Zanubrutinib in Patients With DLBCL and MYD88 or NOTCH1 Mutation or CD5+

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patients must have a documented pathologic diagnosis of DLBCL at any stage. * Must have documented MYD88 L265P, CD79B, or NOTCH1 truncation mutation or be CD5+ by IHC. * Age ≥18 years on the day of signing the informed consent form. * Patients must have measurable disease on Positron Emission Tomography-Computed Tomography scan (CT/PET) imaging. * Patient must have received no more than one cycle of R-CHOP prior to enrollment. Length of time between first R-CHOP treatment and planned 2nd R-CHOP treatment should vary by no more than 21 days ± 3 days. * Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2. * Adequate bone marrow function as defined by: * Absolute neutrophil count (ANC) ≥1000/mm3, except for patients with bone marrow involvement in which ANC must be ≥500/mm3. * Platelet ≥75,000/mm3, except for patients with bone marrow involvement in which the platelet count must be ≥30,000/mm3. * Hemoglobin ≥7 g/dL, after transfusion if necessary * Adequate organ function defined as: * Creatinine clearance ≥30 mL/min as estimated by the Cockcroft-Gault equation. * Aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase, and alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase ≤2.5 × upper limit of normal (ULN). * Serum total bilirubin ≤3 x ULN (except patients with Gilberts syndrome 3g/dl). * Women of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to the start of treatment. * Women of childbearing potential and men must agree to use one of the following highly effective forms of birth control during the treatment and for 1 month following completion of study treatment for women and for 1 week following completion of study treatment for men. * combined (estrogen and progestogen containing) hormonal contraception: * oral * intravaginal * transdermal * progestogen-only hormonal contraception associated with inhibition of ovulation * oral * injectable * implantable * intrauterine device (IUD) * intrauterine hormone-releasing system (IUS) * bilateral tubal occlusion * vasectomized partner * heterosexual abstinence * Patients must not have any known allergies, hypersensitivity or intolerance to corticosteroids or monoclonal antibodies. * Able to provide written informed consent and can understand and agree to comply with the requirements of the study and the schedule of assessments.

Exclusion Criteria:

* Patients with high grade B-cell lymphoma with myelocytomatosis oncogene (MYC) and BCL-2 and/or BCL6 rearrangements. * Patients with brain metastasis. * Patients with peripheral neuropathy CTCAE grade ≥2. * Any uncontrolled or clinically significant cardiovascular disease including the following: * Myocardial infarction within 6 months before screening. * Unstable angina within 3 months before screening. * New York Heart Association class III or IV congestive heart failure. * History of clinically significant arrhythmias (eg, sustained ventricular tachycardia, ventricular fibrillation, torsades de pointes). * Prior malignancy within the past 3 years, except for curatively treated basal or squamous cell skin cancer, non-muscle-invasive bladder cancer, carcinoma in situ of the cervix or breast, or localized Gleason score 6 prostate cancer. * History of severe bleeding disorder such as hemophilia A, hemophilia B, von Willebrand disease, or history of spontaneous bleeding requiring blood transfusion or other medical intervention. * History of stroke or intracranial hemorrhage within 6 months before first dose of study drug. * Severe or debilitating pulmonary disease in the opinion of the treating investigator. * Unable to swallow capsules or disease significantly affecting gastrointestinal function such as malabsorption syndrome, resection of the stomach or small bowel, bariatric surgery procedures, symptomatic inflammatory bowel disease, or partial or complete bowel obstruction. * Active fungal, bacterial and/or viral infection requiring systemic therapy. * Underlying medical conditions that, in the investigator's opinion, will render the administration of study drug hazardous or obscure the interpretation of toxicity or AEs. * Active infection with HIV, or serologic status reflecting active hepatitis B or C infection as follows: * Presence of hepatitis B surface antigen (HBsAg) or hepatitis B core antibody (HBcAb). Patients with presence of HBcAb, but absence of HBsAg, are eligible if hepatitis B virus (HBV) DNA is undetectable (\< 20 IU), and if they are willing to undergo monitoring every 4 weeks for HBV reactivation. * Presence of hepatitis C virus (HCV) antibody. Patients with presence of HCV antibody are eligible if HCV RNA is undetectable. * Major surgery within 4 weeks of the first dose of study drug. * Pregnant or lactating women. * Left ventricular ejection fraction (LVEF) \<55% on screening echocardiogram. * Vaccination or requirement for vaccination with a live vaccine within 28 days prior to the first dose of study drug or at any time during planned study treatment. * Hypersensitivity to zanubrutinib, rituximab, cyclophosphamide, doxorubicin, vincristine, or prednisone. * Requires ongoing treatment with a strong CYP3A inducer (Table 3). * Concurrent participation in another therapeutic clinical trial. * Active and/or ongoing autoimmune anemia and/or autoimmune thrombocytopenia (eg, idiopathic thrombocytopenia purpura). * Requires ongoing treatment with warfarin or warfarin derivatives.

Conditions & Interventions

Interventions:
DRUG: Zanubrutinib
Conditions:
Diffuse Large B-Cell Lymphoma, DLBCL - Diffuse Large B Cell Lymphoma

More Information

Contact(s): Massey IIT Research Operations - masseyepd@vcu.edu
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT06846463

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