FPN 98P: Olaparib in patients with solid tumors with *BRCA1/2* mutation: 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 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 *BRCA1/2* mutations (mut) 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, measurable disease. Tx assigned according to pre-specified matching rules based on genomic tests selected by sites (22/32 pts had an FMI test).
- Recommended dosing was O orally twice daily for total daily dose of 600 mg (tablets) or 800 mg (capsules) until disease progression, unacceptable toxicity or pt choice to discontinue.
- **Primary endpoint:** Disease control (DC) defined as objective response (OR) or stable disease (SD) at 16+ (SD16+) weeks (wks) per RECIST v1.1. Confirmation of response not required. **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 AEs (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:

- 32 pts enrolled July 2016 to December 2018. 13 pts (41%) had *BRCA1* mut; 19 (59%) had *BRCA2* mut. All 32 pts were evaluable for efficacy and safety analyses.
- **Demographics:** Median age 65 y (range 34-89); 72% male; 81% White, 13% Black or African American, 3% Asian/Asian American; 90% non-Hispanic or Latino.
- **Clinical characteristics:** 41% ECOG PS 0, 38% PS 1, 22% PS 2; 50% received ≥3 prior systemic regimens.
- **Outcomes:** 2 pts (6%) achieved CR, 6 pts (19%) PR, 5 pts (16%) SD16+ for a DC rate of 41% (one-sided 90% CI, 29% to 100%) (Table 1, Table 2 and Figure 1). The null DC rate was rejected. Time on O among pts with OR or SD16+ is shown in Figure 2.
- **Safety:** 12 pts (38%) had ≥1 SAE or Grade 3-4 AE at least possibly related to O including anemia (SAE and Grade 3 AE), dyspnea, fatigue (SAE), fever (SAE), generalized muscle weakness, lymphocyte decrease, platelet count decrease (SAE and Grade 3 AE), tumor lysis syndrome (SAE), white blood cell decrease.

(Presenting Author) S. Powell: Advisory Board (institution): Bristol Myers Squibb; Invited Speaker (institution): Alkermes; Local PI (institution): Actuate, AstraZeneca, Bristol Myers Squibb, Genentech, Incyte, Merck, Pfizer, Seattle Genetics, Sorrento, Vyriad.

Conclusion: Olaparib shows anti-tumor activity in heavily pre-treated patients with solid tumors with *BRCA1/2* mutation.

Future Direction: Additional study is warranted to confirm the efficacy of olaparib in this patient population.

Table 1. Tumor Origin and Mut of Pts With OR or SD16+ (N=13)

Response	Primary Tumor Origin	Mut
CR	Sweat gland	*BRCA1* Q1756fs
CR	Stomach	*BRCA2* loss exons 1-12
PR	Stomach	*BRCA1* E908*
PR	Ureter	*BRCA2* W2626C
PR	Sarcoma	*BRCA2* E1493fs*10
PR	Esophagus	*BRCA1* rearrangement intron 21 and *BRCA2* I505T (VUS[a])
PR	Duodenum	*BRCA2* T1067fs*10
PR	Neuroendocrine	*BRCA2* Q893*
SD16+	Fibrous tumor of lung	*BRCA2* deleted, *BRCA1* H1457R (VUS[a]), *BRCA1* LR6VC (VUS[a])
SD16+	Colon	*BRCA2* exon 23 T3033fs
SD16+	Skin	*BRCA2* 12675fs* and S353fs*14
SD16+	Colon	*BRCA2* K2370fs*6
SD16+	Stomach	*BRCA1* c.3756_3759delGTCT

[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.

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Table 2: Efficacy Outcomes (N=32)

DC rate, % (one-sided 90% CI)	41 (29, 100)
OR rate, % (95% CI)	25 (11, 43)
Median PFS, wks (95% CI)	15.7 (8.3, 27.3)
Median OS, wks (95% CI)	45.0 (17.7, 81.4)
Duration of CR, wks (N=2)	24.3 and 84.1
Median duration of PR (range), wks (N=6)	16.0 (8.1, 24.7)
Median duration of SD (range), wks (N=5)	28.1 (26.1, 79.3)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=32)

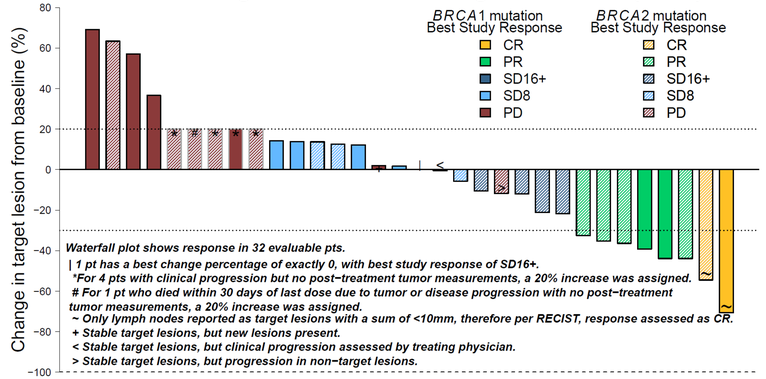

Figure 2: Time on Tx in Pts with OR or SD16+ (N=13)