% was rejected (p<0.001).
- **Safety:** 13 pts (46%) had ≥1 SAE or grade 3 AE at least possibly related to Tala. All were consistent with the drug label except bilirubin increase and hyponatremia (both grade 3 AEs).

Conclusion: Talazoparib demonstrated antitumor activity in patients with advanced solid tumors and *BRCA1/2* mutations.

Future Direction: Additional study is warranted to confirm the efficacy of talazoparib in pts with non-breast/ovarian solid tumors with *BRCA1/2* mutations.

Table 1. Tumor Type and Mut of Pts Meeting Response Criteria (n=16)

Response	Primary Tumor	Mut	Comutations[a]
CR	Non-melanoma skin*	*BRCA2*	*ATM* A188T[b]
PR	Ovary	*BRCA2*	--
PR	Pancreas	*BRCA1, BRCA2*	*MLH1* Gin391Arg[b]
PR	Breast	*BRCA1*	--
PR	HCC*	*BRCA1*	*ATM* K2383I[b]; *MRE11A* R572* and I548T[b]
PR	Mesothelioma, peritoneal*	*BRCA2*	--
PR	Stomach*	*BRCA2*	*CHEK1* T476I[b]; *CHEK2* R474H[b]; *PALB2* E426K[b]
PR	Uterus*	*BRCA2*	--
PR	Breast	*BRCA2*	--
PR	NSCLC*	*BRCA2*	*ARID1A* P570T[b]
SD16+	Prostate	*BRCA2*	--
SD16+	Cervix*	*BRCA2*	--
SD16+	NSCLC*	*BRCA1*	*CHEK2* R117G
SD16+	Uterus*	*BRCA2*	*ARID1A* Q1519fs and Q2037fs; *ATM* R2580S[b]
SD16+	Esophagus*	*BRCA1*	*ATR* V66M[b]
SD16+	Leiomyosarcoma*	*BRCA2*	*ATRX* D1525fs; *NBN* G136V[b]

[a] Of the following genes examined: *ARID1A, ATM, ATR, ATRX, BARD1, BRIP1, CHEK1, CHEK2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, MLH1, MRE11A, NBN, PALB2, RAD51, RAD51B, RAD51D, RAD54L.*
[b] Variant of unknown significance. **No PARP inhibitor is currently FDA approved for this tumor type*

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Table 2: Efficacy Outcomes (N=28)

DC rate, % (90% CI)	57 (43, 100); **p<0.001**
OR rate, % (95% CI)	36 (19, 56)
Median PFS, wks (95% CI)	24 (8, 39)
Median OS, wks (95% CI)	71 (32, inf)
Duration of CR, wks (n=1)	93
Median duration of PR (range), wks (n=9)	20 (11, 80)
Median duration of SD in pts with SD16+, wks (n=6)	36 (19, 108)

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

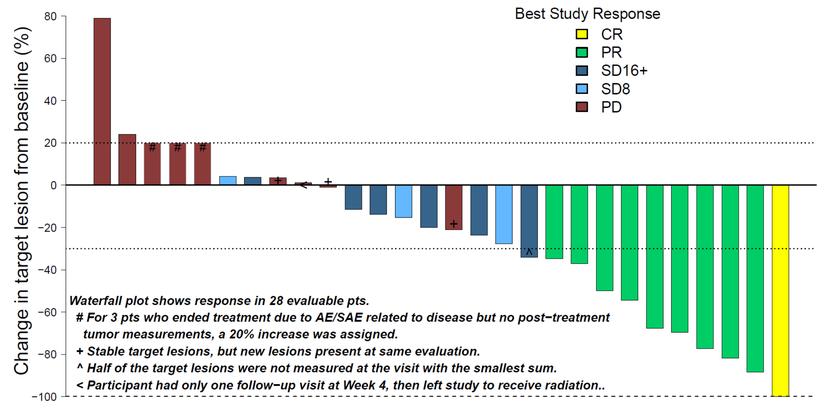

Figure 2: Time on Tx in Pts with OR or SD16+ (n=16)