Palbociclib in Patients with Non-Small Cell Lung Cancer (NSCLC) with *CDKN2A* Alterations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Background

- The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results of a cohort of NSCLC pts with *CDKN2A* loss or mutation treated with palbociclib (P) are reported.

Methods

Study Design:

- Eligible pts had advanced NSCLC without standard treatment options, PS 0-2, adequate organ function and measurable disease. Treatment 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 P at 125 mg orally once daily for 21 days, followed by 7 days off until disease progression. Tumor evaluations were performed at 8 and 16 weeks (wks) after treatment initiation.
- Primary endpoint is disease control (DC) defined as objective response (OR) or stable disease (SD) at 16+ wks per RECIST v1.1. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and toxicity per CTCAE. Grades 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to drug are reported.

Statistical methods:

- Simon's optimal two stage design was used to test the null hypothesis of 15% DC rate versus the alternative of 35%. Power and one-sided type I error rate were set at 85% and 10%, respectively.
- Design requires 10 pts in stage I and if ≥2 pts have DC, the cohort is expanded to stage II with 28 pts. If ≥7 of 28 pts have DC, the drug is considered worthy of further study.

Results

- 29 pts were enrolled between January 2017 and June 2018. One pt was unevaluable for response due to brain metastases requiring immediate radiation. Pt ended study treatment 5 days after treatment initiation, and is included in safety analyses.
- Baseline demographics and clinical characteristics are shown in Table 1.

Table 1: Demographics and Baseline Characteristics (N=29)

Characteristic	N (%)
Median Age, years (range)	63 (41,79)
Sex	
Male	15 (52%)
Race	
White	26 (90%)
Black	3 (10%)
ECOG Performance Status	
0	5 (17%)
1	19 (66%)
2	5 (17%)
Prior systemic regimens	
0	1 (3%)
1-2	8 (28%)
≥3	20 (69%)
Genomic Test Performed	
FoundationOne	19 (66%)
Caris MiProfile	5 (17%)
Guardant Health	3 (10%)
In house laboratory	1 (3%)
Other	1 (3%)

Table 2: Clinical Outcomes of NSCLC Pts with *CDKN2A* Alterations treated with P (N=28)

Clinical Outcomes	
DC rate (OR or SD 16+wks) N (%), [90% CI]	7 (29%), [15%, 37%]
mPFS, wks, (95% CI)	7.9 (7.0, 15.1)
mOS, wks, (95% CI)	20.6 (14.0, 39.0)

Clinical Outcomes

- DC was observed in 29% pts (Table 2). OR rate (CR+PR) was 3.6%. Median PFS (mPFS) and mOS reported in Table 2 and shown in Figure 1.
- Figure 2 shows % change from baseline in target lesions.
- Time on treatment among pts with response is shown in Figure 3.
- Safety was consistent with product label for P (Table 3).

Table 3: SAE/AEs at least possibly related to P experienced by 11 Pts

Grade	SAE	AEs
3	N	white blood cell decrease, lymphocyte count decrease, anorexia, anemia, fatigue, hypophosphatemia, neutrophil count decrease, platelet count decrease
3	Y	vomiting, white blood cell decrease, neutrophil count decrease, anemia
4	Y	sepsis, neutrophil count decrease, platelet count decrease, febrile neutropenia

Figure 1: OS and PFS in Advanced NSCLC Pts with *CDKN2A* Alterations treated with P (N=28)

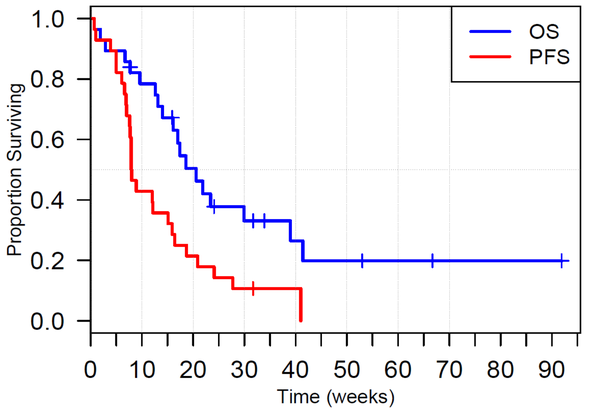


Figure 2: Best percent change from baseline in target lesion size (N=28)

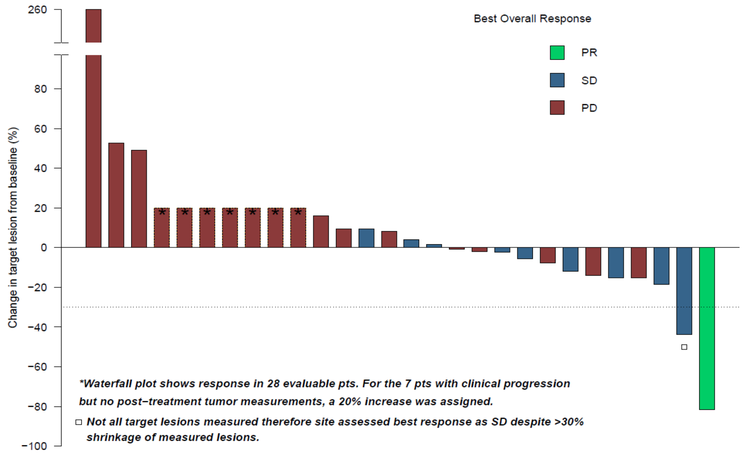
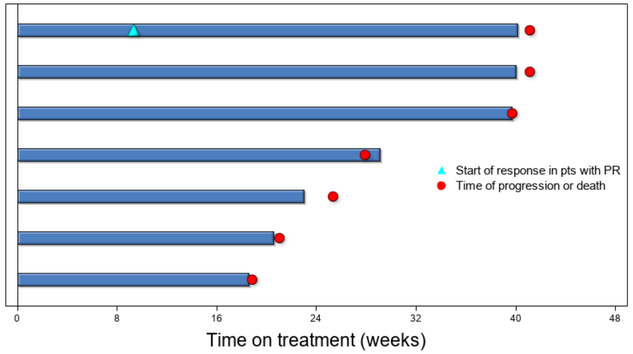


Figure 3: Time on treatment in pts with SD or objective response (N=7)



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Conclusions

Monotherapy with P demonstrated evidence of anti-tumor activity in heavily pre-treated NSCLC pts with *CDKN2A* loss or mutation. Additional study is warranted to confirm the efficacy of P in pts with NSCLC with *CDKN2A* loss or mutation.