Venetoclax, MLN9708 (Ixazomib Citrate) and Dexamethasone for the Treatment of Relapsed or Refractory Light Chain Amyloidosis

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Histologically-proven systemic anti-light chain amyloidosis (AL) confirmed by positive Congo red staining with green birefringence on polarized light microscopy and evidence of a measurable clonal disease that requires active treatment. An underlying plasma cell disorder can be identified by one of the following: clonal plasma cells in the bone marrow (BM), monoclonal protein in the serum or urine, or abnormal free light chain ratio. For patients who are African-American or males \>= 70 years with isolated cardiac involvement, mass spectrometry must be performed to confirm subtyping * Presence of t(11;14) by fluorescence in situ hybridization (FISH) on bone marrow biopsy, either confirmed at screening or documented with a prior biopsy * Patient requires therapy, as determined by the treating physician, following at least one line of treatment (No limit on the number of prior treatments) * Age \>= 18 years. Because no dosing or adverse event data are currently available on the use of venetoclax in combination with MLN9708 (ixazomib citrate) and dexamethasone in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 (Karnofsky \>= 60%) * Leukocytes \>= 3,000/mcL * Absolute neutrophil count \>= 1,000/mcL. Screening absolute neutrophil count (ANC) should be independent of granulocyte- and granulocyte/macrophage colony stimulating factor (G-CSF and GM-CSF) support for at least 1 week and of pegylated G-CSF for at least 2 weeks * Platelets \>= 75,000/mcL. Platelet transfusions to help patients meet eligibility criteria are not allowed within 2 weeks before study enrollment * Total bilirubin =\< 1.5 x institutional upper limit of normal (ULN) * Aspartate aminotransferase (AST)(serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT)(serum glutamate pyruvate transaminase \[SGPT\]) =\< 3 x institutional ULN * Creatinine Calculated clearance \>= 15 mL/min using Cockcroft-Gault equation * 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 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 * AL Amyloidosis Cardiac Risk stage I, II or IIIa disease based on the 2013 European Modification of the 2004 Standard Mayo Clinic Staging in patients with advanced cardiac involvement (Dispenzieri et al., 2004; Wechalekar et al., 2013) * Staging system defined by: NT-proBNP cut off of \< 332 pg/mL and troponin I cut-off of \< 0.10 ng/mL (in the absence of troponin T, troponin I \>= 0.1 ng/mL can be used) as thresholds for stages I, II and III; NT-proBNP \< 8500 pg/ml for stage IIIa * Stage I, both under threshold; * Stage I: Zero markers above threshold: NT-proBNP \< 332 ng/L AND troponin T (TnT) =\< 0.035 ng/mL; NT-proBNP \< 332 ng/L AND TnI =\< 0.1 ng/mL * Stage II, either troponin or NT-proBNP (but not both) over threshold; * Stage II: One marker above threshold: NT-proBNP \>= 332 ng/L OR TnT \>= 0.035 ng/mL; NT-proBNP \>= 332 ng/L OR TnI \>= 0.1 ng/mL * Stage III, both over threshold; * Stage IIIa, both over threshold but NT-proBNP =\< 8500 pg/ml * Stage IIIa: Two markers above threshold: NT-proBNP \>= 332 ng/L BUT =\< 8,500 ng/L AND TnT \>= 0.035 ng/mL; NT-proBNP \>= 332 ng/L BUT =\< 8,500 ng/L AND TnI \>= 0.1 ng/mL * Stage IIIb: Two markers above threshold: NT-proBNP \> 8,500 ng/L AND TnT \>= 0.035 ng/mL; NT-proBNP \> 8,500 ng/L AND TnI \>= 0.1 ng/mL * Life expectancy \>= 3 months * Plasma cell burden =\< 60% * Absence of bone lesions and other end organ disease consistent with multiple myeloma (patients with plasma cell burden between 10 and 60% without end organ disease can be included) * Measurable disease of AL amyloidosis as defined by at least one of the following: 1) serum or urine monoclonal protein \>= 500 mg/dL by protein electrophoresis, or 2) serum free light chain \>= 20 mg/L with an abnormal kappa:lambda ratio or the difference between involved and uninvolved free light chains (dFLC) \>= 20 mg/L * It is not known what effects MLN9708 (ixazomib citrate), venetoclax, and dexamethasone have on human pregnancy or development of the embryo or fetus. Therefore, female patients participating in this study should avoid becoming pregnant, and male patients should avoid impregnating a female partner. Nonsterilized female patients of reproductive age group and male patients should use effective methods of contraception through defined periods during and after study treatment as specified below. * Female patients must meet 1 of the following: * Postmenopausal for at least 1 year before the screening visit, or * Surgically sterile, or * If they are of childbearing potential, agree to practice 2 effective methods of contraception from the time of signing of the informed consent form through 90 days after the last dose of study drug, or * Agree to practice true abstinence, when this is in line with the preferred and usual lifestyle of the subject. (Periodic abstinence \[e.g., calendar, ovulation, symptothermal, postovulation methods\] and withdrawal are not acceptable methods of contraception) * Male patients, even if surgically sterilized (i.e., status postvasectomy) must agree to 1 of the following: * Practice effective barrier contraception during the entire study treatment period and through 90 days after the last dose of study drug, or * Agree to practice true abstinence, when this is in line with the preferred and usual lifestyle of the subject. (Periodic abstinence \[e.g., calendar, ovulation, symptothermal, postovulation methods for the female partner\] and withdrawal are not acceptable methods of contraception) * Left ventricular ejection fraction \>= 35% by echocardiogram. * Ability to understand and the willingness to sign a written informed consent document. Participants with impaired decision-making capacity (IDMC) who have a legally-authorized representative (LAR) and/or family member available will also be eligible

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Exclusion Criteria:

* Patients who have had major surgery or radiotherapy within 14 days prior to entering the study. If the involved radiotherapy field is small, 7 days will be considered a sufficient interval between treatment and administration of the MLN9708 (ixazomib citrate) * Patients who have had anti-plasma cell therapy within 4 weeks (6 weeks for nitrosoureas or mitomycin C) prior to entering the study * 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, within 30 days of the start of this trial and throughout the duration of this trial * Patients with central nervous system involvement * History of allergic reactions attributed to compounds of similar chemical or biologic composition to venetoclax, MLN9708 (ixazomib citrate) (including boron or boron-containing products) or dexamethasone * Strong or moderate CYP3A inhibitors (e.g., erythromycin, ciprofloxacin, diltiazem, fluconazole, verapamil), or strong CYP3A inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort), or moderate CYP3A inducers (e.g., bosentan, efavirenz, etravirine) should be avoided * Venetoclax should be administered using caution with substrates or inhibitors of P-glycoprotein (P-gp) * Patients with uncontrolled intercurrent illness including, but not limited to: ongoing or active serious or systemic infection (within 14 days prior to study enrollment), active hepatitis B or C virus infection, hypertension, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or myocardial infarction (within the past 6 months) * Patients with psychiatric illness/social situations that would limit compliance with study requirements * Female patients who are lactating or have a positive serum pregnancy test during the screening period are excluded from this study because MLN9708 (ixazomib citrate) is a proteasome inhibitor with the potential for embryo-lethal effects, and an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with MLN9708 (ixazomib citrate). Patients must stop breastfeeding while on MLN9708 (ixazomib citrate) and until 90 days have passed since their last dose. These potential risks may also apply to other agents used in this study * Known gastrointestinal disease or gastrointestinal procedure that could interfere with the oral absorption or tolerance of MLN9708 (ixazomib citrate), including difficulty swallowing * Peripheral neuropathy that is \>= grade 3, or grade 2 with pain on clinical examination during the screening period * Patients that have previously been treated with MLN9708 (ixazomib citrate). Patients who have received prior treatment with venetoclax * Patients without measurable disease by serum free light chain, serum m-spike or urine monoclonal protein * Patients with New York Heart Association classification III/IV. Patients with

advanced cardiac amyloidosis, Mayo stage IIIB based on European Modification of the 2004 Standard Mayo Clinic Staging in patients with advanced cardiac involvement with NT-Pro BNP \> 8500 pg/mL (Wechalekar et al., 2013) * Patients with grade 3 or worse diarrhea

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration and Biopsy, PROCEDURE: Computed Tomography, DRUG: Dexamethasone, PROCEDURE: Echocardiography Test, DRUG: Ixazomib Citrate, PROCEDURE: Magnetic Resonance Imaging, PROCEDURE: Positron Emission Tomography, PROCEDURE: Transabdominal Ultrasound, DRUG: Venetoclax, PROCEDURE: X-Ray Imaging
Conditions:
AL Amyloidosis

More Information

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