

Adding Pirtobrutinib to the Usual Treatment for People With Newly Diagnosed Richter Transformation, The PIRAMID Trial

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Participants must have been diagnosed with Richter Transformation (RT) (CLL/small lymphocytic lymphoma [SLL] to LBCL) * Participants must have histologically or cytologically confirmed LBCL * Participants must have measurable disease determined by PET/CT or hematopathology (by morphology or flow cytometry) assessment within 42 days prior to registration * Participants must have staging PET/CT imaging performed within 42 days prior to registration * Participants are allowed prior treatments for CLL/SLL or its complications (autoimmune hemolytic anemia [AIHA], immune thrombocytopenic purpura [ITP]), with the exception of pirtobrutinib * Participants must not have prior treatment for Richter transformation except for corticosteroids up to equivalent dose of prednisone 700 mg total for less than 7 days for disease control. Treatment for CLL/SLL with CLL/SLL directed drugs (including BTK inhibitors with the exception of pirtobrutinib) after the Richter transformation diagnosis is allowed for the purpose of disease control. CLL targeted therapies must be stopped within 3 days before initiation of therapy on protocol. Chemotherapy or anti-CD20 monoclonal antibody therapy must be stopped within 2 weeks before initiation of therapy on protocol * Participants must not have contraindication for receiving anthracycline. Participants must not have received more than a cumulative dose of 100mg/m² in those participants who will receive R-CHOP or not more than 250 mg/m² in those participants who will receive R-mini-CHOP of prior doxorubicin (or equivalent dose of another anthracycline, such as epirubicin) therapy (at any time prior to registration) * Patients requiring strong CYP3A inducers are not eligible and can only be enrolled if * an alternative treatment to the strong CYP3A inducer is available for them and * the last dose of the strong CYP3A inducer is administered at least 7 days before initiation of pirtobrutinib for patients in safety run-in and arm 1 * Participant must be ≥ 18 years old at the time of registration * Participant must have Eastern Cooperative Oncology Group (ECOG)/Zubrod Performance Status of 0-2 * Participant must have a complete medical history and physical exam within 28 days prior to registration * Absolute neutrophil count (ANC) ≥ 0.75 x 10³/μL or ≥ 0.50 x 10³/μL in participants with suspected marrow involvement considered to impair hematopoiesis (within 28 days prior to registration) * Platelets ≥ 50 x 10³/μL or ≥ 30 x 10³/μL in participants with suspected marrow involvement considered to impair hematopoiesis (within 28 days prior to registration) * Hemoglobin ≥ 8 g/dL (≥ 80 g/L) or ≥ 6 g/dL in participants with suspected bone marrow involvement considered to impair hematopoiesis (within 28 days prior to registration) * Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) or ≤ 3 x ULN with documented liver involvement and/or Gilbert's disease (within 28 days prior to registration) * Aspartate aminotransferase (AST) / alanine aminotransferase (ALT) ≤ 3 x institutional ULN or ≤ 5 ULN with documented liver involvement (within 28 days prior to registration) * Participants must have a calculated creatinine clearance ≥ 30 mL/min using the Cockcroft-Gault Formula. This specimen must have been drawn and processed within 28 days prior to registration. For the Cockcroft-Gault formula for calculated creatinine clearance, see the tools on the CRA Workbench <https://txwb.crab.org/TXWB/Tools.aspx> * Participants must have a left ventricular ejection fraction (LVEF) ≥ 45% as measured by echocardiogram or radionuclide (MUGA) ventriculography within 56 days prior to registration * Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, participants must be class 2B or better * HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. Participants' HIV-directed therapy cannot have known interactions with pirtobrutinib * Participants with a known history of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load while on suppressive therapy on the most recent test results obtained within 6 months prior to registration * Participants with a known history of hepatitis C virus (HCV) infection must have been treated and cured. Participants currently being treated for HCV infection must have undetectable HCV viral load test on the most recent test results obtained within 6 months prior to registration * Participants must be able to swallow and retain oral medications and have no known gastrointestinal disorders likely to interfere with absorption of oral medications * Participants must not have a prior or concurrent malignancy in addition to CLL/SLL and Richter transformation whose natural history or treatment (in the opinion of the treating physician) has the potential to interfere with the safety or efficacy assessment of the investigational regimen * Participants must not have had major surgery within 28 days prior to registration * Participants must not have experienced a major bleeding event or grade ≥ 3 arrhythmia on prior treatment with a BTK inhibitor. * NOTE: Major bleeding is defined as bleeding having one or more of the following features: potentially life-threatening bleeding with signs or symptoms of hemodynamic compromise; bleeding associated with a decrease in the hemoglobin level of at least 2g per deciliter; or bleeding in a critical area or organ (e.g., retroperitoneal, intraarticular, pericardial, epidural, or intracranial bleeding or intramuscular bleeding with compartment syndrome) * Participants must not be pregnant or nursing (nursing includes breast milk fed to an infant by any means, including from the breast, milk expressed by hand, or pumped). Individuals who are of reproductive potential must have agreed to use an effective contraceptive method with details provided as a part of the consent process. A person who has had menses at any time in the preceding 12 consecutive months or who has semen likely to contain sperm is considered to be of "reproductive potential." In addition to routine contraceptive methods, "effective contraception" also includes refraining from sexual activity that might result in pregnancy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) including hysterectomy, bilateral oophorectomy, bilateral tubal ligation/occlusion, and vasectomy with testing showing no sperm in the semen * Participants must be offered the opportunity to participate in specimen banking * Participants must agree to have blood and lymphatic tissue specimens submitted for the integrated translational medicine study * For randomized participants only: Participants who can complete PRO-CTCAE and FACIT GP5 questionnaires forms in English or Spanish must be offered the opportunity to participate in the patient-reported outcome

Conditions & Interventions

Interventions:

PROCEDURE: Biospecimen Collection, PROCEDURE: Computed Tomography, DRUG: Cyclophosphamide, DRUG: Doxorubicin Hydrochloride, PROCEDURE: Echocardiography Test, PROCEDURE: Multigated Acquisition Scan, DRUG: Pirtobrutinib, PROCEDURE: Positron Emission Tomography, DRUG: Prednisone, BIOLOGICAL: Rituximab, BIOLOGICAL: Rituximab and Hyaluronidase Human, OTHER: Survey Administration, DRUG: Vincristine

Conditions:

Richter Syndrome, Transformed Chronic Lymphocytic Leukemia to Diffuse Large B-Cell Lymphoma, Transformed Small Lymphocytic Lymphoma to Diffuse Large B-Cell Lymphoma

More Information

Contact(s): ctrrecruit@vcu.edu

Principal Investigator:

IRB

Number:

System ID: NCT07220187

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