FPN 207P: Palbociclib in patients with solid tumors with *CDK4* or *CDK6* amplifications: 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 the antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- **Results of two cohorts of pts with solid tumors with *CDK4* amplification (amp) or *CDK6* amp treated with palbociclib (P) 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 prespecified matching rules based on genomic tests performed in CLIA-certified, CAP-accredited labs selected by clinical sites. Amp cut-offs were defined per test providers.
- Pts received P at 125 mg orally once daily for 21 days followed by 7 days off, 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.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response (DOR), duration of SD, and toxicity per CTCAE v 4.0. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to P are reported.
- Low accruing histology-specific cohorts with the same genomic alteration and tx were collapsed into two histology-pooled cohorts for these analyses. The *CDK6* cohort collapsed with 15 pts and was closed for futility. The *CDK4* cohort reached 29 pts but was separated for analysis into the cohort analyzed here and a histology-specific cohort that will be presented separately. Both cohorts were reviewed for approval and release of data.

Statistical Methods:

- Inferences are based on a 1-sided exact binomial test with a null hypothesis of DC rate of 15%. Alpha was set to 10% for each cohort; power was 65% for the *CDK4* cohort and 58% for the *CDK6* cohort. Two-sided 95% confidence intervals (CI) are used for other parameter estimates.

Results:

- Pts with solid tumors with *CDK4* amp (n=16) or *CDK6* amp (n=15) were enrolled between June 2016 and January 2020. Pt demographics and clinical characteristics are summarized in **Table 1**.
- **Outcomes:** 1 pt from each cohort was not evaluable for efficacy. 2 pts with *CDK4* amp had SD16+ for a DC rate of 13% (p=0.72); 1 pt with *CDK6* amp and pancreatic cancer had an 8-wk long PR for a DC rate of 7% (p=0.90) (**Table 2**). The null DC rate was not rejected for either cohort. The duration of SD for the 2 pts with SD16+ were 28 (ovarian cancer) and 52 (adrenal cancer) wks. 1 pt with PD in the *CDK4* cohort had both *CDK4* and *CDK6* amp.
- **Safety:** 6 of 31 pts (19%) across both cohorts had ≥1 SAE or grade 3 AE of neutropenia or thrombocytopenia at least possibly related to tx.

(First and Presenting Author) MF Khalil: No conflicts of interest to declare.

Conclusion: Palbociclib did not declare antitumor activity in patients with non-sarcoma solid tumors with *CDK4* or *CDK6* amplifications.

Table 1. Clinical Characteristics (N=31)

Characteristic		*CDK4* Cohort, n=16 No. (%)	*CDK6* Cohort, n=15 No. (%)
Median Age	Years (range)	61 (32-77)	64 (45-74)
Sex	Female	9 (56)	9 (60)
Race	Asian/Asian American	1 (6)	--
	Black/African American	3 (19)	2 (13)
	White	12 (75)	12 (80)
	Other	--	1 (7)
Ethnicity	Hispanic or Latino	--	2 (13)
	Not Hispanic or Latino	16 (100)	12 (80)
	Prefer not to answer	--	1 (7)
ECOG PS	0	3 (19)	4 (27)
	1	10 (63)	10 (67)
	2	3 (19)	1 (7)
Prior Systemic Regimens	0	1 (6)	--
	1	1 (6)	2 (13)
	2	3 (19)	4 (27)
	≥3	11 (69)	9 (60)
Primary Tumor Type	Adrenal	1 (6)	--
	Ampulla of Vater	1 (6)	--
	Chordoma	1 (6)	--
	Colorectal	--	3 (20)
	Esophagus	1 (6)	3 (20)
	Gallbladder	1 (6)	4 (27)
	Non-Small Cell Lung	4 (25)	--
	Ovarian	1 (6)	--
	Pancreatic	1 (6)	4 (27)
	Prostate	2 (13)	--
	Small Intestine	--	1 (7)
	Uterine	3 (19)	--

Table 2: Efficacy Outcomes (n=29)

	CDK4 Cohort (n=15)	*CDK6* Cohort (n=14)
DC rate, % (1-sided 90% CI) (p-value)	13 (3, 100) (p=0.72)	7 (0.7, 100) (p=0.90)
OR rate, % (95% CI)	0 (0, 21)	7 (<1, 34)
Median PFS, wks (95% CI)	8 (8, 12)	8 (5, 8)
Median OS, wks (95% CI)	36 (11, 71)	14 (7, 26)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=29)

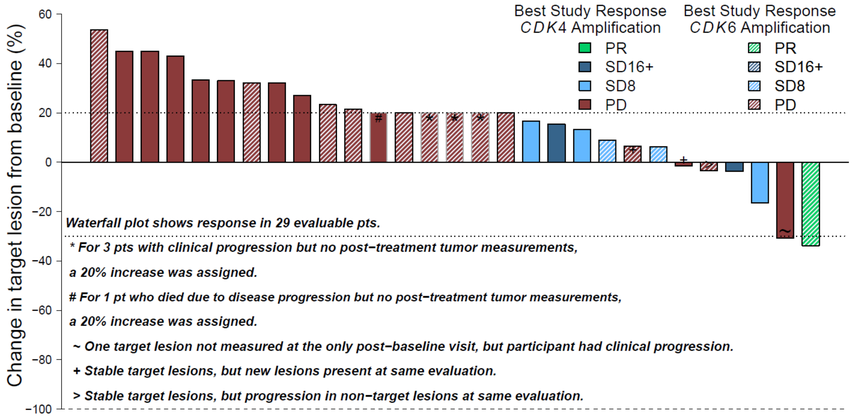
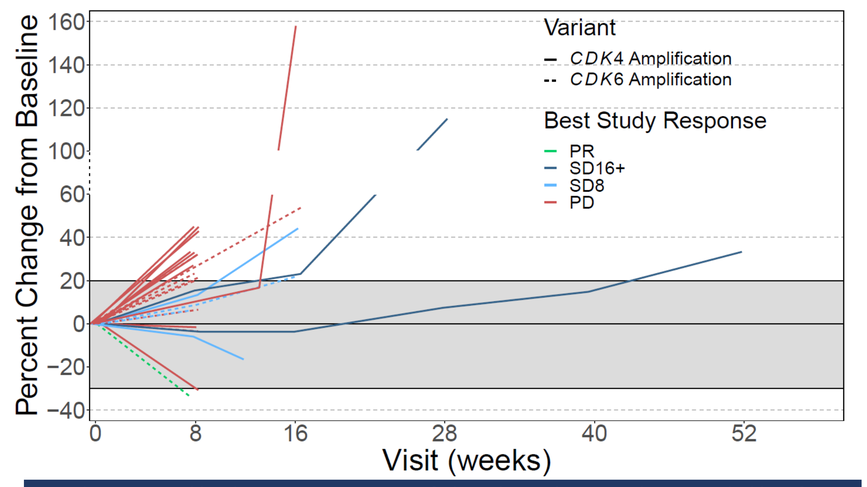


Figure 2: Percent Change in Tumor Burden Over Time (n=29)



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