Palbociclib in patients with solid tumors with *CCND1* amplification or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Abstract #: CT268

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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.
- Results in a cohort of pts with solid tumors with *CCND1* amplification (amp) or mutation (mut) treated with palbociclib (P) 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 matching rules based on genomic tests performed in CLIA-certified, CAP-accredited labs selected by 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) defined 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 v. 4.0 at least possibly related to tx are reported.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.

Statistical Methods:

- Inferences are based on a one-sided 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

- 38 pts with *CCND1* amp (n=36), *CCND1* rearrangement (n=1), or both (n=1) were enrolled from April 2016 to November 2019. Baseline demographics and clinical characteristics are shown in **Table 1**.

Outcomes:

- Two pts left the study before the 8-wk post-baseline tumor evaluation and were unevaluable for efficacy.
- One pt had CR, one pt had PR and four pts had SD16+ (**Table 2**).
- The pt with CR had a DOR of 191 wks. The pt with PR had a DOR of 9 wks. Median duration of SD was 33 wks (range, 28-49) for the pts with SD16+.
- DC rate was 17% (1-sided 90% CI, 9%-100%); the null DC rate was not rejected. OR rate was 6% (**Table 3**).

Safety:

- 14 pts (37%) experienced 8 tx-related grade 3-4 AEs or SAEs. All were consistent with drug label except hyponatremia, lymphopenia, and leukopenia.

Table 1. Baseline Characteristics (N=38)

Characteristic		No. (%)[a]
Median Age	Years (range)	66 (38-83)
Sex	Female	15 (40)
Race	Black/African American	4 (11)
	Native Hawaiian/Pacific Islander	1 (3)
	White	32 (84)
	Prefer not to answer	1 (3)
Ethnicity	Hispanic or Latino	1 (3)
	Not Hispanic or Latino	36 (95)
	Prefer not to answer	1 (3)
ECOG PS	0	9 (24)
	1	23 (61)
	2	6 (16)
Prior systemic regimens	1-2	14 (37)
	≥3	24 (63)
Primary Tumor Origin	HNSCC	7 (18)
	Melanoma	5 (13)
	Endometrium	4 (11)
	Esophagus	4 (11)
	Prostate	4 (11)
	Anus	2 (5)
	Colon	2 (5)
	Gallbladder	2 (5)
	Bile duct	1 (3)
	Bladder	1 (3)
	Fallopian tube	1 (3)
	Ovary	1 (3)
	Renal pelvis	1 (3)
	Small intestine	1 (3)
	Stomach	1 (3)
	Ureter	1 (3)

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

Table 2. Tumor Origin and Alterations in Pts with OR or SD16+ (n=6)

Response	Tumor Origin	*CCND1* Alteration	Comutations[a]
CR	Melanoma	*CCND1* amp	*PTEN* Y155fs
PR	Melanoma	*CCND1* amp, rearrangement[b]	*AURKA* amp
SD16+	Bile duct	*CCND1* amp	*TP53* R196Q
SD16+	Bladder	*CCND1* amp	*ARID1A* G414* *ATM* A1089S[b] *ERBB2* amp, L755S, R103Q[b] *FGFR2* G793A[b] *MTOR* S2120Y[b]
SD16+	Prostate	*CCND1* amp	--
SD16+	Prostate	*CCND1* amp	--

[a] Comutations in the following genes were examined: *AKT1, AKT2, AKT3, ARID1A, ATM, AURKA, CCNE1, CDK4, CDK6, CDKN2A, ERBB2, ESR1, FAT1, FGFR1, FGFR2, KRAS, MTOR, PIK3CA, PTEN, RB1, TP53*
[b] Variant of unknown significance

Table 3. Efficacy Outcomes (n=36)

DC rate, % (1-sided 90% CI)	17 (9, 100)
OR rate, % (95% CI)	6 (<1, 19)
Median PFS, wks (95% CI)	8 (6, 8)
Median OS, wks (95% CI)	20 (15, 31)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=36)

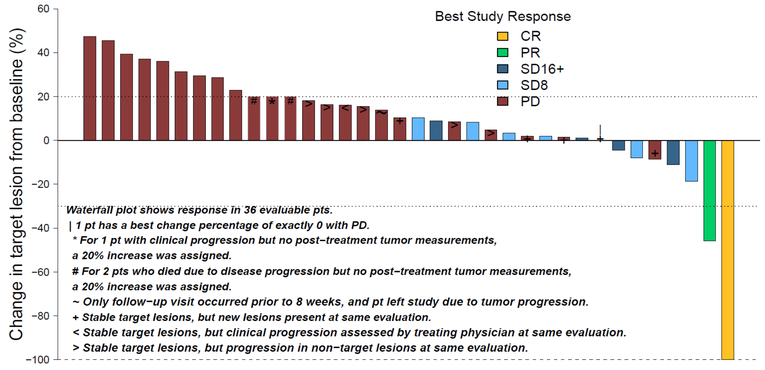


Figure 2: Time on Tx in Pts with SD16+ or OR (n=6)

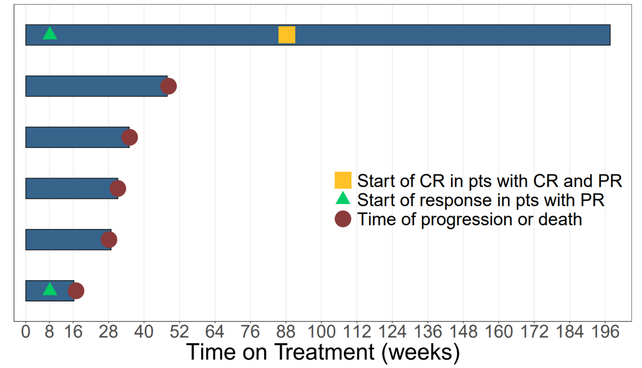
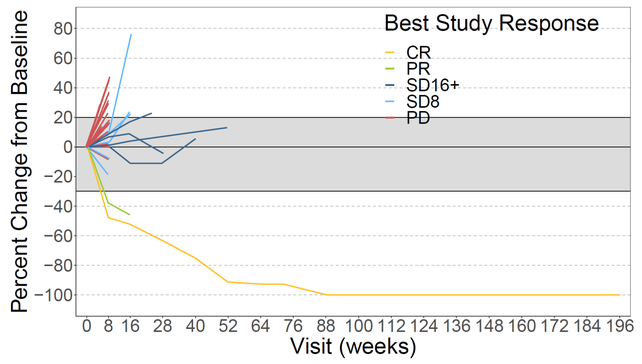


Figure 3: Percent Change from Baseline of Tumor Burden During Tx of P in Pts with Advanced Solid Tumors with *CCND1* Amp or Mut (n=36)



Conclusions

P did not show evidence of antitumor activity in pts with solid tumors with *CCND1* alterations. Other tx should be considered for these pts, including tx offered in clinical trials.

Acknowledgements

Funding provided by Pfizer. The authors would like to thank the patients who participated in this cohort, the clinical centers and staff, as well as Betty "B" Thompson of Pfizer, a TAPUR supporting pharmaceutical company.

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