Epcoritamab Plus Ibrutinib for the Treatment of Relapsed or Refractory Aggressive B-Cell Non-Hodgkin Lymphoma

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* One of the following CD20+ B-cell non-Hodgkin lymphoma subtypes (note, documentation of CD20 positivity by flow cytometry and/or immunohistochemistry is based on any representative pathology report) * Diffuse large B-cell lymphoma (DLBCL), including DLBCL, not otherwise specified (NOS); T-cell/histiocyte-rich large B-cell lymphoma; and Epstein-Barr virus-positive DLBCL, NOS * High-grade B-cell lymphoma (HGBL) with MYC and BCL2 and/or BCL6 rearrangements (double-hit or triple-hit lymphoma) or HGBL, NOS * Primary mediastinal B-cell lymphoma (PMBCL) * Follicular lymphoma, grade 3b (also known as follicular large B-cell lymphoma in the 5th edition of World Health Organization \[WHO\] classification of lymphoid neoplasms) * Patients with previously diagnosed indolent lymphoma (follicular lymphoma or marginal zone lymphoma but not lymphoplasmacytic lymphoma or small lymphocytic lymphoma/chronic lymphocytic leukemia) who have transformed to any of the above lymphoma subtypes are eligible * Patients must have relapsed or refractory aggressive B-cell lymphoma and received prior treatment with an anthracycline in combination with an anti-CD20 monoclonal antibody: * ≥ 2 prior systemic lymphoma treatments OR * ≥ 1 prior systemic lymphoma treatment in patients with high-risk disease defined as primary refractory or relapsed within 12 months of completing anthracycline-based frontline treatment who are ineligible for chimeric antigen receptor (CAR) T cells per the treating physician. The reason for CAR T-cell treatment ineligibility should be documented * Prior treatment with a BTK inhibitor is allowed if stopped due to lymphoma progression or treatment completion but not intolerance * Prior treatment with autologous stem cell transplant (ASCT) is allowed if ≥ 100 days prior to enrollment * Prior treatment with CAR T cells is allowed if ≥ 30 days prior to enrollment * Age ≥ 18 years. Because no dosing or adverse event data are currently available on the use of ibrutinib or epcoritamab in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 * Measurable disease (defined as \> 1.5 cm in diameter) or at least one PET fludeoxyglucose F-18 (FDG) avid area of disease * Absolute neutrophil count (ANC) ≥ 1,000/mcL * Platelet count ≥ 75,000/mcL. Platelet count ≥ 50,000/mcL is allowed in case of bone marrow involvement and/or splenomegaly * Hemoglobin ≥ 8 g/dL * Transfusion and/or growth factor support within 7 days (or 14 days in case of long-acting growth factors such as pegylated granulocyte colony-stimulating factor \[G-CSF\]) of enrollment to meet these requirements is not permitted * Total bilirubin ≤ 1.5 x the upper limit of the normal range (ULN) (unless due to Gilbert's disease or hemolysis in which case bilirubin must be \< 3 x ULN) * Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \[SGOT\]) \< 3 x institutional ULN * Alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase \[SGPT\]) \< 3 x institutional ULN * Creatinine clearance \> 45 mL/min calculated by Cockcroft-Gault. Patients on dialysis are not eligible * The effects of ibrutinib and epcoritamab on the developing human fetus are unknown. For this reason, women of child-bearing potential and men must agree to use adequate contraception (double barrier method of birth control or abstinence) 2 weeks before initiation of treatment, for the duration of study participation and for 12 months after completing treatment. Should a woman become pregnant or suspect that she is pregnant while she or her partner is participating in this study, she should inform the treating physician immediately. Men must agree to refrain from sperm donation for at least 12 months after the last dose of epcoritamab * Women of childbearing potential must have a negative serum (beta-human chorionic gonadotropin \[β-hCG\]) or urine pregnancy test at Screening. Women who are pregnant or breastfeeding are ineligible for this study * Patients must have the ability to understand and the willingness to sign a written informed consent document and Health Insurance Portability and Accountability Act (HIPAA) consent document. Voluntary written consent must be given before the performance of any study-related procedure not part of standard medical care, with the understanding that consent may be withdrawn by the patient at any time without prejudice to future medical care

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Exclusion Criteria:

* Prior therapy with a bispecific antibody targeting CD3 and CD20 * Prior lymphoma therapy should be completed greater than two weeks before the start of protocol therapy, except for corticosteroids used for palliation of symptoms * Patients who require immediate cytoreductive therapy for their lymphoma per the treating physician's assessment are ineligible * Patients with a history of allogeneic stem cell transplantation are excluded unless the transplant was \> 180 days before the first scheduled dose of ibrutinib AND the patient does not have evidence of active acute or chronic graft versus host disease AND the patient must not have taken immunosuppressive medications associated with the transplant for at least 1 month before the first scheduled dose of ibrutinib * Ongoing systemic treatment with a strong CYP3A inhibitor or inducer. Treatment with any strong CYP3A inhibitor or inducer needs to be stopped for 5 half-lives prior to starting treatment on trial * Major surgery within 4 weeks before the start of treatment other than surgery performed for lymphoma diagnosis * Known active central nervous system (CNS) involvement by lymphoma. Patients who are enrolled and subsequently identified to have pathologic confirmation of CNS involvement by lymphoma may be continued on the study at the discretion of the principal investigator * Active uncontrolled infection or infection requiring intravenous (IV) antibiotic therapy for \> 2 consecutive days within 2 weeks prior to the first dose of study drug * Evidence of current uncontrolled or symptomatic cardiovascular conditions, including, uncontrolled cardiac arrhythmias, history of or symptomatic congestive heart failure (New York Heart Association \[NYHA\] class III or greater), unstable angina, or myocardial infarction within the past 6 months. Poorly controlled or clinically significant atherosclerotic vascular disease including angioplasty, cardiac or vascular stenting within 6 months of enrollment * Known liver cirrhosis with moderate to severe hepatic impairment (Child-Pugh class B or C) * Clinically significant pulmonary disease or history of bronchospasm requiring intubation, or clinically significant active interstitial lung disease or pneumonitis * History of cerebrovascular accident or transient ischemic attack within the 6 months before day 1, cycle 1 of treatment * Any prior history of intracranial hemorrhage * Clinically significant known bleeding diatheses or platelet dysfunction disorders. * Receiving treatment with coumadin/warfarin * Known gastrointestinal disease or gastrointestinal procedure that will significantly interfere with the oral absorption or tolerance of ibrutinib including the inability to swallow pills/capsules * Any serious medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with the completion of treatment according to this protocol * Known allergy to any of the study medications, their analogues, or excipients in the various formulations of any agent * Prior solid organ transplant * History of other malignancies that could affect compliance with the protocol or interpretation of results in the opinion of the investigator * Participation in other interventional clinical trials, including those with other investigational agents not included in this trial, within 21 days of the first scheduled dose of ibrutinib (cycle 1 day -7) * Known history of HIV, active hepatitis C infection (HCV ribonucleic acid \[RNA\] polymerase chain reaction \[PCR\]-positive) and/or active hepatitis B infections (HBV DNA PCR-positive). If hepatitis B core (HBc) antibody is positive, the patient must be evaluated for the presence of HBV DNA by PCR. If HCV antibody is positive, the patient must be evaluated for the presence of HCV RNA by PCR. Patients with positive HBc antibody and negative HBV DNA by PCR are eligible. Patients with positive HCV antibody and negative HCV RNA by PCR are eligible * Pregnant or breastfeeding women are excluded from this study. Because there is an unknown, but potential risk for adverse events in nursing infants secondary to treatment of the mother with ibrutinib or epcoritamab, breastfeeding should be discontinued if the mother is treated with ibrutinib or epcoritamab * Patients with ongoing clinically significant grade ≥ 2 toxicity from prior therapy

Conditions & Interventions

Interventions:

PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Computed Tomography, BIOLOGICAL: Epcoritamab, DRUG: Ibrutinib, PROCEDURE: Positron Emission Tomography

BIOLOGICAL: Epcoritamab; DRUG: Ibrutinib; PROCEDURE: Positron Emission Tomography

Conditions:

Recurrent Diffuse Large B-Cell Lymphoma, Refractory Diffuse Large B-Cell Lymphoma, Recurrent Transformed Non-Hodgkin Lymphoma, Refractory Transformed Non-Hodgkin Lymphoma, Recurrent High Grade B-Cell Lymphoma With MYC and BCL2 or BCL6 Rearrangements, Recurrent High Grade B-Cell Lymphoma With MYC, BCL2, and BCL6 Rearrangements, Recurrent High Grade B-Cell Lymphoma, Not Otherwise Specified, Refractory High Grade B-Cell Lymphoma With MYC and BCL2 or BCL6 Rearrangements, Refractory High Grade B-Cell Lymphoma With MYC, BCL2, and BCL6 Rearrangements, Refractory High Grade B-Cell Lymphoma, Not Otherwise Specified, Recurrent Grade 3b Follicular Lymphoma, Recurrent Primary Mediastinal Large B-Cell Lymphoma, Refractory Grade 3b Follicular Lymphoma, Refractory Primary Mediastinal Large B-Cell Lymphoma

More Information

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