Study Of Palbociclib Combined With Chemotherapy In Pediatric Patients With Recurrent/Refractory Solid Tumors

Status: Recruiting

Eligibility Criteria

Age: 2 years to 20 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion: 1. Histologically confirmed relapsed or refractory solid tumor as follows:

• For dose escalation and dose determination parts: Histologically confirmed relapsed or refractory solid tumor (including CNS tumors but not lymphomas). Patients with Diffuse Intrinsic Pontine Glioma do not require histological only radiographic confirmed relapse to enroll.

• For dose expansion and tumor specific cohorts: Histologically confirmed relapsed or refractory solid tumor including but not limited to EWS, rhabdoid tumor, rhabdomyosarcoma, neuroblastoma, and medulloblastoma. Patients with Diffuse Intrinsic Pontine Glioma do not require histological only radiographic confirmed relapse to enroll. EWS is not eligible for TOPO and CTX tumor-specific cohorts.

• For randomized Phase 2 part: Histologically confirmed Ewing sarcoma at diagnosis or at relapse, with presence of EWSR1-ETS or FUS-ETS rearrangement. Histopathology confirmation of both EWSR1-ETS or FUS-ETS rearrangement partners is required OR availability of formalin fixed paraffin embedded (FFPE) tumor tissue sample for central testing. Patient must have relapsed or have refractory disease and at least evaluable disease in at least one site other than bone marrow that can be followed by imaging. 2. Age ≥2 and <21 years at the time of study entry. 3. Lansky performance status ≥50% for patients ≤16 years of age, or Eastern Cooperative Oncology Group (ECOG) 0, 1 or 2 for patients >16 years of age. 4. Adequate bone marrow function.

• Absolute neutrophil count ≥1000/mm3;

• Platelet count ≥100,000/mm3 (transfusion independent, no platelet transfusion in past 7 days prior study entry);

• Hemoglobin ≥8.5 g/dL (transfusion allowed). 5. Adequate renal function: Serum creatinine level based on age/gender must within protocol specified limits. 6. Adequate liver function, including:

• Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5 × upper limit of normal (ULN) or ≤5 × ULN for age, if attributable to disease involvement of the liver;

• Total bilirubin ≤1.5 × ULN for age, unless the patient has documented Gilbert's syndrome. 7. Patients enrolled to Phase 1 portion of the study and tumor specific cohorts must have measurable disease as defined by RECIST version 1.1 or modified RANO criteria for CNS disease or INRC for neuroblastoma. Patients with EWS enrolled to Phase 2 portion of the study are eligible with evaluable disease (eg, bone only disease with no soft tissue component). 8. Recovered to CTCAE Grade ≤1, or to baseline, from any non-hematological acute toxicities of prior surgery, chemotherapy, immunotherapy, radiotherapy, differentiation therapy or biologic therapy, with the exception of alopecia. 9. Serum/urine pregnancy test (for all girls ≥8 years of age) negative at screening and at the baseline visit. Exclusion: 1. Phase 1 and tumor specific cohorts: For palbociclib with IRN and TMZ combination, prior treatment with a CDK4/6 inhibitor or progression while on treatment with an IRN-containing regimen that includes TMZ. Patients who have received the combination of IRN and TMZ and did not progress while on these medications are eligible. For patients enrolling in the palbociclib with TOPO and CTX combination, prior treatment with a CDK4/6 inhibitor or progression while on treatment with a TOPO-containing regimen that includes CTX. Patients who have received the combination of TOPO and CTX and did not progress while on these medications are eligible. Phase 2 portion: prior treatment with a CDK4/6 inhibitor or progression while on treatment with an IRN-containing or TMZ-containing regimen. Patients who have received IRN and/or TMZ and did not progress while on these medications are eligible. 2. Prior intolerability to IRN and/or TMZ plus/minus palbociclib with IRN and TMZ combination and prior intolerability to TOPO and/or CTX for TOPO and CTX combination. 3. Use of strong cytochrome P450 (CYP) 3A inhibitors or inducers. Patients who are receiving strong uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) inhibitors within 12 days of Cycle 1 Day 1 (C1D1) are not eligible for the palbociclib with IRN and TMZ combination. Patients who are receiving strong UGT1A1 inhibitors within 12 days of C1D1 are eligible for the palbociclib with TOPO and CTX combination (See Section 5.7.1 for list of products.) 4. Systemic anti cancer therapy within 2 weeks prior to study entry and 6 weeks for nitrosoureas. 5. Prior irradiation to >50% of the bone marrow (see Appendi 9). 6. Participation in other studies involving investigational drug(s) within 2 weeks or 5 half lives, whichever is longer, prior to study entry. 7. Major surgery within 4 weeks prior to study entry. Surgical biopsies or central line placement are not considered major surgeries. 8. For IRN and TMZ with/without palbociclib combinations: known or suspected hypersensitivity to palbociclib, IRN and/or TMZ. For combination of palbociclib with TOPO and CTX: known or suspected hypersensitivity to palbociclib, TOPO and/or CTX. 9. Patients with known symptomatic brain tumors or brain metastases and require steroids, unless they have been on a stable or on a decreasing steroid dose for >14 days. 10. Patients with previously diagnosed brain metastases are eligible if they have completed their prior treatment and have recovered from the acute effects of radiation therapy or surgery prior to study entry for these metastases for at least 14 days post radiation and 4 weeks post-surgery and are neurologically stable. 11. Hereditary bone marrow failure disorder. 12. QTc >470 msec. 13. History of clinically significant or uncontrolled cardiac disease, including:

• History of or active congestive heart failure; if patient had congestive heart failure resolve and >1 year from resolution, patient will be considered eligible;

• Clinically significant ventricular arrhythmia (such as ventricular tachycardia, ventricular fibrillation or Torsades de Pointes);

• Diagnosed or suspected congenital or acquired prolonged QT syndrome;

• Need for medications known to prolong the QT interval;

• Uncorrected hypomagnesemia or hypokalemia because of potential effects on the QT interval;

• Left ventricular ejection fraction <50% or shortening fraction <28%. 14. Recent or ongoing clinically significant gastrointestinal disorder that may interfere with absorption of orally administered drugs (eg, gastrectomy). 15. Severe acute or chronic medical or laboratory test abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results, and in the judgment of the Investigator, would make the patient inappropriate for entry into this study. 16. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or patients who are Pfizer employees, including their family members, directly involved in the conduct of the study.

Conditions & Interventions

Interventions:

Drug: Palbociclib, Drug: Temozolomide, Drug: Irinotecan, Drug: Topotecan, Drug: Cyclophosphamide

Conditions:

Ewing Sarcoma, Solid Tumors, Rhabdoid Tumor, Rhabdomyosarcoma, Neuroblastoma, Medulloblastoma, Diffuse Intrinsic Pontine Glioma

Keywords:

Ewing Sarcoma, EWS, Solid Tumor, Recurrent Solid Tumors, Refractory Solid Tumors, Bone Cancer, Bone Tumor, Bone Sarcoma, Soft Tissue Cancer, Soft Tissue Sarcoma, Recurrent Ewing Sarcoma, Refractory Ewing Sarcoma, Relapsed Ewing Sarcoma, Pediatric Cancer, Childhood Cancer, Ewing Sarcoma Treatment, Palbociclib, CDK4/6 Inhibitor, Irinotecan, Temozolomide, Topotecan, Cyclophosphamide

More Information

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