Venetoclax in Combination With ASTX727 for the Treatment of Chronic Myelomonocytic Leukemia and Other Myelodysplastic Syndrome/Myeloproliferative Neoplasm

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* A diagnosis of an MDS/MPN "overlap" syndrome with \>= 5% marrow blasts (including monocytic blast equivalent in case of CMML). Hydroxyurea may be used to control counts up until the start of therapy * White blood cell (WBC) \< 25,000/mm\^3. Treatment with hydroxyurea is permitted to lower the WBC to reach this criterion * Age \>= 18 years. Because no dosing or adverse event data are currently available on the use of ASTX727 in combination with venetoclax in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 * Total bilirubin =\< 1.5 x upper limit of normal (ULN) (unless considered due to Gilbert's syndrome) * Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \[SGPT\]) =\< 3.0 x institutional ULN OR =\< 5.0 x institutional ULN for patients with liver metastases * Glomerular filtration rate (GFR) \>= 30 mL/min/1.73 m\^2 * 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. Hormonal therapy for prior or concurrent malignancy is allowed * 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 should be class 2B or better * 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 * Ability to swallow pills

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Exclusion Criteria:

* Patients with need for emergent disease-directed therapy excluding hydroxyurea * More than one cycle of previous MDS/MPN-directed therapy, or MDS-directed therapy including lenalidomide and hypomethylating agent (HMAs) such as decitabine or azacitidine, excluding hydroxyurea. Prior use of erythropoietin stimulating agents (ESA) and thrombopoietic agents is allowed, but must be discontinued 4 weeks prior to study treatment * Patients currently or previously receiving an investigational agent or device within 4 weeks of the first dose of treatment * Patients with symptomatic uncontrolled central nervous system (CNS) disease. Imaging to confirm the absence of brain metastases is not required. Patients with spinal cord compression unless considered to have received definitive treatment for this and evidence of clinically stable disease for 28 days * Patients who have consumed grapefruit, grapefruit products, Seville oranges (including marmalade containing Seville oranges) or starfruit within 3 days prior to the initiation of study treatment and are unwilling to discontinue consumption of these throughout the receipt of study drug * History of allergic reactions attributed to compounds of similar chemical or biologic composition to ASTX727 or venetoclax * Patients with uncontrolled intercurrent illness (e.g. requiring intravenous therapy) at the discretion of the investigator * Pregnant women are excluded from this study because venetoclax and ASTX727 have the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with venetoclax, breastfeeding should be discontinued if the mother is treated with venetoclax. These potential risks may also apply to other agents used in this study. Patients must be post-menopausal or with evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy test within 28 days of study treatment and confirmed prior to treatment on day 1 * Post-menopausal is defined as: * Amenorrheic for 1 year or more following cessation of exogenous hormonal treatments * Luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels in the post-menopausal range for women under 50 years of age * Radiation-induced oophorectomy with last menses \> 1 year ago * Chemotherapy-induced menopause with \> 1 year interval since last menses * Surgical sterilization (bilateral oophorectomy or hysterectomy) * Women of child-bearing potential must agree to use adequate contraception (hormonal birth control or abstinence) prior to study entry and for the duration of study participation, and for 6 months following completion of study treatment. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men treated or enrolled on this protocol must also agree to use adequate contraception (latex or synthetic condom or abstinence) prior to the study, for the duration of study participation, and 3 months after completion of venetoclax and ASTX727 administration * Patients with any other medical condition for which the expected survival is below 12 months * Patients with a prior or concurrent malignancy whose natural history or treatment has the potential to interfere with the safety or assessment of the investigational regimen * Patients with uncontrolled infection at the time of study entry

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, DRUG: Decitabine and Cedazuridine, DRUG: Venetoclax

Conditions:
Chronic Myelomonocytic Leukemia, Myelodysplastic Syndrome, Myelodysplastic Syndrome With Excess Blasts, Myelodysplastic/Myeloproliferative Neoplasm, Myeloproliferative Neoplasm

More Information

Contact(s): ctrrecruit@vcu.edu
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT05600894
