Palbociclib in Patients With Pancreatic and Biliary Cancer With CDKN2A Alterations: Results From the Targeted Agent and Profiling Utilization Registry Study

Tareq Al Baghdadi, MD1; Susan Halabi, PhD2; Elizabeth Garrett-Mayer, PhD3; Pam K. Mangat, MS3; Eugene R. Ahn, MD4; Vaibhav Sahai, MBBS, MS5; Ricardo H. Alvarez, MD, MSc6; Edward S. Kim, MD7; Kathleen J. Yost, MD8; Andrew Lawrence Rygiel, MPH3; Kaitlyn R. Antonelli3; Nicole L. Butler, MPH3; Suanna S. Bruinooge, MPH3; and Richard L. Schilsky, MD3

Abstract

PURPOSE The Targeted Agent and Profiling Utilization Registry (TAPUR) Study identifies signals of antitumor activity of commercially available targeted agents in patients with advanced cancers that harbor genomic alterations known as drug targets. In this article, data from two cohorts of patients with pancreatic and biliary cancers with CDKN2A loss or mutation treated with palbociclib are reported.

METHODS Eligible patients age 12 years and older with advanced measurable or evaluable solid tumors are provided treatment according to protocol-specified genomic matching rules. The primary study end point is objective response or stable disease of at least 16 weeks duration. For each cohort, a Simon two-stage design was used with a futility evaluation after 10 patients. Secondary end points include safety, progression-free survival (PFS), and overall survival (OS).

RESULTS Between July 2016 and November 2017, 12 and 10 patients with pancreatic and biliary cancer, respectively, with CDKN2A loss or mutation were treated with palbociclib. Twenty evaluable patients (10 per cohort) were included in the analysis. No patients had objective response or stable disease at 16 weeks, and both cohorts were closed. Two patients, neither with response, were determined to be ineligible. All patients were evaluated for safety, PFS, and OS. A median PFS of 7.2 weeks (90% CI, 4.0 to 8.0 weeks) and median OS of 12.4 weeks (90% CI, 4.7 to 23.1 weeks) were observed in the pancreatic cohort. A median PFS of 7.3 weeks (90% CI, 3.9 to 7.9 weeks) and median OS of 11.1 weeks (90% CI, 5.1 to 14.0 weeks) were observed in the biliary cohort. No unexpected toxicities were observed.

CONCLUSION Palbociclib monotherapy does not have clinical activity in patients with advanced pancreatic or biliary cancers with CDKN2A loss or mutation. Toxicity is similar to reported experience with palbociclib in other tumor types.

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Introduction

Cytotoxic chemotherapy is the cornerstone of treatment of patients with advanced biliary and pancreatic adenocarcinoma. Despite recent advances, outcomes remain poor with a median overall survival (OS) of less than 12 months in stage IV biliary and pancreatic cancers, and new therapies are urgently needed.

Cyclin-dependent kinase (CDK) inhibitor 2A (CDKN2A) encodes p16INK4a, which plays an important role in cell-cycle regulation through inhibition of CDK4/6. CDKN2A loss or mutation is found in a wide array of malignancies and may lead to increased CDK activity. In a report of the mutational landscape of advanced pancreatic cancer, 46.5% of tumors harbored alterations in CDKN2A. Palbociclib is an orally available selective CDK inhibitor approved for the treatment of hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative breast cancer in combination with endocrine therapy. The Targeted Agent and Profiling Utilization Registry (TAPUR) Study is a prospective, phase II, pragmatic basket trial designed to identify signals of antitumor activity of commercially available targeted agents in patients with advanced cancers that harbor genomic alterations known to be drug targets. In this analysis, data for two cohorts of patients with pancreatic and biliary cancers with CDKN2A loss or mutation treated with single-agent palbociclib are reported.
The results demonstrated that palbociclib monotherapy has no meaningful clinical activity in patients with CDKN2A mutated or deleted advanced pancreatic or biliary adenocarcinoma.

Relevance
Off-label prescribing of palbociclib for the treatment of patients with pancreatic and biliary tract cancers with CDKN2A loss or mutation is not recommended. These patients should be offered participation in clinical trials of new treatment approaches.

METHODS

Trial Design
The rationale and study design have been reported previously in detail. Patients with advanced cancer and no standard treatment options are eligible if they have a tumor that harbors a genomic alteration known to be a target of or to predict sensitivity to one of the available study drugs. The primary study end point is antitumor activity, defined as objective response (OR) at 8 weeks or later or stable disease (SD) at 16 weeks or later from the time of enrollment. Secondary end points include progression-free survival (PFS), OS, and toxicity. For patients with solid tumors, OR is defined as complete or partial response per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. All serious adverse events and grade 3 to 5 treatment-related adverse events are reported per National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0). Patients are matched to one of the study drugs according to prespecified protocol matching rules on the basis of genomic testing performed by laboratories selected by clinical sites that have certification under the Clinical Laboratory Improvement Amendments and accreditation from the College of American Pathologists. Patients may not be matched to treatments that are already approved by the US Food and Drug Administration for their cancer type. Treating physicians may choose to consult with the TAPUR Molecular Tumor Board for appropriate targeted treatment options where none or multiple treatment matches surface within the TAPUR matching rules or if the treating physician would like to propose a treatment match outside the matching rules. Study treatments are administered per the treating physician in accordance with the recommended starting dose and schedule described in the package insert of each drug. Study treatment is continued until progressive disease is documented or withdrawal because of patient preference or physician recommendation. Radiographic assessment and clinical evaluation for response evaluation are performed at 8 and 16 weeks after initiation of treatment; then every 12 weeks while the patient remains in the study; and then at the end of study treatment, where possible. Patients are placed in multiple parallel cohorts defined by study drug, genomic alteration, and tumor type.

Each cohort has the same optimal Simon two-stage design, with a total possible cohort size of 28 patients. Within each cohort, the null hypothesis is 15% if patients have OR or SD of at least 16 weeks’ duration versus the alternative of 35%. Power and a one-sided type I error rate were set at 85% and 10%, respectively. The design requires 10 patients to be enrolled in a cohort in stage I and if fewer than two patients have OR or SD of at least 16 weeks’ duration, the cohort is permanently closed. If two or more patients have OR or SD at 16 weeks, the cohort expands to stage II and enrolls an additional 18 patients. If at least seven patients in the total cohort have a response of at least 16 weeks’ duration, the null hypothesis is rejected, and it is concluded that a signal of activity has been identified.

Patients
Eligible patients are required to meet both protocol- and drug-specific inclusion and exclusion criteria. Protocol-specific eligibility criteria include advanced measurable or evaluable solid tumors per RECIST version 1.1; Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0, 1, or 2; and a protocol-specified genomic target identified by a test performed in a laboratory that has Clinical Laboratory Improvement Amendments certification and College of American Pathologists accreditation. The general eligibility criteria for TAPUR permit enrollment of patients ages 12 years or older; however, to meet eligibility criteria specific to palbociclib, patients must be 18 years of age or older. All patients in this cohort have an advanced cancer that has CDKN2A loss or mutation or amplification of CDK4, CDK6, or CCND1 and without any Rb mutations. In
addition, to match to palbociclib, patients must have a cancer type other than breast and not have received food or drugs within 7 days before the start of study treatment that are known to be CYP3A4 inhibitors or inducers. Detailed inclusion and exclusion criteria for TAPUR have been previously reported.7

Patients treated with palbociclib received standard doses (125 mg orally daily for 21 days followed by 7 days off treatment to complete a 28-day cycle) until disease progression. Radiographic tumor evaluations were performed at 8 and 16 weeks after treatment initiation.

Eligible patients in this analysis had advanced pancreatic or biliary cancer with CDKN2A loss or mutation. All patients were tested for alterations using next-generation sequencing (NGS) platforms, with more than half the patients determined to have CDKN2A loss (Table 1). Patients in both cohorts continued treatment with palbociclib until disease progression, and no patients withdrew from the study.

**Trial Oversight**

The TAPUR Study protocol was reviewed and approved by a central institutional review board and, in some cases, by the local institutional review board at participating sites. Patients provide written consent before any screening activities or data collection. The TAPUR Study was designed by ASCO staff with input from ASCO volunteer members and the participating pharmaceutical companies. The TAPUR Data and Safety Monitoring Board (DSMB) is an independent board appointed by ASCO and meets biannually to monitor the study and review the safety and efficacy findings. The DSMB reviews all cohorts after stage I enrollment is complete and recommends cohorts for either closure or expansion. For expanded cohorts, the DSMB will review all completed cohorts before release of the cohort data. In the case of the cohorts reported herein, the DSMB reviewed the safety and efficacy data and determined that both cohorts should permanently close at the end of stage I enrollment and that the findings be released.

**Study End Points**

The primary end point is OR, defined as complete or partial response at or before 16 weeks, or SD at 16 weeks or later as reported per RECIST version 1.1. Secondary end points are PFS, OS, and toxicity per Common Terminology Criteria for Adverse Events (version 4.0).

**Data Analysis**

OR analyses were conducted for the 20 evaluable patients in the palbociclib cohorts, known as the efficacy population. All 22 patients were included in the safety, PFS, and OS analyses. The primary end point was summarized as proportion, and 90% CIs were computed. Kaplan-Meier curves were used to estimate the PFS and OS distributions.

**TABLE 1.** Molecular Alterations and Testing Methods for Pancreatic and Biliary Cancer Cohorts

<table>
<thead>
<tr>
<th>Target</th>
<th>Test Platform</th>
<th>Molecular Alteration</th>
<th>Pancreatic Cancer, No. (%)</th>
<th>Biliary Cancer, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDKN2A</td>
<td>NGS</td>
<td>Loss</td>
<td>8 (67)</td>
<td>5 (50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mutation</td>
<td>3 (25)</td>
<td>5 (50)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VUS</td>
<td>1 (8)</td>
<td>0 (0)</td>
</tr>
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**TABLE 2.** Baseline Demographic and Clinical Characteristics for Each Cohort

<table>
<thead>
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<th>Characteristic</th>
<th>Pancreatic Cancer</th>
<th>Biliary Cancer</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>62 (52-70)</td>
<td>63 (54-81)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (67)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (33)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Race</td>
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<td></td>
</tr>
<tr>
<td>White</td>
<td>10 (84)</td>
<td>8 (80)</td>
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<tr>
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<td>1 (10)</td>
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<td>ECOG performance status</td>
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<td>0</td>
<td>3 (25)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>1</td>
<td>8 (67)</td>
<td>6 (60)</td>
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<td>2</td>
<td>1 (8)</td>
<td>3 (30)</td>
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<td>Prior treatments</td>
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</tr>
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<td>Radiation therapy</td>
<td>2 (17)</td>
<td>2 (20)</td>
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<tr>
<td>No. of systemic therapies</td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>0 (0)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>2</td>
<td>6 (50)</td>
<td>2 (20)</td>
</tr>
<tr>
<td>3</td>
<td>6 (50)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Genomic test performed</td>
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<td></td>
</tr>
<tr>
<td>FoundationOne</td>
<td>10 (83)</td>
<td>9 (90)</td>
</tr>
<tr>
<td>MSK-IMPACT</td>
<td>2 (17)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>MI-ONCOSEQ</td>
<td>0 (0)</td>
<td>1 (10)</td>
</tr>
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</table>

Patients with additional genomic alterations reported

<table>
<thead>
<tr>
<th>No. of genomic alterations reported</th>
<th>Pancreatic Cancer</th>
<th>Biliary Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 (0)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>1</td>
<td>11 (92)</td>
<td>5 (50)</td>
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<tr>
<td>2</td>
<td>1 (8)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>3</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Abbreviations: ECOG, Eastern Cooperative Oncology Group; MI-ONCOSEQ, Michigan Oncology Sequencing Project; MSK-IMPACT, Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets.
RESULTS

Patients With Pancreatic Cancer

Twelve patients with pancreatic cancer and CDKN2A loss or mutation treated with palbociclib were enrolled in the study across seven sites from July 25, 2016, to April 28, 2017. The median age was 62 years (range, 52 to 70 years); 67% of patients were male; and 10 patients were white, one black, and one other. Three, eight, and one patient had an ECOG PS of 0, 1, and 2, respectively (Table 2).

All patients had NGS tests performed using either FoundationOne (83%; Foundation Medicine, Cambridge, MA) or Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (17%; Memorial Sloan Kettering Cancer Center, Boston, MA). Detailed information from the test reports that identified the specific CDKN2A variant information is listed in Table 3. The majority of patients in the cohort (67%) were identified with a CDKN2A loss. The remaining patients were determined to have a CDKN2A mutation, with the exception of one patient identified as having a CDKN2A variant of unknown significance. However, this patient was not included in the efficacy analysis because the patient was determined as not evaluable for response. The most common alterations identified in addition to CDKN2A alterations for each patient are shown in Figure 1. Other common genomic alterations noted in this cohort were mutations in BRAF, FGFR1, FRS2, KRAS, and TP53, with KRAS mutations being the most commonly reported in 10 of 12 patients.

Two patients who were enrolled and received treatment were subsequently found to be ineligible because they had not met the eligibility requirement for a hemoglobin level of 9.0 g/dL or greater at the time of enrollment. Neither ineligible patient demonstrated OR. Of the 10 eligible patients, nine experienced progression at or before 8 weeks; and eight patients were white, one black, and one with race not specified. One, six, and three patients had an ECOG PS of 0, 1, and 2, respectively (Table 2).

On the basis of these findings, the cohort was closed as a result of futility. Median PFS was 7.2 weeks (90% CI, 4.0 to 8.0 weeks) and median OS was 12.4 weeks (90% CI, 4.7 to 23.1 weeks; Fig 2A).

One of the 12 patients experienced grade 3 fatigue possibly related to palbociclib. No other grade 3 or higher adverse event or serious adverse event was observed as at least possibly related to palbociclib.

Patients With Biliary Cancer

Ten patients with biliary cancer with CDKN2A loss or mutation treated with palbociclib were enrolled in the study across six sites from August 9, 2016, to November 11, 2017. The median age was 63 years (range, 54 to 81 years); 50% of patients were male; and eight patients were white, one black, and one with race not specified. One, six, and three patients had an ECOG PS of 0, 1, and 2, respectively (Table 2).

Most patients in this cohort (90%) had a FoundationOne test performed, with the exception of one patient (10%) who had the NGS test performed by the Michigan Oncology Sequencing Project laboratory. Detailed information from the tests that identified the specific CDKN2A variant information is listed in Table 4. Equal numbers of patients in the cohort were identified with either CDKN2A loss or CDKN2A mutation. The most common alterations identified in addition to CDKN2A for each patient are shown in Figure 1. Other genomic alterations noted in this cohort included ARID1A, ATM, BRAF, FGFR2, FH, KRAS, NRAS, PIK3CA, and VHL.

All 10 patients experienced progression at or before 10 weeks. On the basis of these findings, the cohort was closed as a result of futility. The median PFS was 7.3 weeks (90% CI, 3.9 to 7.9 weeks), and median OS was 11.1 weeks (90% CI, 5.1 to 14.0 weeks; Fig 2B).

One of the 10 patients enrolled experienced a grade 3 serious adverse event of muscle weakness and port

### TABLE 3. Detailed CDKN2A Information From Test Assay for Patients in the Pancreatic Cancer Cohort

<table>
<thead>
<tr>
<th>Loss/Mutation</th>
<th>Specific CDKN2A Variant</th>
<th>NGS Test</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss CDKN2A exon 1 and CDKN2B</td>
<td>FoundationOne</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>p16INK4a loss and p14ARF loss exon 1 and CDKN2B loss</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mutation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p16INK4a L78fs<em>41 and p14ARF H93fs</em>41+, p16INK4a R80* and p14ARF P94L</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>p14ARF exon2 p.A121_C123del; p16INK4A exon2 p.R167_A169del</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>CDKN2A14ARF S127F (c.380C&gt;T) exon2; CDKN2A14ARF P101S (c.301C&gt;T) exon2; CDKN2A14ARF chr9:18389532_c.317-3482: C DKN2A14ARF INV exon2; CDKN2A14ARF chr9:18389532_c.138:CDKN2A14ARFINV exons 1-3</td>
<td>MSK-IMPACT</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>VUS A127fs*19</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: MSK-IMPACT, Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets; NGS, next-generation sequencing; VUS, variant of unknown significance.
infection possibly related to palbociclib. Four patients experienced grade 3 or 4 adverse events of thrombocytopenia at least possibly related to palbociclib.

DISCUSSION

This phase II study in patients with advanced pancreatic or biliary cancers with CDKN2A loss or mutation treated with single-agent palbociclib demonstrated no clinical activity. The toxicity is similar to previous reports of monotherapy with palbociclib.

CDKN2A is a tumor suppressor gene frequently altered by mutations, deletions, and epigenetic silencing. Its product, p16INK4a, regulates entry into the DNA synthetic phase of the cell cycle in a retinoblastoma protein (RB)–dependent manner. The p16INK4a level increases with aging and induces cellular senescence in response to stress.

![Graph showing overall survival (OS) and progression-free survival (PFS) in patients with pancreatic and biliary cancer treated with palbociclib that targeted CDKN2A loss or mutation.](image)

**FIG 1.** Genomic alterations reported in patients with pancreatic and biliary cancer treated with palbociclib that targeted CDKN2A loss or mutation.

**FIG 2.** Overall survival (OS) and progression-free survival (PFS) in patients with (A) pancreatic and (B) biliary cancer treated with palbociclib that targeted CDKN2A loss or mutation.
**CDKN2A** mutations/deletions occur frequently in pancreatic adenocarcinoma.\(^ {11}\) Moreover, alterations that abrogate the RB/p16 tumor suppressor pathway are seen in virtually all pancreatic carcinomas.\(^ {12}\) **CDKN2A** mutations occur in a minority of cholangiocarcinomas and are associated with a poor prognosis.\(^ {13,14}\)

Prior studies of multiple RB-positive tumors have shown that most are sensitive to some degree to CDK4/6 inhibition.\(^ {15-18}\) Preclinical studies assessing the impact of CDK4/6 inhibition on pancreatic cancer cell lines and xenograft models showed conflicting data. For example, one study showed that palbociclib inhibited the growth of pancreatic cancer cell lines but resulted in upregulation of the expression of genes that promote invasion and metastasis.\(^ {19}\) Another showed that established pancreatic cell lines displayed a relatively weak response to palbociclib, but palbociclib had potential activity in patient-derived xenografts.\(^ {20}\)

Palbociclib is approved for the treatment of patients with advanced hormone receptor–positive, HER2-negative breast cancer in combination with an aromatase inhibitor or fulvestrant.\(^ {21,22}\) Palbociclib showed promising activity in patients with liposarcoma\(^ {23}\) and **CDKN2A**-mutated non–small-cell lung cancer.\(^ {24}\) However, palbociclib was not effective in unselected patients with squamous cell lung cancer\(^ {25}\) or urothelial cancer.\(^ {26}\) Prior studies have suggested several mechanisms of resistance to CDK4/6 inhibitors in human cancer cell lines and xenograft models, including **CDK4** amplification, **RB** loss, and cyclin E1 amplification.\(^ {27-31}\) The potential for prior exposure to systemic chemotherapy to induce resistance to palbociclib through these or other mechanisms has not been explored but might have contributed to the lack of efficacy of palbociclib in this trial. It is conceivable, therefore, that the use of palbociclib alone or in combination earlier in the treatment course could be beneficial.

The association of **CDKN2A** mutations/deletions with clinical activity of CDK4/6 inhibitors is undetermined. In patients with hormone receptor–positive, HER2-negative breast cancer, **CDKN2A** mutations do not predict activity of either palbociclib or ribociclib.\(^ {32,33}\) A report revealed that **CDKN2A** mutant cancers show only intermediate sensitivity to CDK4/6 inhibition with abemaciclib, whereas genetic events that activate \(\alpha\)-type cyclins were associated with high sensitivity.\(^ {30}\)

The effects of combining other targeted agents with palbociclib in pancreatic adenocarcinoma cell lines have been explored. The addition of a MEK inhibitor\(^ {31}\) and a mammalian target of rapamycin inhibitor\(^ {30,34}\) was synergistic. The latter may relate to metabolic reprogramming of pancreatic cancer cells by CDK4/6 inhibition, which results in increased oxidative phosphorylation, increased consumption of glucose and glutamine, and activation of the mammalian target of rapamycin pathway.\(^ {34}\) These and other novel combinations hopefully will allow successful treatment of pancreatic adenocarcinoma and other malignancies on the basis of a sound understanding of mechanisms that underlie cancer cell resistance. The development of relevant predictive biomarkers whereby treatment decisions are based on comprehensive genomic profiling is a promising and increasingly pursued strategy. To this end, studies using comprehensive genomic assessment have identified therapeutically relevant genomic alterations in 48% of patients with advanced pancreatic adenocarcinoma\(^ {6}\) and 47% of patients with cholangiocarcinoma.\(^ {14}\)

In conclusion, these results from the TAPUR Study demonstrate that single-agent palbociclib has no meaningful clinical activity in patients with **CDKN2A** mutated or deleted advanced pancreatic adenocarcinoma and cholangiocarcinoma.

**TABLE 4.** Detailed **CDKN2A** Information From Test Assay for Patients in the Biliary Cancer Cohort

<table>
<thead>
<tr>
<th>Loss/Mutation</th>
<th>Specific <strong>CDKN2A</strong> Variant</th>
<th>NGS Test</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss</td>
<td><strong>CDKN2A</strong> homozygous loss</td>
<td>MI-ONCOSEQ</td>
<td>1</td>
</tr>
<tr>
<td>p16INK4a A4_P11del, p16INK4a L16fs*9, loss exons 2-3</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mutation</td>
<td>Splice site 151-2A&gt;G</td>
<td>FoundationOne</td>
<td>1</td>
</tr>
<tr>
<td>p16INK4a R58X and p14ARF P72L</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
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<tr>
<td>p16INK4a A36fs<em>17, p16INK4a N71fs</em>49 and p14ARF Q85fs*50+</td>
<td>FoundationOne</td>
<td>1</td>
<td></td>
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<td>Splice site 151-1G&gt;C</td>
<td>FoundationOne</td>
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</tr>
<tr>
<td>Truncation exon 2</td>
<td>FoundationOne</td>
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</table>

Abbreviations: MI-ONCOSEQ, Michigan Oncology Sequencing Project; NGS, next-generation sequencing.

**AFFILIATIONS**

1Michigan Cancer Research Consortium, Ypsilanti, MI
2Duke University Medical Center, Durham, NC
3American Society of Clinical Oncology, Alexandria, VA
4Cancer Treatment Centers of America, Chicago, IL
5University of Michigan Rogel Cancer Center, Ann Arbor, MI
6Cancer Treatment Centers of America, Atlanta, GA
7Levine Cancer Institute, Atrium Health, Charlotte, NC
8Cancer Research Consortium of West Michigan, Grand Rapids, MI
CORRESPONDING AUTHOR
Pam K. Mangat, MS, American Society of Clinical Oncology, 2318 Mill Rd, Alexandria, VA 22314; e-mail: pam.mangat@asco.org.

PRIOR PRESENTATION
Presented at the 2018 American Society of Clinical Oncology Annual Meeting, Chicago, IL, June 1-5, 2018.

AUTHOR CONTRIBUTIONS
Conception and design: Susan Halabi, Elizabeth Garrett-Mayer, Pam K. Mangat, Edward S. Kim, Suanna S. Bruninooge, Richard L. Schilsky
Administrative support: Andrew Lawrence Rygier, Kaitlyn R. Antonelli, Nicole L. Butler
Provision of study material or patients: Eugene R. Ahn, Vaibhav Sahai, Ricardo H. Alvarez, Kathleen J. Yost
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
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Tareq Al Baghdadi
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Honoraria: Cardinal Health, Medscape
Consulting or Advisory Role: Celgene, Bristol-Myers Squibb, Heron Therapeutics
Travel, Accommodations, Expenses: Cardinal Health, Celgene, Bristol-Myers Squibb, Heron Therapeutics

Susan Halabi
Consulting or Advisory Role: Eisai, Ferring Pharmaceuticals

Elizabeth Garrett-Mayer
Stock and Other Ownership Interests: Abbott Laboratories, AbbVie, Tactical Therapeutics, Okawa Pharmaceuticals
Consulting or Advisory Role: Deciphera, Tyne

Eugene R. Ahn
Employment: Cancer Treatment Centers of America
Leadership: Cancer Treatment Centers of America

Vaibhav Sahai
Consulting or Advisory Role: Celgene, Halozyme, NewLink Genetics, Ipsen, Incyte
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Ricardo H. Alvarez
Employment: Cancer Treatment Centers of America
Leadership: Cancer Treatment Centers of America
Consulting or Advisory Role: Eisai, Puma Biotechnology, R-Pharma, Pfizer
Speakers’ Bureau: Eisai, Pfizer
Other Relationship: Eisai, Puma Biotechnology, Pfizer

Edward S. Kim
Honoraria: AstraZeneca, Boehringer Ingelheim, Pfizer, Merck, Takeda Pharmaceuticals, Roche, Genentech
Consulting or Advisory Role: AstraZeneca, Boehringer Ingelheim, Pfizer, Merck, Takeda Pharmaceuticals, Roche, Genentech
Research Funding: Boehringer Ingelheim, Merck, Ignyta, Genentech, Roche
Travel, Accommodations, Expenses: AstraZeneca, Boehringer Ingelheim, Takeda Pharmaceuticals, Genentech, Roche, Pfizer, Merck

Kathleen J. Yost
Stock and Other Ownership Interests: Pfizer (I)
Research Funding: Pfizer
Other Relationship: Pfizer, AstraZeneca

Richard L. Schilsky
Research Funding: AstraZeneca (Inst), Bayer AG (Inst), Bristol-Myers Squibb (Inst), Genentech (Inst), Roche (Inst), Eli Lilly (Inst), Merck (Inst), Pfizer (Inst), Boehringer Ingelheim (Inst), Varian (Inst)

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REFERENCES

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