Palbociclib in Participants with Pancreatic Cancer and Gallbladder or Bile Duct Cancer with *CDKN2A* Alterations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Tareq Al Baghdadi[1], Susan Halabi[2], Elizabeth Garrett-Mayer[3], Pam K. Mangat[3], Eugene R. Ahn[4], Vaibhav Sahai[5], Ricardo H. Alvarez[6], Edward S. Kim[7], Kathleen J. Yost[8], Kuo Guo[3], Andrew Lawrence Rygiel[3], Kaitlyn R. Antonelli[3], Nicole L. Butler[3], Suanna S. Bruinooge[3], Richard L. Schilsky[3]

[1.] Michigan Cancer Research Consortium, Ypsilanti, MI, USA; [2.] Duke University Medical Center, Durham, NC, USA; [3.] American Society of Clinical Oncology, Alexandria VA, USA; [4.] Cancer Treatment Centers of America, Chicago, IL, USA; [5.] University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [6.] Cancer Treatment Centers of America, Newnan, GA, USA; [7.] Carolinas HealthCare System's Levine Cancer Institute, Charlotte, NC, USA; [8.] Cancer Research Consortium of West Michigan, Grand Rapids, MI, USA

Background

- The TAPUR Study is a phase II multi-basket study designed to identify signals of anti-tumor activity of commercially available targeted agents used in patients (Pts) with advanced cancers that harbor genomic alterations known to be drug targets.
- In this report, data for two cohorts of Pts with 1) pancreatic and 2) gallbladder or bile duct cancers with *CDKN2A* loss or mutation treated with palbociclib are reported.

Methods

Study Design:

- Pts meeting protocol inclusion and exclusion criteria are assigned treatment according to pre-specified protocol matching rules based on genomic testing performed using commercially available tests selected by clinical sites.
- Eligible pts in this analysis had advanced pancreatic or gallbladder/bile duct cancer with CDK2NA loss or mutation.
- Pts received standard doses of palbociclib (P) (125 mg orally daily for 21 days, followed by 7 days off treatment to complete a 28 day cycle) until disease progression. Tumor evaluations were performed at weeks 8 and 16 after treatment initiation.
- Primary endpoint is objective response (OR) at or before 16 weeks (wks) 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.

Statistical methods:

- Simon's optimal two stage design was used to test the null hypothesis of 15% response rate versus the alternative of 35%.
- Power and alpha were set at 85% and 10%, respectively.
- Design requires 10 pts in stage 1 and if <2 pts have OR or SD at 16 wks, the cohort is closed.

Table 1: Demographics and Baseline Characteristics

Characteristic	Palbociclib targeting *CDKN2A*, N (%)	
Tumor Type	Pancreatic Cancer (N=12)	Gallbladder or Bile Duct Cancer (N=10)
Age, years Median (range)	62 (52-70)	63 (54-81)
Sex		
Male	8 (67%)	5 (50%)
Female	4 (33%)	5 (50%)
Race		
White	10 (84%)	8 (80%)
African-American	1 (8%)	1 (10%)
Other	1 (8%)	1 (10%)
ECOG Performance Status		
0	3 (25%)	1 (10%)
1	8 (67%)	6 (60%)
2	1 (8%)	3 (30%)
Prior Treatments		
#Pts with radiation therapy	2 (17%)	2 (20%)
#Pts prior systemic therapies		
1	0 (0%)	2 (20%)
2	6 (50%)	2 (20%)
3	6 (50%)	6 (60%)
Genomic Test Performed		
FoundationOne	9 (75%)	9 (90%)
Caris MIProfile	0 (0%)	0 (0%)
Guardant 360	0 (0%)	0 (0%)
Other	3 (25%)	1 (10%)
#Pts with additional genomic alterations reported		
0	5 (42%)	4 (40%)
1	5 (42%)	4 (40%)
2	1 (8%)	1 (10%)
3	1 (8%)	1 (10%)

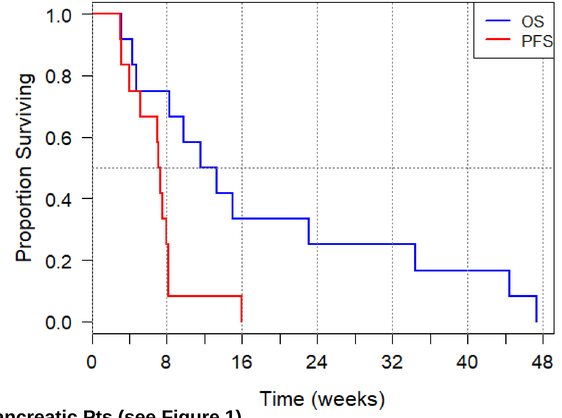
Results

- Baseline demographics and clinical characteristics are shown in Table 1. Other genomic alterations noted in both cohorts included *ARID1A, BRAF, FGFR1, FGFR2, FH, FRS2, KRAS, NRAS, PIK3CA, RAF1*, and *TP53* with *KRAS* being the most commonly reported in 7 of 22 pts.

Clinical Outcomes

- No ORs or SD at 16 wks were observed in the pancreatic or gallbladder/bile duct pts and both cohorts were therefore closed.

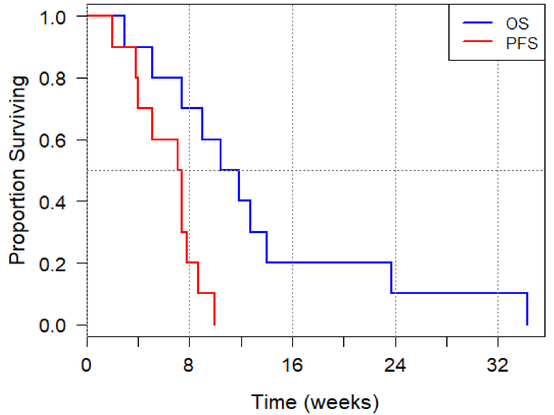
Figure 1: OS and PFS in Pancreatic Cancer Pts treated with palbociclib targeting *CDKN2A loss or mutation*



Pancreatic Pts (see Figure 1)

- 12 pts were enrolled from July 2016 to April 2017, but two were subsequently found to be ineligible. They are included in the data analysis for safety, PFS and OS.
- mPFS, wks, (90% CI) =7.2, (4.0, 8.0); mOS, wks, (90%CI)=12.4 (4.7, 23.1)
- One pt experienced grade 3 fatigue possibly related to P. No other grade 3, 4 or 5 AEs or SAEs reported as at least possibly related to P.

Figure 2: OS and PFS in Gallbladder and Bile Duct Cancer Pts treated with palbociclib targeting *CDKN2A loss or mutation*



Gallbladder and Bile Duct Pts (see Figure 2)

- 10 pts were enrolled from August 2016 to November 2017.
- mPFS, wks, (90% CI) =7.3, (3.9, 7.9); mOS, wks, (90%CI)=11.1 (5.1, 14.0)
- One pt experienced grade 3 SAE of muscle weakness and port infection possibly related to P. No other grade 3, 4, or 5 SAEs reported as at least possibly related to P. Four pts experienced grade 3 or 4 AEs of thrombocytopenia at least possibly related to P.

Conclusions

Monotherapy with P does not have clinical activity in pts with advanced pancreatic or gallbladder/bile duct cancers with *CDKN2A* loss or mutation. Toxicity is similar to previous experience with palbociclib. These pts should be offered other treatments, particularly clinical trials.

Acknowledgments

The authors would like to acknowledge the pts who participated in these cohorts as well as the following clinical leads of Pfizer, a TAPUR supporting pharmaceutical company: Lynn McRoy, MD; Ronit Simantov, MD.