University of Wisconsin
Carbone Cancer Center

CO 10906 FAST FACT SHEET

CO 10906, "Phase 1 Study of LY573636-sodium in Patients with Essential Thrombocythemia and Acute Myeloid Leukemia"
Principal Investigator: Ryan Mattison, M.D.
Study Chair: NA
Study Sponsor: Eli Lilly
Background: LY573636-sodium is a novel acylsulfonamide compound.
LY573636-sodium appears to induce apoptosis via a mitochondrial dependent mechanism, associated with decreased adenosine triphosphate (ATP) generation. LY573636-sodium is active against multiple malignant cell types in vitro, including leukemia, non-small cell lung cancer (NSCLC), colon cancer, melanoma, ovarian cancer, renal cancer, and breast cancer. It has activity seen against myeloid, lymphoid leukemia and megakaryocytic cell lines.
There have been 400+ patients have received LY573636-sodium in various phase I clinical studies, primarily refractory solid tumors. The DLT's include thrombocytopenia, neutropenia, and anemia. There has been some life-threatening bleeding with concomitant warfarin use

Objectives: The primary purpose is to determine recommended phase II dose. The secondary objectives are: to assess safety, tolerability of drug; to estimate PK parameters; to explore PD biomarkers of apoptosis, cell cycle progression, gene expression; and lastly to estimate response rates in ET and R/R AML.

Treatment Plan:
Subjects will receive a 2-hour infusion of LY573636-sodium on cycle 1 day 1. Subjects may receive additional cycles if benefit is seen. The cycle length is 35 days for Acute Myeloid Leukemia (AML) patients or 28 days for Essential Thrombocythemia (ET) patients. There will be PK sampling cycle 1 day 1 at 0, 1, 2 hours and 1, 2, and 4 hours after the infusion is complete; Cycle 1 Day 8, 14, 21, and 28. There will be bone marrow biopsies for AML patients (required) on Day 14 day 28 of cycle 1.

Eligibility:

RN reconsent patient Day 1 if consent form outside protocol window OR patient consented via phone (remember to review consent form v. date & IRB expiration date in Oncore)
"Based on currently available clinical information, it is felt that the subject meets the defined life expectancy criterion. (Dr. Mattison confirms that this criterion is 3 months.
Must have either Essential Thrombocytemia (ET) or AML who have relapsed or refractory disease after at least 1 prior standard treatment. If patients have APL, they must be resistant and/or intolerant of both all-trans retinoic acid (ATRA) and arsenic trioxide. A baseline bone marrow assessment is required ≤14 days prior to the first dose of study drug for patients with AML.
Must be ≥18 years of age.
Must have given written informed consent approved by Lilly and the ethical review board (ERB)/institutional review board (IRB) governing the site.

Must have adequate organ function including: ▪ Hepatic: Bilirubin ≤1.5 times upper limits of normal (ULN) ▪ alanine transaminase (ALT) ≤ 2.5 times ULN ▪ aspartate transaminase (AST) ≤ 2.5 times ULN ▪ alkaline phosphatase ≤ 2.5 times ULN, and ▪ serum albumin level ≥3.0 g/dL (30 g/L) ▪ Renal: Serum creatinine ≤1.5 times ULN
Must have performance status of ≥2 on the Eastern Cooperative Oncology Group (ECOG) scale
Must have discontinued all previous therapies for cancer, including chemotherapy, radiotherapy, immunotherapy, cancer-related hormonal therapy, or other investigational therapy for at least 21 days for myelosuppressive agents (such as cytarabine, daunorubicin, and gemtuzumab ozogamicin) or 14 days for non-myelosuppressive agents prior to receiving study drug, and recovered from the acute effects of therapy (such as neurotoxicity, diarrhea, and mucositis) except for residual myelosuppression and alopecia. Hydroxyurea used to control peripheral blood blast count is permitted within these respective periods, but it must be stopped at least 24 hours before study drug administration.
Must be reliable and willing to make themselves available for the duration of the study and are willing to follow study procedures.
Males and females with reproductive potential must agree to use medically approved contraceptive precautions during the trial and for 6 months following the last dose of study drug.
Females of child bearing potential must have had a negative serum pregnancy test ≤ 7 days prior to the first dose of study drug.
Must have a serum albumin level □3.0 g/dL or □30 g/L less than or equal to 72 hours prior to dosing with LY573636.
Must not have 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 non-myelosuppressive or myelosuppressive agent, respectively.
Must not have myeloproliferative disorders (for example, chronic myeloid leukemia, polycythemia vera, and primary myelofibrosis) other than ET.
Must not have received an autologous or allogenic stem cell transplant within 75 days of the initial dose of study drug for the dose escalation phase or within 60 days of the initial dose of study drug for the dose confirmation phase. In addition, recipients of an allogeneic stem cell transplant must have discontinued immunosuppressive therapy at least 24 hours before study drug administration with no more than Grade 1 acute graft-versus-host disease. Please see protocol attachment JZAJ.6 for grading and staging of graft-versus-host disease.
Must not have previously completed or withdrawn from this study or any other study investigating LY573636.
Must not have serious preexisting medical conditions that in the opinion of the investigator would preclude participation in this study.
Must not have leukemic involvement of the CNS as shown by spinal fluid cytology or imaging. Patients with signs or symptoms of leukemic meningitis or a history of leukemic meningitis must have a negative lumbar puncture within 14 days of study enrollment.
Must not have serious concomitant disorders, including active bacterial, fungal, or viral infection, incompatible with the study (at the discretion of the investigator).
Must not have a second primary malignancy that could affect interpretation of the results.
Must not have a known coagulopathy or bleeding disorder, other than leukemia-related thrombocytopenia. Patients with severe or life-threatening bleeding refractory to platelet transfusion are also excluded from this study.
Must not have had major surgery within 4 weeks of study enrollment.
Must not be receiving warfarin (Coumadin®).
Must not be female who is pregnant or lactating.
Must not have known positive test results in human immunodeficiency virus (HIV), hepatitis B surface antigen (HBSAg), or hepatitis C antibodies (HCAb).

Potential Toxicities:
Very common side effects (10% or more of patients) that were reported as possibly related to LY573636 include:
Decrease in the number of cells in the blood responsible for blood clotting, (which may increase the chance of bruising and bleeding), decreased red blood cells (which may cause feelings of being tired), decreased white blood cells (can increase chance of developing infection), feeling sick to the stomach, feeling tired, rash, unusually frequent or loose stools, sores in the mouth and throat

Study Contact: Phase I Program, Carbone Cancer Center (608) 263-6222