Testing the Safety of the Anti-cancer Drugs Tazemetostat and Belinostat in Patients With Lymphomas That Have Resisted Treatment

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* DOSE ESCALATION PHASE: Patients with relapsed or refractory non-Hodgkin lymphoma including both B-cell non-Hodgkin lymphoma (NHL) and T-cell NHL. Refractory cutaneous T-cell lymphoma (CTCL) will be allowed if greater or equal to stage 1B and have previously failed two systemic therapies * DOSE EXPANSION PHASE: Patients with relapsed or refractory follicular, transformed lymphoma or germinal center B-cell diffuse large B-cell Lymphoma (GCB-DLBCL) as defined by Hans criteria, as well as T-cell lymphomas. For patients with B-cell lymphomas, equal numbers of patients will be enrolled onto one of 2 arms: (1) mutated EZH2 or (2) wild-type EZH2. EZH2 mutations will be identified by polymerase chain reaction (PCR) * Patients must not be eligible for, or have refused, stem cell transplantation or chimeric antigen receptor T-cell (CAR T-cell) therapy * Patients who have undergone 1-5 prior treatments of any type (progression after transplant/cellular therapy allowed) are eligible * Patients must have measurable disease according to the Lugano classification * Age \>= 18 years. Because no dosing or adverse event data are currently available on the use of tazemetostat in combination with belinostat in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 (Karnofsky \>= 60%) * Absolute neutrophil count \>= 1,000/mcL * If there is documented lymphomatous involvement of the bone marrow as assessed by bone marrow biopsy within 90 days prior to registration, participants should have: absolute neutrophil count (ANC) \>= 0.75 × 10\^9/L * Platelets \>= 75,000/mcL * If there is documented lymphomatous involvement of the bone marrow as assessed by bone marrow biopsy within 90 days prior to registration, participants should have: platelets \>= 50 x 10\^9/L * Total bilirubin =\< 1.5 institutional upper limit of normal (ULN); unless due to Gilbert's disease, hemolysis, or lymphomatous involvement of liver, in which case total bilirubin should be =\< 5 x institutional ULN * Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \[SGPT\]) =\< 3 x institutional ULN; unless due to Gilbert's disease, hemolysis, or lymphomatous involvement of liver, in which case AST(SGOT)/ALT(SGPT) should be =\< 5 x institutional ULN * Glomerular filtration rate (GFR) \>= 30 mL/min/1.73 m\^2 * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial * For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated * Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load * Patients with treated brain metastases are eligible if follow-up brain imaging after central nervous system (CNS)-directed therapy shows no evidence of progression * Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. Patients whose lymphoma has transformed from a less aggressive histology remain eligible * Patients should be New York Heart Association Functional Classification of class II or better * Patients must have a QT interval corrected by Fridericia's formula (QTcF) =\< 450 msec * Able to swallow and retain orally-administered medication and does not have any clinically significant gastrointestinal abnormalities that may alter absorption, such as malabsorption syndrome or major resection of the stomach or bowels * The effects of tazemetostat and belinostat on the developing human fetus are unknown. For this reason, women of child-bearing potential must agree to use two reliable methods of contraception simultaneously prior to study entry and for the duration of study participation and for 6 months after the last dose of the study treatment. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 3 months after completion of tazemetostat and belinostat administration. Male participants must not donate semen or sperm from first dose of study drug, during study treatment (including during dose interruptions), and for 3 months after study drug discontinuation * Ability to understand and the willingness to sign a written informed consent document. Participants with impaired decision-making capacity who have a legally-authorized representative (LAR) and/or family member available will also be eligible * Patients that have received prior chemotherapy or radiotherapy must have completed their last treatment at least 2 weeks before entering the study. Rituximab given between EZH2 analysis and initiation of study drugs will be allowed

---

Exclusion Criteria:

* Patients who have not recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities \> grade 1) with the exception of alopecia * Patients who are receiving any other investigational agents * Patients with active central nervous system (CNS) metastases, including lymphomatous meningitis, as the study drugs are not known to effectively treat CNS disease * History of allergic reactions attributed to belinostat or tazemetostat, or to compounds of similar chemical or biologic composition to these agents * Patients receiving any medications or substances that are strong or moderate inhibitors or inducers of CYP3A4 within 14 days prior to study treatment are ineligible. Patients receiving strong UGT1A1 inhibitors are ineligible due to expected increased exposure to belinostat and potential for increased toxicity. Because the list of these agents is constantly changing, it is important to regularly consult a frequently-updated medical reference. As part of the enrollment/informed consent procedures, the patient will be counseled on the risk of interactions with other agents, and what to do if new medications need to be prescribed or if the patient is considering a new over-the-counter medicine or herbal product * Patients with known UGT1A1 genetic polymorphisms, such as UGT1A1*28, are excluded as they can have reduced UGTA1A activity and may be at risk for increased belinostat exposure * Patients with uncontrolled intercurrent illness * Pregnant women are excluded from this study because belinostat, as an HDAC inhibitor, and tazemetostat, as an EZH2 inhibitor, both have the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with belinostat and tazemetostat, breastfeeding should be discontinued if the mother is treated with belinostat and tazemetostat. Women of childbearing potential must have negative urine or serum pregnancy test to be eligible for this study * Systemic steroids that have not been stabilized to the equivalent of =\< 10 mg/day prednisone prior to the start of the study drugs and throughout the study. Patients are allowed to receive dexamethasone as premedication during belinostat infusion * Has thrombocytopenia, neutropenia, or anemia of grade \>= 3 (per Common Terminology Criteria for Adverse Events \[CTCAE\] 5.0 criteria) or any prior history of myeloid malignancies, including myelodysplastic syndrome (MDS) * Has abnormalities known to be associated with MDS (e.g. 5q deletion \[del 5q\], chromosome 7 abnormality \[chr 7 abn\]) and multiple primary neoplasms (MPN) (e.g. JAK2 V617F) observed in cytogenetic testing and deoxyribonucleic acid (DNA) sequencing * Has a prior history of T lymphoblastic lymphoma/T acute lymphoblastic leukemia (T-LBL/T-ALL)

Conditions & Interventions

Interventions:

DRUG: Belinostat, PROCEDURE: Biopsy Procedure, PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, OTHER: Pharmacokinetic Study, PROCEDURE: Positron Emission Tomography and Computed Tomography Scan, DRUG: Tazemetostat

Conditions:

Recurrent B-Cell Non-Hodgkin Lymphoma, Recurrent Diffuse Large B-Cell Lymphoma Germinal Center B-Cell Type, Recurrent Follicular Lymphoma, Recurrent Non-Hodgkin Lymphoma, Recurrent Primary Cutaneous T-Cell Non-Hodgkin Lymphoma, Recurrent T-Cell Non-Hodgkin Lymphoma, Recurrent Transformed Non-Hodgkin

Hodgkin Lymphoma, Recurrent Primary Cutaneous T-Cell Non-Hodgkin Lymphoma, Recurrent T-Cell Non-Hodgkin Lymphoma, Recurrent Transformed Non-Hodgkin Lymphoma, Refractory B-Cell Non-Hodgkin Lymphoma, Refractory Diffuse Large B-Cell Lymphoma Germinal Center B-Cell Type, Refractory Follicular Lymphoma, Refractory Non-Hodgkin Lymphoma, Refractory Primary Cutaneous T-Cell Non-Hodgkin Lymphoma, Refractory T-Cell Non-Hodgkin Lymphoma, Refractory Transformed Non-Hodgkin Lymphoma

More Information

Contact(s): ctrrecruit@vcu.edu
Principal Investigator:
Phase: PHASE1
IRB
Number:
System ID: NCT05627245
