A Randomized Study of ASTX727 With or Without Iadademstat in Advanced Myeloproliferative Neoplasms (MPNs)

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patients must have morphologically confirmed diagnosis of Philadelphia-chromosome negative MPN in accelerated-phase (10-19% myeloid blasts) or blast-phase (≥ 20% myeloid blasts) arising from polycythemia vera, essential thrombocythemia, primary myelofibrosis, secondary myelofibrosis, or MPN not otherwise specified, as per the World Health Organization (WHO) 2016 classification OR myelodysplastic syndrome (MDS)/MPN overlap syndromes (e.g., chronic myelomonocytic leukemia \[CMML\]) with ≥ 10% blasts * Patients must not have received prior DNMTi. Previous use of janus kinase (JAK) inhibition, hydroxyurea, and interferon is allowed. There is no required washout period * Age ≥ 18 years * Because no dosing or adverse event data are currently available on the use of ASTX727 (35 mg decitabine + 100 mg cedazuridine) in combination with iadademstat in patients \< 18 years of age, children are excluded from this study * Eastern Cooperative Oncology Group (ECOG) performance status ≤ 3 (Karnofsky ≥ 30) * Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (unless elevated due to Gilbert's syndrome, thought to be related to MPN-AP/BP, or due to extrasvascular hemolysis. In these cases conjugated bilirubin should be ≤ 2.0 x ULN) * Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamic pyruvic transaminase \[SGPT\]) ≤ 3 x institutional ULN * Glomerular filtration rate (GFR) ≥60 mL/min/1.73 m\^2 by Modification of Diet in Renal Disease (MDRD) * 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 * 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 II or better * The effects of ASTX727 (35 mg decitabine + 100 mg cedazuridine) and/or iadademstat on the developing human fetus are unknown. For this reason and because DNMT inhibitor and LSD1 inhibitor agents are known to be teratogenic, women of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) for the duration of study participation and 6 months after completion of ASTX727 (35 mg decitabine + 100 mg cedazuridine) and/or iadademstat administration. 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 for the duration of study participation and 6 months after completion of ASTX727 (35 mg decitabine + 100 mg cedazuridine) and/or iadademstat administration * Women of child-bearing potential must agree not to donate or freeze egg(s) during the course of this study or within 180 days after receiving their last dose of study drug. Male patients must agree not to donate sperm during the course of this study or within 180 days after receiving their last dose of study drug * Ability to understand and the willingness to sign a written informed consent document. Legally authorized representatives may sign and give informed consent on behalf of study participants * Patient is able to swallow oral medications * Patients must have a body weight of at least 50 kg due to the use of flat doses. If a patient is on continued treatment and is receiving benefit, but falls below 50 kg, they may stay on the study per investigator discretion. Otherwise, they will have to come off the study * Peripheral white blood cell (WBC) count \<25 x 10\^9/L on day 1 prior to treatment initiation. Hydroxyurea is allowed for cytoreduction until 24 hours prior to study treatment

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Exclusion Criteria:

* 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 or had received any investigational products within 3 weeks or 5 half-lives (whichever is shorter) prior to first dose of study treatment * Patients with a QTcF \> 450 ms * History of allergic reactions attributed to compounds of similar chemical or biologic composition to ASTX727 (35 mg decitabine + 100 mg cedazuridine) or iadademstat * Patients medicated with anti-depressants reported to have KDM1A/LSD1 inhibitory activity: tranylcypromine or phenelzine * Patients with IDH1-mutated MPN blast phase (≥20% blasts). Patients with an IDH1-mutation with MPN-AP (10-19%) blasts are eligible for this study * Iadademstat concomitant medication considerations: Patients are not allowed to receive prophylactic hematopoietic colony stimulating factors, any complementary or alternative medicine \[any of various systems of healing or treating disease (as non-prescription supplements, herbal medicine and homeopathy)\]. Of note, patients may receive granulocyte colony-stimulating factor for management of febrile neutropenia or for prolonged neutropenia * Patients may not receive administration of live or live-attenuated vaccines. Administration of non-live vaccines included ribonucleic acid (RNA)-based vaccines is allowed and is recommended for pneumococcal, coronavirus, and influenza vaccines * Patients with uncontrolled intercurrent illness or any other significant condition(s) that would make participation in this protocol unreasonably hazardous * Pregnant women are excluded from this study because iadademstat is an LSD1 inhibitor agent with 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 iadademstat, breastfeeding should be discontinued if the mother is treated with iadademstat. These potential risks also apply to the ASTX727 (35 mg decitabine + 100 mg cedazuridine) used in this study * Patients who require treatment while on study with concomitant drugs that target the 5HT2B receptor or the sigma nonspecific receptor (e.g., escitalopram, fluoxetine, sertraline) except for drugs that are considered absolutely essential for the care of the patient and with appropriate treatment monitoring

Conditions & Interventions

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

Conditions:
Accelerated Phase Myeloproliferative Neoplasm, Blast Phase Myeloproliferative Neoplasm, Essential Thrombocythemia, Myelodysplastic/Myeloproliferative Neoplasm, Myeloproliferative Neoplasm, Not Otherwise Specified, Polycythemia Vera, Primary Myelofibrosis, Secondary Myelofibrosis

More Information

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