ORIGINAL ARTICLE

A Phase 2 Study of Palbociclib for Recurrent or Refractory Advanced Thymic Epithelial Tumors (KCSG LU17-21)

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ABSTRACT

Introduction: Thymic epithelial tumors (TETs) are rare but are the most common tumors of the anterior mediastinum. Platinum-based combination chemotherapy is the standard of care for such tumors and is associated with a 50% to 90% objective response rate (ORR) in metastatic disease. Nevertheless, there is no standard chemotherapeutic option after failure of platinum-based combination chemotherapy. Genetic alterations associated with the cell cycle, including pRB, $p16^{INK4A}$, and cyclin D1, are most often observed in TETs. On the basis of these results, we conducted a phase 2 trial to evaluate the efficacy and safety of palbociclib in patients with recurrent or refractory advanced TETs.

Methods: This is a phase 2, multicenter, open-label, single-arm study of palbociclib monotherapy in patients with recurrent or metastatic advanced TETs who failed one or more cytotoxic chemotherapies. The patients received 125 mg of oral palbociclib daily for 21 days, followed by a 7-day break. The primary end point was progression-free survival (PFS). The secondary end points were ORR, duration of response, overall survival, and safety.

Results: Between August 2017 and October 2019, a total of 48 patients were enrolled. The median number of previous chemotherapies was one (range: one to four), and 21 (43.7%) of 48 patients received thymectomy. By the WHO classification, the patients were type A (n = 1), type B1 (n = 2), type B2 (n = 8), type B3 (n = 13), thymic carcinoma (n = 23), and unknown (n = 1). With a median follow-up of 14.5 months (range: 0.8–38.2), the median number of cycles of palbociclib monotherapy was 10 (range: 1–40). The ORR was 12.5% (four partial responses in thymoma and two partial responses in thymic carcinoma). The PFS at 6 months was 60.2%, and the median PFS was 11.0 months (95% confidence interval: 4.6–17.4). The median overall survival was 26.4 months (95% confidence interval:

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17.4–35.4). The most common treatment-related adverse events of any grade were neutropenia (62.5%), anemia (37.5%), and thrombocytopenia (29.1%), and the most common grade 3/4 treatment-related hematologic adverse event was neutropenia (41.7%). Neutropenia above grade 3 was reversible, and there were no cases with neutropenic fever.

Conclusions: Palbociclib monotherapy was well tolerated and had encouraging efficacy in patients with TETs who failed platinum-based combination chemotherapy.

Keywords: Thymic epithelial tumors; Palbociclib; Platinum-based combination chemotherapy; Thymoma; Thymic carcinoma

Introduction

Thymic epithelial tumors (TETs) are the most common tumor of the anterior mediastinum, with a wide spectrum of anatomical, clinical, histologic, and morphologic features.[1,2] The WHO classification is the most widely used system for histologic classification of TETs. Patients with thymoma, especially WHO type B1 or B2, have a high risk of developing autoimmune diseases such as myasthenia gravis, systemic lupus erythematosus, or red cell aplasia. The rarity and clinical complexity of TETs warrant multidisciplinary management of all diagnostic–therapeutic approaches.[3] Surgery is the mainstay of curative-intent primary treatment, as complete resection represents the most significantly favorable prognostic factor for overall survival. Nevertheless, in metastatic disease, palliative chemotherapy is indicated. The TETs are sensitive to chemotherapy, and platinum-based combination chemotherapy as a first-line regimen is the standard of treatment and is associated with a 50% to 90% objective response rate (ORR).[4,5] There is, however, no standard chemotherapeutic option after failure of platinum-based combination chemotherapy. Several studies with cytotoxic chemotherapy have documented 10% to 30% ORRs with various drugs such as ifosfamide, octreotide, fluorouracil, pemetrexed, or gemcitabine in recurrent TETs.[6]

The EGFR was overexpressed in approximately 70% of thymoma and 50% of thymic carcinomas. Although several agents targeted to inhibit these pathways, such as EGFR tyrosine kinase inhibitors (gefitinib and erlotinib), have been studied in patients with TETs, their clinical activity was modest. The low frequency of EGFR mutations in TETs might explain why responses to EGFR tyrosine kinase inhibitor have rarely been observed. As another potential target, KIT is overexpressed in 2% of thymomas and 79% of thymic carcinomas. Sunitinib had a 14.5% ORR in a phase 2, single-arm study.[7] Recently, cixutumumab, an IGF-1R inhibitor, was found to have a 14% ORR in thymoma, but no response in thymic carcinoma.[8] There were reports of vascular epithelial growth factor overexpression in 86% to 88% of TETs. As angiogenesis inhibitors, a phase 2 trial of bevacizumab was tested in combination with erlotinib in TETs, and the disease control rate (DCR) was 60%. Belinostat, a histone deacetylase inhibitor, had a 2-year survival rate of 8% in thymoma and 77% in thymic carcinoma in a phase 2 trial.[9] Pembrolizumab treatment for patients with TETs resulted in a median progression-free survival (PFS) of 4 to 6 months and an ORR of 21% to 22%.[10,11] Owing to its relevant antitumoral activity, pembrolizumab has been recently added to the National Comprehensive Cancer Network guidelines for treatment of patients with thymic carcinoma that was refractory to chemotherapy.[12]

Phosphorylation of pRB by CDK4 and CDK6, which are activated by cyclin D, initiates the transition from the G1 phase to the S phase.[13] Overexpression or amplification of cyclin D or dysregulation of CDK4/6 causes abnormalities in the G1–S checkpoint, which plays an important role in the pathogenesis of many malignancies. In tumors with functional pRB in which cellular proliferation is driven by cyclin D, inhibition of CDK4/6 is a promising potential therapeutic approach. Genetic alterations associated with the cell cycle, including mutations of pRB, p16INK4A, and cyclin D1, are most often observed in TETs.[14]

Palbociclib is an orally bioavailable small-molecule inhibitor of CDK4 and CDK6, which prevents phosphorylation of pRB, resulting in cell cycle arrest at the G1/S phase.[15] Palbociclib has been found to have antitumor activities in pRB-expressing tumor cell lines and was approved for treatment of hormone receptor-positive breast cancer.[16] In 2015, Keijzers et al.[17] reported the expression of pRB and phosphorylated pRB in approximately 95% and 84% of TETs, respectively. On the basis of these results, in this prospective trial, we investigated the efficacy of palbociclib in patients with recurrent or refractory advanced TETs.

Materials and Methods

Participants

Patients diagnosed with having histologically confirmed TETs were eligible. Other major inclusion criteria were patients who had previously received at least one platinum-based cytotoxic chemotherapy regimen administered for inoperable or metastatic disease; had at least one measurable lesion on the basis of the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1; and had an Eastern Cooperative

Oncology Group performance status score of 0 to 2. Patients with previously treated and radiologically stable brain metastases were enrolled. Detailed guidance regarding study participation was included in the protocol and available as a Supplementary Material. All patients provided written informed consent, and this study was performed under the supervision of an institutional review board of each institute. This study was conducted in accordance with the Declaration of Helsinki (ClinicalTrials.gov number: NCT03219554).

Study Design and Treatment Schedule

This is an open-label, single-arm, multicenter, phase 2 study of palbociclib monotherapy. This study was conducted at seven academic institutes of the Korean Clinical Study Group in the Republic of Korea. The patients received 125 mg of oral palbociclib daily for 21 days, followed by a 7-day break. This cycle was repeated every 28 days. The patients received palbociclib monotherapy until objective disease progression, symptomatic deterioration, unacceptable toxicity, death, or withdrawal of consent, whichever occurred first. Continuation of the treatment beyond progression was allowed by physician's judgment.

Disease assessments were performed by chest computed tomography (CT) with or without abdominal CT every 8 weeks from the date of initiation of treatment (abdominal CT was optional by clinician's decision). Each assessment was performed as scheduled according to the calendar, regardless of any dosing delays, to prevent the introduction of bias into the assessment of efficacy. Tumor assessments were performed until radiographically or clinically (i.e., photographed or palpable lesions) documented progressive disease (PD) as per RECIST version 1.1, initiation of new anticancer therapy, or discontinuation of a patient from overall study participation (e.g., death, patient request, loss to follow-up), whichever occurred first. The safety objectives were evaluated according to Common Terminology Criteria for Adverse Events version 4.3.

Study End Points

The primary end point of this study was PFS, and the secondary end points were ORR, duration of response, overall survival, and safety.

Calculation of Sample Size

On the basis of a previous study, a median PFS of 3.5 months with a 6-month PFS of 30% was observed in patients with TET who progressed to platinum-based cytotoxic chemotherapy.[18,19] We expected the median PFS to be 5.67 months with a 6-month PFS rate of 50%, leading to a 0.61 hazard ratio for palbociclib monotherapy. We expected an accrual time of 12 months and an additional follow-up period of 24 months. On the basis of this hypothesis, a total of 36 progression or death events and a sample size of 43 patients were required to satisfy a power of 95% for a one-sample log-rank test with a one-sided alpha of 5%. This study was designed to enroll a total of 48 patients by accounting for up to 10% attrition owing to dropouts.

Statistical Analysis

The PFS was calculated as the interval between the first date of palbociclib monotherapy and the date of disease progression or all-cause mortality. Overall survival was calculated as the interval between the first date of the study treatment and the date of all-cause mortality. The Kaplan-Meier curve was used to estimate the survival distribution. The ORR was defined as the proportion of patients with complete response (CR) or partial response (PR), and DCR was defined as CR, PR, or stable disease using RECIST criteria version 1.1.

All p values were two sided, and a p value less than 0.05 was considered statistically significant. All data were analyzed using the Statistical Package for Social Sciences software (version 24.0; IBM Corp., Armonk, NY).

NanoString Gene Expression Analysis

Total RNA was extracted from formalin-fixed, paraffin-embedded tissue using a RNeasy formalin-fixed, paraffin-embedded kit (Qiagen). The RNA concentration and purity were assessed using a DS11 Spectrophotometer (Denovix Inc., Wilmington, DE). Total RNA (100 ng) was analyzed using the nCounter Human PanCancer Pathway Panel (NanoString Technologies Inc., Seattle, WA). The mRNA data were analyzed using the nSolver (version 4.0) software.

Results

Study Population and Clinical Characteristics

Between August 2017 and October 2019, 50 patients signed the informed consent form and were enrolled. Two patients withdrew consent before starting palbociclib monotherapy. A total of 48 patients (24 patients with thymoma and 24 patients with thymic carcinoma) was enrolled and received at least one cycle of treatment. Four patients discontinued palbociclib monotherapy without tumor assessment after one cycle. Thus, 44 patients were included in the tumor response evaluation, and all 48 patients were included in the safety evaluation and survival analysis. The data lock was performed on February 28, 2021, at which point 37 events of disease progression or death had occurred. Table 1 reveals the patients' baseline characteristics. The patients had an Eastern Cooperative Oncology Group

Table 1. Baseline Characteristics

Patient Characteristics	Thymoma (n = 24)	Thymic Carcinoma (n = 23)	Unknown (n = 1)	Total (N = 48)
Age (y), median (range)	48 (32-69)	57 (34-92)	48	54 (32-92)
<60 y	19 (79.2%)	13 (56.5%)	1 (100%)	33 (68.8%)
≥60 y	5 (20.8%)	10 (43.5%)	0	15 (31.2%)
Sex				
Male	10 (41.7%)	15 (65.2%)	1 (100%)	26 (54.2%)
Female	14 (58.3%)	8 (34.8%)	0	22 (45.8%)
ECOG performance status				
0	1 (4.2%)	1 (4.3%)	1 (100%)	2 (4.2%)
1	23 (95.8%)	22 (95.7%)	0	46 (95.8%)
Smoking status				
Never smoker	16 (66.7%)	11 (47.8%)	1 (100%)	27 (56.3%)
Ex-smoker	6 (25%)	11 (47.8%)	0	18 (37.5%)
Current smoker	2 (8.3%)	1 (4.3%)	0	3 (6.2%)
WHO classification				
A	1 (4.2%)			1 (2.1%)
B1	2 (8.3%)			2 (4.2%)
B2	8 (33.3%)			8 (16.7%)
B3	13 (54.2%)			13 (27.1%)
C		23 (100%)		23 (47.9%)
Unknown			1 (100%)	1 (2.1%)
Masaoka stage				
IV-A	10 (41.7%)	3 (13.0%)		13 (27.1%)
IV-B	12 (50.0%)	20 (87.0%)		33 (68.8%)
unknown	2 (8.3%)	0		2 (4.2%)
Distant metastasis				
Lung	5 (20.8%)	9 (39.1%)	1 (100%)	15 (31.3%)
Pleura	18 (75.0%)	14 (60.9%)	0	32 (66.7%)
Liver	8 (33.3%)	7 (30.4%)	0	15 (31.3%)
Bone	3 (12.5%)	4 (17.4%)	0	7 (14.6%)
Brain	0	3 (13.0%)	0	3 (6.2%)
Others	7 (29.2%)	15 (65.2%)	1 (100%)	23 (47.9%)
Lines of previous chemotherapy				
1	17 (70.8%)	14 (60.9%)	0	31 (64.6%)
2	5 (23.8%)	6 (26.1%)	0	11 (22.9%)
3	2 (9.5%)	2 (8.7%)	1 (100%)	5 (10.4%)
4	0	1 (4.3%)	0	1 (2.1%)

ECOG, Eastern Cooperative Oncology Group.

performance status of 0 (4.2%) or 1 (95.8%). Most of the patients had WHO classification of C (47.9%) or B3 (27.1%) and had received at least one prior palliative chemotherapy (87.5%).

Palbociclib Treatment

With a median follow-up period of 14.5 (range: 0.8–38.2) months, the median number of cycles of palbociclib monotherapy was 10 (range: 1–40), and the median dose administered was 125 (range: 75–125) mg/d. At least one dosing interruption was required in 14 patients (29.2%), and a dose reduction to 100 mg/d occurred in eight patients (16.7%) and to 75 mg/d in four patients (8.3%), primarily owing to adverse events of neutropenia, anemia, and pneumonitis. Study discontinuations were primarily owing to disease progression (n = 22, 45.8%).

Objective Response and Duration of Treatment Response

The ORR was 12.5% (four PR in thymoma and two PR in thymic carcinoma), and the DCR was 79.2% (15 stable disease in thymoma, 16 stable disease in thymic carcinoma, and one stable disease in other) (Fig. 1*A* and Table 2). Supplementary Figure 1 reveals the largest percentage change from baseline in the sums of longest target tumor lesion diameters per patient. Figure 1*B* illustrates the duration of palbociclib monotherapy and best response by swimmer plot. Approximately half of the patients (53.1%) who achieved stable disease

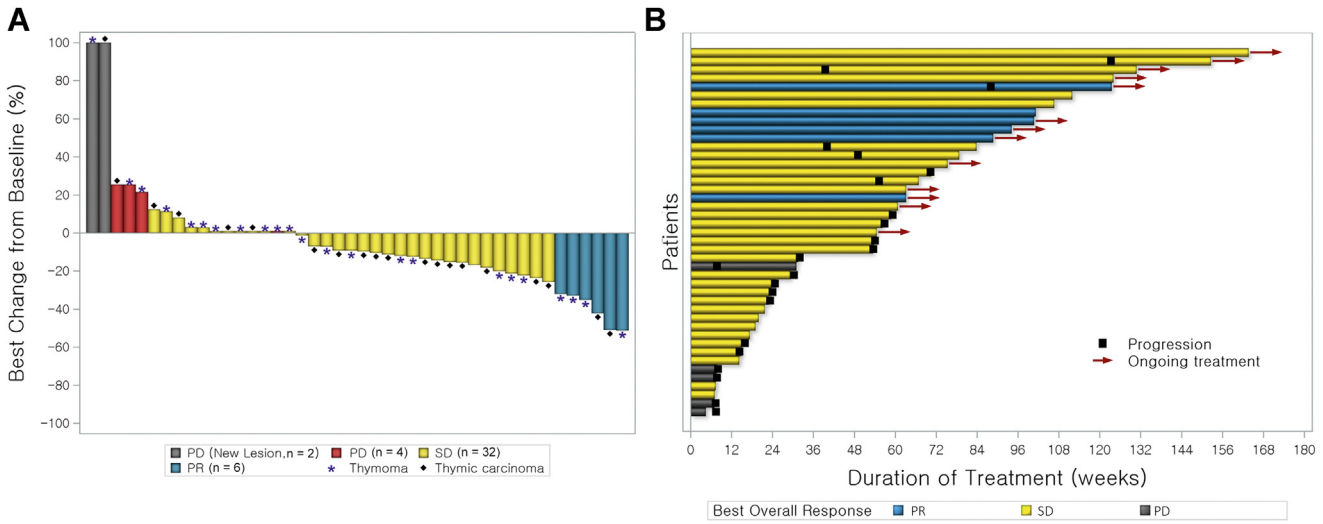

Figure 1. (*A*) Waterfall plot. (*B*) Swimmer plot. PD, progressive disease; PR, partial disease; SD, stable disease.

continued the treatment longer than 12 months. In addition, 22.9% (13 of 48) were still receiving ongoing palbociclib monotherapy with PR or stable disease at the time of data lock. Six patients received palbociclib monotherapy beyond progression on the basis of their physician's decision.

PFS and Overall Survival

The PFS at 6 months was 60.2%, the median PFS was 11.0 months (95% CI: 4.6–17.4), and the median overall survival was 26.4 months (95% CI: 9.4–43.4) (Fig. 2*A* and *B*). Between thymoma and thymic carcinoma, the median PFS and overall survival did not differ. The median PFS was 13.0 months (95% CI: 1.0–25.0) for thymoma and 9.2 months (95% CI: 0.6–17.8) for thymic carcinoma (p value = 0.10) (Supplementary Fig. 2*A*). The median overall survival was 26.4 months (95% CI: 12.9–39.4) for thymoma and 25.6 months (95% CI: 0–51.4) for thymic carcinoma (p value = 0.30) (Supplementary Fig. 2*B*).

Safety Profile

All patients who received at least one dose of palbociclib monotherapy (N = 48) were assessable for safety. The most common nonhematologic all-causality adverse events of any grade were fever (n = 9, 18.8%), fatigue (n = 8, 16.7%), anorexia (n = 5, 10.4%), and diarrhea (n = 5, 10.4%) (Table 3). The most common grade 3/4 nonhematologic all-causality adverse event was pneumonitis (n = 2, 4.2%). The frequency of any-grade treatment-related hematologic adverse events was 79.1% (38 of 48) and that of grade 3/4 treatment-related hematologic adverse events was 54.2% (26 of 48) (Table 3). The most common grade 3/4 treatment-related hematologic adverse event was neutropenia (n = 20, 41.7%). Neutropenia was related with palbociclib monotherapy; however, it was reversible with treatment interruption and dose modification. There were no cases of neutropenic fever. In addition, two patients (4.2%) discontinued treatment owing to adverse events (bacterial pneumonia, n = 2), none of which were considered related to palbociclib.

Table 2. Treatment Outcomes of Palbociclib in Thymoma and Thymic Carcinoma

Treatment Outcomes	Thymoma (n = 24)	Thymic Carcinoma (n = 23)	Total (N = 48)
Best response, no. (%)			
Partial response	4 (16.7%)	2 (8.7%)	6 (12.5%)
Stable disease	15 (62.5%)	16 (69.6%)	32 (66.7%)
Progression	4 (16.7%)	2 (8.7%)	6 (12.5%)
Overall response rate, %	4 (16.7%)	2 (8.7%)	6 (12.5%)
Disease control rate, %	19 (79.2%)	18 (78.3%)	38 (79.2%)
Proportion PFS at 6 mo, %	66.4%	52.2%	60.2%
No. of cycles, median (range)	10 (1-40)	6 (1-31)	10 (1-40)

PFS, progression-free survival.

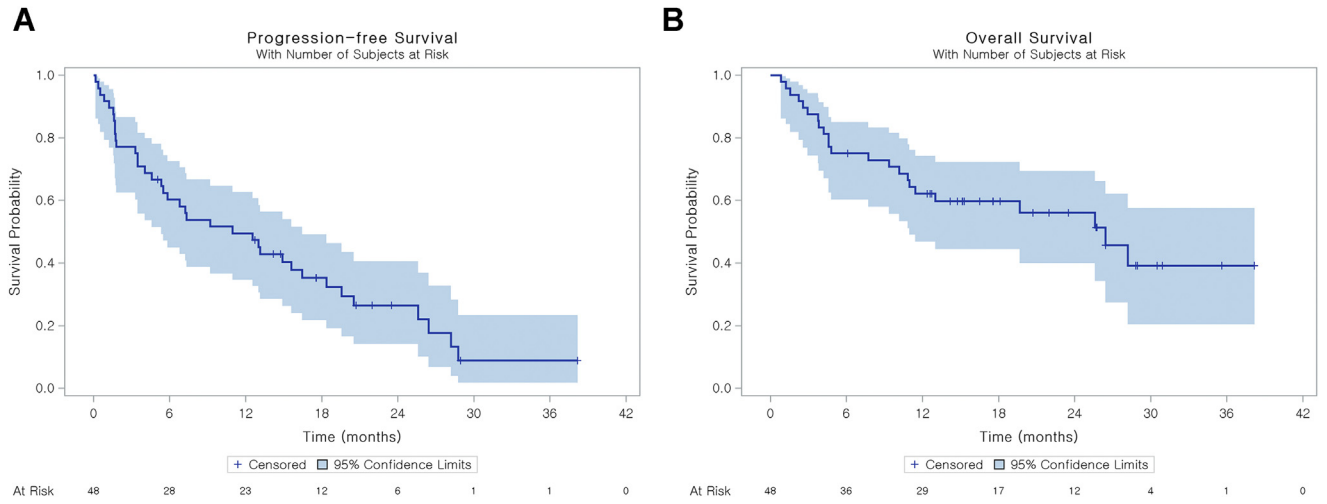

Figure 2. Kaplan-Meier curves for (*A*) progression-free survival and (*B*) overall survival in all study population.

Exploratory Biomarker Study

Among the 48 patients in this study, mRNA expression was analyzed in 12 (five with thymoma and seven with thymic carcinoma) who had available tumor tissue. The expression of 33 cell cycle- or DNA damage-related genes between thymoma and thymic carcinoma is presented as a heatmap (Supplementary Fig. 3*A*). In all analyzed genes, KIT and PAX5 were most differentially expressed between thymic carcinoma and thymoma (Supplementary Fig. 3*B*).

When analyzing gene perturbation according to clinical outcomes (PR or stable disease longer than 12 mo versus PD or stable disease for less than 12 mo), six cell cycle- or DNA damage-related genes (*WEE1*, *POLE2*, *TGFB2*, *IL1R1*, *FANCC*, and *MYD88*) were associated with a durable clinical response to palbociclib treatment (PR or stable disease longer than 12 mo, p value < 0.05) (Fig. 3*A*). A volcano plot of differentially expressed genes between the group with PR or stable disease for longer than 12 months and the group with PD or stable disease for less than 12 months is depicted (Fig. 3*B*). The top 10 differentially expressed genes were *IGF1*, *VEGFA*, *WNT5B*, *WEE1*, *TGFB2*, *IL11RA*, *BNIP3*, *TSPAN7*, *CD19*, and *WNT2B* (p value < 0.01). Among them, two cell cycle-related genes (*WEE1* and *TGFB2*) were highly expressed in the group with PD or stable disease for less than 12 months.

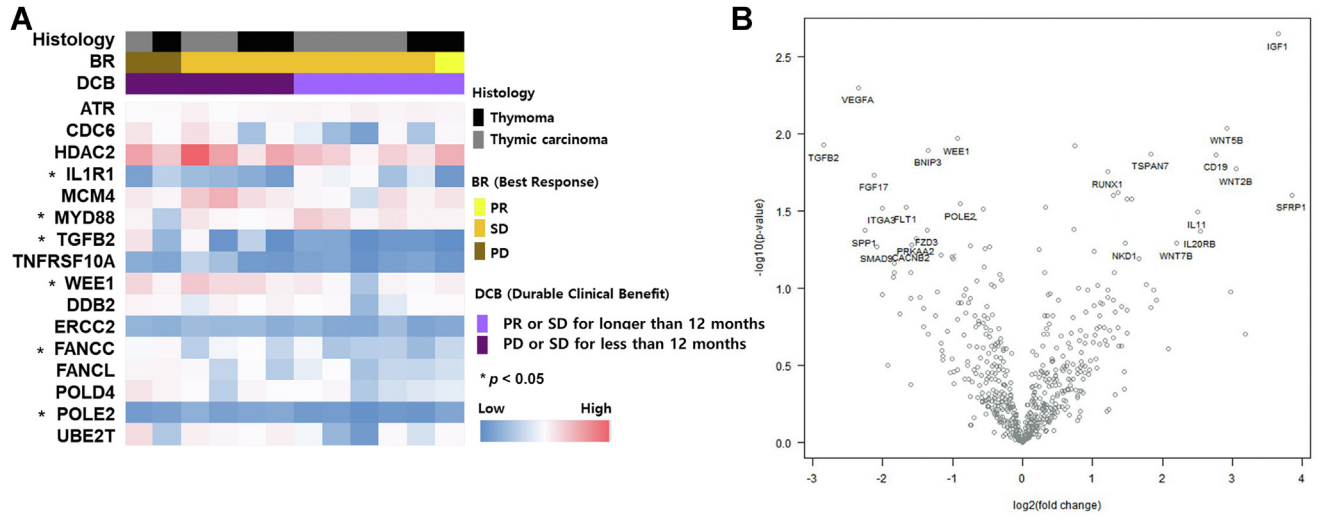

Figure 3. Gene expression analysis according to clinical response (partial response or stable disease for longer than 12 mo versus progressive or stable disease for shorter than 12 mo) in patients with thymoma or thymic carcinoma who received palbociclib. (*A*) Heatmap of cell cycle- and DNA damage-related genes. (*B*) Volcano plot depicting differentially expressed genes according to clinical responses. PD, progressive disease; PR, partial response; SD, stable disease.

Table 3. Summary of Adverse Events During Palbociclib Treatment in Thymoma and Thymic Carcinoma

Adverse Events	Any Grade	Grade ≥3
Hematologic adverse events		
Neutropenia[a]	30 (62.5)	20 (41.7)
Anemia[a]	18 (37.5)	7 (14.6)
Thrombocytopenia[a]	13 (27.1)	5 (10.4)
Nonhematologic adverse events		
Fever	9 (18.8)	0 (0)
Fatigue[a]	8 (16.7)	0 (0)
Anorexia	5 (10.4)	0 (0)
Diarrhea	5 (10.4)	0 (0)
Nausea[a]	4 (8.4)	0 (0)
Constipation	4 (8.4)	0 (0)
Alopecia	4 (8.4)	0 (0)
Pneumonitis	4 (8.4)	2 (4.2)
Herpes zoster	3 (6.25)	0 (0)
Increased blood creatinine	2 (4.2)	0 (0)
Increased AST[a]	1 (2.1)	0 (0)
Increased ALT[a]	1 (2.1)	1 (2.1)
Increased bilirubin	1 (2.1)	0 (0)

Note: All values are n (%).
[a]Treatment related.
ALT, alanine aminotransferase; AST, aspartate transaminase.

Discussion

To our knowledge, this is the first prospective study to reveal the efficacy and safety of palbociclib monotherapy in patients with TETs after disease progression on platinum-based chemotherapy. Palbociclib was found to have clinically meaningful antitumor activity with a long duration of disease control and tolerable safety profiles in previously treated patients with TETs. Palbociclib had a 12.5% ORR and 79.2% DCR. Half of the patients continued having good disease control with PR or stable disease at 12 months, and 22.9% were continuing palbociclib monotherapy with PR or stable disease at the time of data lock. Palbociclib also had encouraging PFS and overall survival data in both thymoma and thymic carcinoma.

Recent studies with targeted therapy or immunotherapy in patients with TETs have revealed high incidences of treatment-related adverse events, which is a main challenge. In a phase 2 study of pembrolizumab for patients with TETs, pembrolizumab had a high incidence of grade greater than or equal to 3 immune-related adverse events observed in 71.4% of the patients with thymoma and 15.4% of the patients with thymic carcinoma.[10,20] Given the risk of immune-related adverse events, patients with thymoma should not receive pembrolizumab. Furthermore, even in patients with thymic carcinoma, early detection and management of immune-related adverse events are critical in immune checkpoint inhibitor treatment.

Similarly, sunitinib had a 90% DCR, but 8% of the patients experienced grade 3 decline of left ventricular ejection fraction, including one case of cardiac arrest. In addition, 21% of the patients discontinued sunitinib owing to adverse events.[7] In contrast, palbociclib monotherapy was associated with low toxicities, which can allow long durations of treatment. In our study, four of six patients who achieved PR still continued palbociclib monotherapy for longer than 20 months without any treatment-related adverse events over grade 3. Although the treatment-related adverse events warranted treatment interruption in 14 patients (29.2%) and dose modification in eight patients (16.7%), primarily owing to adverse events such as neutropenia, anemia, and pneumonitis, these adverse events were manageable and reversible after a temporary dosing interruption or dose modification. Furthermore, no patients discontinued palbociclib monotherapy owing to treatment-related adverse events. Milciclib (PHA-848125AC) is a CDK inhibitor that has been evaluated in TET and had PFS at 3 months of 46.7%.[21] Lenvatinib had an ORR of 38% in patients with thymic carcinoma, and it could be a kind of reasonable treatment option after failing platinum-based chemotherapy.[22] The most frequent grade 3 treatment-related adverse events of lenvatinib was hypertension (64%) and palmar-plantar erythrodysesthesia syndrome (7%).

We performed gene expression analysis to find the potential biomarkers of palbociclib in 12 patients. Cell cycle- and DNA damage-related genes including *WEE1* and *TGFB2* were related with durable clinical benefits (PR or stable disease for longer than 12 mo). Previous biomarker analysis of CDK4, CDK6, cyclin D, cyclin E,

p16, and RB in the PALOMA-2 study did not reveal any predictive biomarkers related to the benefits of palbociclib in breast cancer.[23] Loss of p16 expression and homozygous deletion of CDKN2A are promising prognostic biomarkers in thymic carcinoma.[24] Further biomarker study is warranted to select patients who will most likely benefit from palbociclib.

Currently, several clinical trials of combination therapy using anti–programmed cell death protein 1/programmed death-ligand 1 with anticytotoxic T-lymphocyte antigen 4 or antiangiogenic drugs are ongoing. A phase 2 study of avelumab and axitinib is ongoing in patients with WHO type B3 thymoma or thymic carcinoma. The combination of pembrolizumab and sunitinib is under evaluation in a phase 2 trial enrolling patients with advanced and pretreated thymic carcinoma (NCT03463460). Two phase 2 trials are currently testing the activity of selinexor, which is a selective inhibitor of XPO1 in advanced and pretreated TETs (NCT03193437, NCT03466827).

Despite palbociclib monotherapy encouraging antitumor activity and having an acceptable safety profile in pretreated thymoma and thymic carcinoma in this study, there are limitations. Considering the response rate of less than 20% with palbociclib monotherapy, combination trials should be considered to improve the efficacy in TET. Given the indolent nature of TET in some patients, a randomized controlled study against cytotoxic chemotherapy or immunotherapy is warranted to confirm the efficacy of palbociclib monotherapy. As a limitation, this study included both thymoma and thymic carcinoma which are different disease spectrum.

In conclusion, our study revealed the efficacy and safety of palbociclib monotherapy in patients who progressed to platinum-based chemotherapy. Therefore, palbociclib monotherapy might be a salvage therapy for patients with TETs who failed platinum-based chemotherapy.

CRediT Authorship Contribution Statement

Hyun Ae Jung: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing—original draft/review and editing, Visualization.

Miso Kim: Software, Formal analysis, Investigation, Writing—original draft, Visualization.

Hae Su Kim: Conceptualization, Methodology, Project administration, Writing—review and editing.

Joo-Hang Kim: Software, Formal analysis, Investigation, Visualization, Writing—review and editing.

Yoon Hee Choi: Formal analysis, Investigation, Resources, Data curation, Writing—review and editing.

Jinhyun Cho: Conceptualization, Methodology, Investigation, Writing—review and editing.

Ji Hyun Park: Conceptualization, Methodology, Investigation, Writing—review and editing.

Keon Uk Park: Conceptualization, Methodology, Investigation, Writing—review and editing.

Bo Mi Ku: Conceptualization, Methodology, Investigation, Writing—review and editing.

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Se-Hoon Lee: Conceptualization, Methodology, Investigation, Writing—review and editing.

Jin Seok Ahn: Conceptualization, Methodology, Investigation, Writing—review and editing.

Keunchil Park: Conceptualization, Methodology, Investigation, Writing—review and editing.

Myung-Ju Ahn: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing—review and editing, Supervision, Project administration, Funding acquisition.

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Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *Journal of Thoracic Oncology* at www.jto.org and at https://doi.org/10.1016/j.jtho.2022.10.008.

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