

# 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	<i>BRCA1</i> Q1756fs
CR	Stomach	<i>BRCA2</i> loss exons 1-12
PR	Stomach	<i>BRCA1</i> E908*
PR	Ureter	<i>BRCA2</i> W2626C
PR	Sarcoma	<i>BRCA2</i> E1493fs*10
PR	Esophagus	<i>BRCA1</i> rearrangement intron 21 and <i>BRCA2</i> I505T (VUS <sup>a</sup> )
PR	Duodenum	<i>BRCA2</i> T1067fs*10
PR	Neuroendocrine	<i>BRCA2</i> Q893*
SD16+	Fibrous tumor of lung	<i>BRCA2</i> deleted, <i>BRCA1</i> H1457R (VUS <sup>a</sup> ), <i>BRCA1</i> LR6VC (VUS <sup>a</sup> )
SD16+	Colon	<i>BRCA2</i> exon 23 T3033fs
SD16+	Skin	<i>BRCA2</i> 12675fs* and S353fs*14
SD16+	Colon	<i>BRCA2</i> K2370fs*6
SD16+	Stomach	<i>BRCA1</i> c.3756_3759delGTCT

<sup>a</sup> Variant of unknown significance

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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)

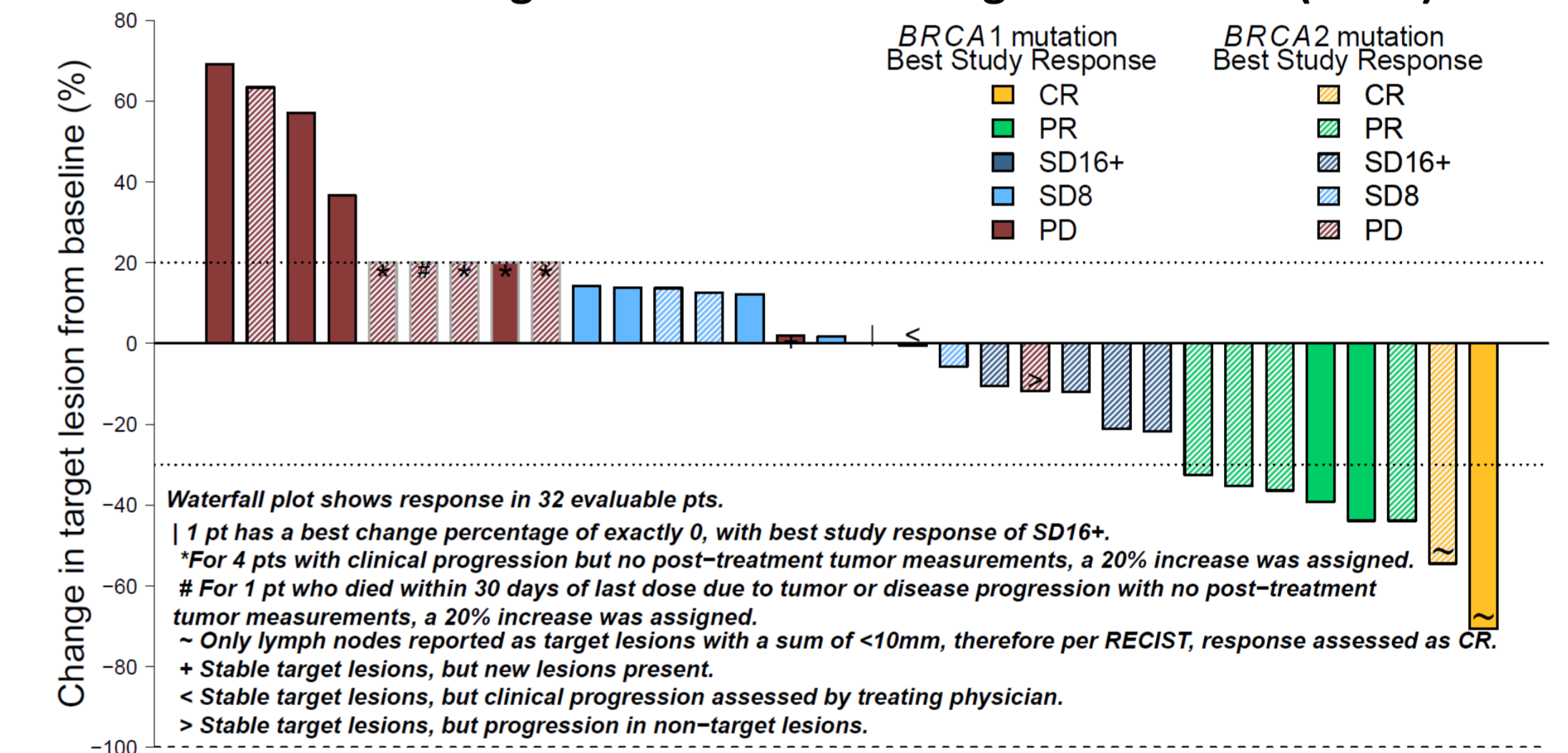


Figure 2: Time on Tx in Pts with OR or SD16+ (N=13)

