

Unique Protocol ID: 13199

Secondary ID: I3Y-MC-JPBA

Brief Title: Phase 1 Study of CDK4/6 Dual Inhibitor in Patients with Cancer

Official Title: Phase 1 Study of a CDK4/6 Dual Inhibitor in Patients with Advanced Cancer

Study Type: Interventional

Sponsor: Eli Lilly and Company

Collaborators: N/A

Brief Summary:

The objective of this Phase 1 study is to evaluate the safety and tolerability of CDK4/6 Dual Inhibitor in patients with advanced cancer. The study includes dose escalation and dose confirmation components.

Overall Status: Recruiting

Study Start Date: December 2009

Study Completion Date: April 2012 Anticipated

Study Design:

Primary Purpose: Treatment

Study Phase: Phase 1

Interventional Model: Single Group Assignment

Number of Arms: 1

Masking: Open Label

Allocation: Non-Randomized

Endpoint Classification: Safety

Enrollment: 84 Anticipated

Primary Outcome Measure:

Measure: Evaluate the safety and tolerability of CDK4/6 Dual Inhibitor when administered orally to patients with advanced cancer.

Timeframe: Throughout study

Secondary Outcome Measure:

Measure: Determine maximum plasma concentration (Cmax)

Timeframe: Cycle 1

Measure: Determine area under the concentration/time curve (AUC)

Timeframe: Cycle 1

Measure: Evaluate pharmacodynamic effects in surrogate tissues and tumors

Timeframe: Cycle 1

Measure: Document the antitumor activity of CDK4/6 inhibitor

Timeframe: Cycle 2, then every other cycle

Measure: Establish a recommended dose range for Phase 2 studies

Timeframe: End of study

Condition(s):

Advanced Cancer (Solid Tumor or Lymphoma)

Arms	Assigned Interventions
Experimental: CDK4/6 Dual Inhibitor This study involves dose escalation followed by dose confirmation.	Drug: CDK4/6 Dual Inhibitor The CDK4/6 Dual Inhibitor is administered orally once daily during 28-day cycles. Dose escalation will continue until the MTD is identified. Patients will receive two cycles but may have additional cycles if receiving clinical benefit.

Eligibility Criteria:

Inclusion Criteria:

- Must be an appropriate candidate for experimental therapy after available standard therapies have ceased to provide clinical benefit for his/her disease.
- Must have histological or cytological evidence of cancer, either a solid tumor or a lymphoma, which is advanced and/or metastatic.
- For Dose Confirmation, must have measurable disease.
- Must be at least 18 years of age.
- Must have given written informed consent prior to any study-specific procedures
- Must have adequate organ function including:
 - Hematologic: Absolute neutrophil count (ANC) $\geq 1.5 \times 10^9/L$, platelets $\geq 100 \times 10^9/L$, and hemoglobin ≥ 8 g/dL.
 - Hepatic: Bilirubin ≤ 1.5 times upper limits of normal (ULN) and alanine aminotransferase (ALT) ≤ 3.0 times ULN.
 - Renal: Serum creatinine ≤ 1.5 times ULN.
- Must have a performance status ≤ 1 for Dose Escalation and ≤ 2 for Dose Confirmation on the Eastern Cooperative Oncology Group (ECOG) scale.
- Must have discontinued all previous therapies for cancer (including chemotherapy, radiotherapy, immunotherapy, and investigational therapy) for at least 21 days for myelosuppressive agents or 14 days for nonmyelosuppressive agents prior to receiving study drug, and recovered from the acute effects of therapy (treatment related toxicity resolved to baseline) except for residual alopecia. At the discretion of the investigator, patients with breast or prostate cancers progressing on endocrine therapies may have that treatment continued while receiving study drug.
- Must be reliable, available for the duration of the study, and willing to follow study procedures.
- For males and females with reproductive potential, must agree to use medically approved contraceptive precautions during the trial and for 3 months following the last dose of study drug.
- For females with child bearing potential, must have a negative serum pregnancy test within 3 days of the first dose of study drug.
- Must have an estimated life expectancy of ≥ 12 weeks.
- Must be able to swallow capsules.

Exclusion Criteria:

- Has received treatment with a drug that has not received regulatory approval for any indication within 14 or 21 days of the initial dose of study drug for a nonmyelosuppressive or myelosuppressive agent, respectively.
- Has a personal history of any of the following conditions: presyncope or syncope of either unexplained or cardiovascular etiology, ventricular arrhythmia (including but not limited to ventricular tachycardia and ventricular fibrillation), sudden cardiac death,

sudden cardiac arrest, myocardial infarction, coronary artery bypass grafting, or congestive heart failure.

- Has a baseline ECG with any of the following abnormal findings: ventricular arrhythmia, evidence of acute myocardial ischemia, evidence of prior myocardial infarction, heart block (of any degree), or prolongation (QTc \geq 450 milliseconds) of the QTc interval.
- Has serious preexisting medical conditions that, in the judgment of the investigator, would preclude participation in this study.
- For Dose Escalation, has CNS malignancy or metastasis. For Dose Confirmation, has symptomatic CNS malignancy or metastasis. Patients with previously-treated CNS malignancy or metastasis are eligible if they are not currently receiving anticoagulants and their disease is radiographically stable for at least 14 days prior to receiving study drug, regardless of whether they are receiving corticosteroids.
- Has an acute leukemia.
- Has received an autologous or allogeneic stem-cell transplant within 75 days of the initial dose of study drug.
- For a female, is pregnant or lactating.
- Has active bacterial, fungal, and/or known viral infection.

Minimum Age: 18 years

Maximum Age: N/A

Gender: both

Contact for Public Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST)

Contact for Scientific Queries: Call 1-877-CTLILLY (1-877-285-4559) or 1-317-615-4559 Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, EST)

Locations:

Lilly Clinical Trial Site
Santa Monica, CA
Recruiting

Lilly Clinical Trial Site
San Antonio, TX
Recruiting

Lilly Clinical Trial Site
Boston, MA
Recruiting