

Metronomic Decitabine-Cedazuridine and Venetoclax in R/R AML, HR-MDS, HR/AP MPN

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Age ≥18 years at time of enrollment * Diagnosis of one of the following by World Health Organization (WHO) International Consensus Classification (ICC) criteria as determined by local assessment: * Relapsed/ refractory acute myeloid leukemia (R/R AML) as defined by ≥5% marrow blasts or unequivocal, measurable extramedullary disease * High Risk Myelodysplastic Syndrome (HR-MDS) (high/very high risk MDS by Revised International Prognostic Scoring System (IPSS-R) or Molecular International Prognostic Scoring System (IPSS-M) * high-risk accelerated-phase myeloproliferative neoplasm (HR/AP-MPN) defined by ≥10% blasts in blood or bone marrow * Eastern Cooperative Oncology Group (ECOG) Performance status 0-3 * White blood cell (WBC) count ≤25 × 10⁹/Liter (L) (cytoreduction with hydroxyurea or steroids is allowed to achieve this) * Aspartate Aminotransferase (AST)/ Alanine Aminotransferase (ALT) ≤3 × upper limit of normal (ULN) (≤5 × ULN if due to leukemic involvement) * Total bilirubin ≤2 × ULN (unless the elevation is due to Gilbert's or hemolysis) * Creatinine clearance ≥ 30 milliliters / minute (mL/min) * Women of child-bearing potential must not be pregnant or breastfeeding and must have a negative pregnancy test at screening. Women of non-childbearing potential are those who have had a hysterectomy or bilateral oophorectomy, or who have completed menopause (no menses for at least one year and age ≥65 or follicle-stimulating hormone levels in the menopausal range). * Subjects and their partners with reproductive potential must agree to use effective contraceptive measures during the study and for 3 months after the last dose of study treatment. Effective contraception includes methods such as oral contraceptives or double-barrier method.

Exclusion Criteria:

* Prior use of hypomethylating agent and venetoclax in combination (Note, use of hypomethylating agent and/or venetoclax separately in alternative combinations with other drugs is allowed) * Inability to tolerate oral therapies, or medical co-morbidities that significantly impact parenteral absorption * Acute promyelocytic leukemia myeloproliferative neoplasm (MPN) with the Philadelphia chromosome translocation (BCR:ABL) translocation * Clinically significant cardiovascular disease as defined by unstable angina * New York Heart Association class III/IV congestive heart failure * Treatment with any investigational drug or therapy within 2 weeks of study treatment or 5 half-lives before the first dose of study treatment, whichever is shorter * Known hypersensitivity to azacitidine, venetoclax, decitabine or cedazuridine * Cytotoxic chemotherapy or prior azacitidine or decitabine within 2 weeks of first dose of study treatment * Concurrent use of AML/MDS/MPN therapies including lenalidomide, erythropoietin, luspatercept, cytotoxic chemotherapies, targeted agents, etc Note: hydroxyurea is allowed in Cycle 1 if necessary for cytoreduction and/or cytarabine not exceeding a maximum dose of 1 gram per meter squared (g/m²) in Cycle 1 is also allowed for cytoreduction * Uncontrolled intercurrent illness or infection (those with controlled HIV, hepatitis, or other chronic infections are eligible) * Untreated central nervous system disease * Pregnancy or breastfeeding * Other active malignancy requiring systemic therapy during duration of trial or otherwise would confound endpoints (eg, second malignancy present where survival is expected to be less than 6 months)

Conditions & Interventions

Interventions:

DRUG: Decitabine-cedazuridine plus venetoclax (DEC-C+VEN), DRUG: Azacitidine plus venetoclax (AZA+VEN)

Conditions:

Relapsed / Refractory AML, High Risk Myelodysplastic Syndrome, High Risk Myeloproliferative Neoplasms

Keywords:

Relapsed / Refractory AML, High Risk Myelodysplastic Syndrome, High Risk Myeloproliferative Neoplasms

More Information

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Principal Investigator:

IRB

Number:

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