

Testing the Addition of Anti-Cancer Drug Sonrotoclax, to the Standard Treatment Zanubrutinib, for Previously Untreated CLL/SLL

Status: RECRUITING

Eligibility Criteria

Age: 65 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* STEP 0: This bone marrow or peripheral blood submission to Adaptive is mandatory prior to registration/randomization for real-time identification of the clone needed for MRD testing. The bone marrow sample should be from the first aspiration (i.e., first pull). Aspirate needle should be redirected if needed to get first pull bone marrow aspirate. It should be obtained as soon after pre-registration as possible to confirm registration eligibility * STEP 0: Patients must be diagnosed with CLL/SLL according to International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2018 criteria that includes all of the following: * $\geq 5 \times 10^9$ /L B lymphocytes (5000/ μ L) in the peripheral blood (CLL) or a lymph node biopsy demonstrating SLL with the below immunophenotype (SLL) * On morphologic review, the leukemic cells must be small mature lymphocytes * Immunophenotype of CLL cells (performed locally) must reveal a clonal B-cell population, which coexpress the B cell surface markers of CD19 and CD20, as well as the T-cell antigen CD5. Patients with bright surface immunoglobulin expression or lack of CD23 expression in $> 10\%$ of cells must lack t(11;14) translocation by interphase cytogenetics * STEP 0: Patients must meet criteria for treatment as defined by IWCLL 2018 guidelines which includes at least one of the following criteria: * Evidence of marrow failure as manifested by the development or worsening of anemia or thrombocytopenia (not attributable to autoimmune hemolytic anemia or thrombocytopenia), typically hemoglobin (Hb) < 10 g/dL, platelet count $< 100,000/\text{mm}^3$ * Massive (> 6 cm below the costal margin), progressive or symptomatic splenomegaly * Massive nodes (ie, > 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy * Autoimmune anemia and/or thrombocytopenia that is poorly responsive to standard therapy * Constitutional symptoms, which include any of the following: * Unintentional weight loss of $\geq 10\%$ within the previous 6 months * Significant fatigue (ie. Eastern Cooperative Oncology Group [ECOG] performance status [PS] ≥ 2) * Fevers $> 100.5^\circ\text{F}$ or 38.0°C for 2 weeks or more without evidence of infection * Night sweats > 1 month without evidence of infection * STEP 0: Patients must not have had prior therapy for CLL (except palliative steroids or treatment of autoimmune complications of CLL with rituximab or steroids) * STEP 0: Treatment with rituximab and/or high-dose corticosteroids for autoimmune complications of CLL must be completed prior to enrollment. Palliative steroids must be at a dose not higher than 20 mg/day of prednisone or equivalent corticosteroid at the time of registration * STEP 0: Age ≥ 65 years * STEP 0: ECOG performance status ≤ 2 * STEP 0: Patients with known HIV infection on effective anti-retroviral therapy with undetectable viral load within 6 months prior to registration are eligible for this trial * STEP 0: For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated * STEP 0: 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 * STEP 0: Patients must not be receiving active systemic anticoagulation with warfarin. Patients must be off warfarin therapy for at least 5 half-lives washout and with normal INR prior to enrollment * STEP 0: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients must be class 2B or better. Patients with acute cardiac events within 6 months prior to registration should be carefully evaluated for their suitability for enrollment * STEP 0: No patients with a history of a severe bleeding disorder or a history of hemorrhagic stroke or intracranial hemorrhage * STEP 0: No patients with known active progressive central nervous system (CNS) disease * STEP 0: No known medical condition causing an inability to swallow oral formulations of agents * STEP 1: The adaptive report confirming a measurable and trackable B cell clone * STEP 1: Patients may not have had major surgery within 7 days of enrollment, or minor surgery within 5 days of enrollment. Examples of minor surgery include dental surgery, insertion of a venous access device, skin biopsy, or aspiration of a joint. The decision about whether a surgery is major or minor can be made at the discretion of the treating physician * STEP 1: No patients with ongoing active fungal, bacterial or viral infection requiring systemic therapy except those described in the protocol document * STEP 1: Patients must not require more than 20 mg prednisone or equivalent corticosteroid daily * STEP 1: Patients must not have uncontrolled active systemic infection requiring intravenous antibiotics * STEP 1: Patients must not have continued requirement for therapy with a strong CYP3A4/5 inhibitor or inducer. Any such inhibitor or inducer must have been discontinued at least 14 days or 5 half-lives (whichever is shorter) before the first dose of study drug * STEP 1: Absolute neutrophil count (ANC) $\geq 1,000/\text{mm}^3$ unless due to marrow involvement * STEP 1: Platelet count $\geq 30,000/\text{mm}^3$ * STEP 1: Total bilirubin $\leq 1.5 \times$ upper limit of normal (ULN) (unless due to liver involvement, hemolysis or Gilbert's disease) * STEP 1: Aspartate aminotransferase (AST)(serum glutamic oxaloacetic transaminase [SGOT])/ alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase [SGPT]) $\leq 3.0 \times$ upper limit of normal (ULN) unless due to disease infiltration of the liver * STEP 1: Calculated (calc.) creatinine clearance by Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) ≥ 30 mL/min * STEP 1: Urine protein to creatinine ratio < 1 or urine protein $\leq 1+$ * STEP 2: Detectable MRD ≥ 10 residual clonal cells per million nucleated cells in peripheral blood at the C15 restaging evaluation from ClonoSEQ * STEP 2: Response of PR, PR-L, CR, CCR or CRi to zanubrutinib sonrotoclax therapy

Conditions & Interventions

Interventions:

DRUG: Zanubrutinib, DRUG: Sonrotoclax, PROCEDURE: Computed Tomography, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Biospecimen Collection,

OTHER: Survey Administration

Conditions:

Chronic Lymphocytic Leukemia, Small Lymphocytic Leukemia

More Information

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Principal Investigator:

IRB

Number:

System ID: NCT07321652

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