TAK-243 in Treating Patients With Relapsed or Refractory Acute Myeloid Leukemia or Myelodysplastic Syndromes With Increased Blasts

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Diagnosis of AML or MDS with increased blasts (MDS-IB) assessed by local laboratory review according to the 2022 World Health Organization (WHO) criteria for myeloid neoplasms. Both patients with MDS-IB1 (5-9% bone marrow blasts) and MDS-IB2 (10-19% bone marrow blasts) are eligible. * Patients must have relapsed or refractory disease after receiving at least one prior line of therapy * AML-specific inclusion criteria: Patients with relapsed or refractory AML with \>= 5% bone marrow blasts after receiving at least two courses of intensive induction chemotherapy (including, but not limited to, 7+3 regimen, fludarabine, cytarabine, idarubicin and filgrastim \[FLAG-Ida\] and mitoxantrone, etoposide, and cytarabine \[MEC\]) or 2 cycles of venetoclax-based lower intensity regimen (azacitidine plus venetoclax or low-dose cytarabine plus venetoclax), and without any other approved therapies available that would be more appropriate in the investigator's judgment. Patients who have received only one course of intensive induction chemotherapy but are not eligible for a second course because of decreased performance status or clear disease progression may be eligible for participation after discussion with the study principal investigator (PI). Patients with concomitant extramedullary disease relapse are eligible to participate, but not patients with isolated extramedullary relapse without bone marrow disease. * MDS-specific inclusion criteria: Patients with relapsed or refractory MDS-IB with \>= 5% bone marrow blasts after at least 4 cycles of hypomethylating agent (HMA)-based therapy or at least two courses of intensive induction chemotherapy and meet criteria for stable disease (SD), progressive disease (PD) or disease relapse according to the International Working Group 2023 response criteria for higher-risk MDS. Patients must not have access to any other approved therapies that would be more appropriate in the investigator's judgment. Patients who have received less than 4 cycles of HMA-based therapy may be eligible to participate after discussion with the study PI if there is clear evidence of progression or intolerance to HMA-based therapy that precludes its continuation. * Patients must have recovered from the effects of any prior systemic therapy, radiotherapy or surgery: * Patients should not have received other investigational therapy within 2 weeks. * Patients should not have received standard chemotherapy within 1 week of administration of study drug; hydroxyurea administration (for leukocyte count control) is permitted. * Age \>=18 years. Because no dosing or adverse event data are currently available on the use of TAK-243 in patients \<18 years of age, children are excluded from this study. * Eastern Cooperative Oncology Group (ECOG) performance status =\< 2 (Karnofsky \>= 50%). * Serum bilirubin =\< 1.5 × institutional upper limit of normal (ULN). * Patients with a known history of Gilbert's syndrome may enroll. * Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \[SGOT\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \[SGPT\]) =\< 3 × institutional ULN. * Serum creatinine \< 176 mcmol/L (2 mg/dL) OR * Creatinine clearance \> 60 mL/min based on the Cockcroft-Gault equation. * Documented normal cardiac function (\>= 50%) by echocardiogram or multi-gated acquisition (MUGA) scan. * HIV-infected patients on effective anti-retroviral therapy with undetectable viral load withing 6 months are eligible for this trial. * For patients with evidence of chronic hepatitis B virus (HBV) infection, 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. * The effects of TAK-243 on the developing human fetus are unknown and ubiquitin-activating enzyme inhibitors are known to be teratogenic. For this reason, female patients must be: * Postmenopausal (age-related amenorrhea \>= 12 consecutive months or follicle-stimulating hormone \> 40 mIU/mL), for at least 1 year before the screening visit, OR * Surgically sterile (i.e., who had undergone hysterectomy or bilateral oophorectomy), OR If they are of childbearing potential: * Agree to practice 1 highly effective method and 1 additional effective (barrier) method of contraception, at the same time, from the time of signing the informed consent through 4 months after the last dose of study drug (female and male condoms should not be used together), OR * Agree to practice true abstinence, when this is in line with the preferred and usual lifestyle of the patient. (Periodic abstinence \[e.g., calendar, ovulation, symptothermal, postovulation methods\] withdrawal, spermicides only, and lactational amenorrhea are not acceptable methods of contraception.) 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. * Male patients, even if surgically sterilized (i.e., status post-vasectomy), who: * Agree to practice effective barrier contraception during the entire study treatment period and through 4 months after the last dose of study drug (female and male condoms should not be used together), OR * Agree to practice true abstinence, when this is in line with the preferred and usual lifestyle of the subject. (Periodic abstinence \[e.g., calendar, ovulation, symptothermal, postovulation methods for the female partner\] withdrawal, spermicides only, and lactational amenorrhea are not acceptable methods of contraception.) * 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. * Patients should have a minimum life expectancy of 1 month.

Exclusion Criteria:

* Patients with acute promyelocytic leukemia (APL) or AML with t(15;17)(q22;q12)

•PML::RARA). * Patients who have not recovered from adverse events due to prior anti-cancer therapy (i.e., have residual toxicities \> grade 1), except anemia, neutropenia or thrombocytopenia of any grade and grade 2 peripheral neuropathy. * Presence of any other malignancy requiring active therapy. * Patients who are receiving any other investigational agents. * History of allergic reactions attributed to compounds of similar chemical or biologic composition to TAK-243. * Concomitant treatment with organic anion transport protein (OATP) and BCRP inhibitors or strong inducers/inhibitors of cytochrome P450 (CYP)3A4/5. Treatment with these agents must be discontinued at least 14 days prior to TAK-243 dosing. Because the lists of these agents are constantly changing, it is important to regularly consult a frequently updated medical reference. As part of the enrollment/informed consent procedures, the patient will be counseled on the risk of interactions with other agents, and what to do if new medications need to be prescribed or if the patient is considering a new over-the-counter medicine or herbal product. * Presence of an active uncontrolled infection or severe infectious disease, such as severe pneumonia, meningitis, or septicemia. * Presence of active graft-versus-host disease (GVHD) or continued treatment with systemic immunosuppressive agents following allogeneic hematopoietic stem cell transplantation (HSCT). * Presence of any co-morbid condition that, in the opinion of the investigator, might compromise the patient's safety, might interfere with participation in the trial or might interfere with the interpretation of trial results. * Pregnant and lactating/breast-feeding women are excluded from this study because TAK-243 is a UAE-inhibiting agent with the potential for teratogenic or abortifacient effects and there is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with TAK-243. Females of child-bearing potential must have a negative serum pregnancy test within 7 days before enrollment and should not be lactating/breast-feeding. Breastfeeding should be discontinued if the mother is treated with TAK-243. * Major surgery within 14 days before the first dose of any study drug or a scheduled surgery during study period. * Patients with uncontrolled coagulopathy or bleeding disorder. * Patients with known hepatic cirrhosis. * Patients with known active cardiopulmonary disease defined as: * Unstable angina withing 3 months prior to first dose of TAK-243; * Myocardial infarction (MI) within 6 months prior to first dose of TAK-243 (patients who had MI and/or coronary revascularization more than 6 months before screening and who are without cardiac symptoms may enroll); * Congestive heart failure (New York Heart Association \[NYHA\] Class III or IV; * Cardiomyopathy with left ventricular ejection fraction (LVEF) \< 50%; * Symptomatic pulmonary hypertension. * Presence of active central nervous system (CNS) involvement (patients with prior CNS leukemia who have negative CNS cytology and who receive periodic prophylactic intrathecal chemotherapy are eligible). * Patients with clinically significant arrhythmia: * History of ventricular fibrillation or torsade de pointes at any time, * Episode of grade \>= 3 atrial fibrillation

or flutter in the last 3 months, defined as symptomatic episode, requiring urgent intervention (cardioversion, pacemaker or ablation) or with life-threatening consequences. * Uncontrolled high blood pressure (i.e., systolic blood pressure \>180 mm Hg, diastolic blood pressure \> 95 mm Hg). * Prolonged rate corrected QT (QTc) interval \>= 480 msec, calculated using the Fridericia method. * Patients with known severe or very severe chronic obstructive pulmonary disease (defined as forced expiratory volume in one second (FEV1) less than 30% or less than 50% of predicted), interstitial lung disease, or pulmonary fibrosis. * Female patients who intend to donate eggs (ova) during the course of this study or 4 months after receiving their last dose of study drug(s). * Male patients who intend to donate sperm during the course of this study or 4 months after receiving their last dose of study drug(s). * Patients with history of neutrophilic dermatosis (e.g. Sweet syndrome, pyoderma gangrenosum), relapsing polychondritis, polyarteritis nodosa and/or giant cell arteritis. * Patients with VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic syndrome) or any other autoinflammatory disease.

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Echocardiography Test, PROCEDURE: Multigated Acquisition Scan, DRUG: UAE Inhibitor TAK-243
Conditions:
Myelodysplastic Syndrome With Excess Blasts, Recurrent Acute Myeloid Leukemia, Recurrent Myelodysplastic Syndrome, Recurrent Myelodysplastic Syndrome/Acute Myeloid Leukemia, Refractory Acute Myeloid Leukemia, Refractory Myelodysplastic Syndrome, Refractory Myelodysplastic Syndrome/Acute Myeloid Leukemia

More Information

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