A Study to Find the Highest Dose of Cedazuridine and Decitabine Combination With Filgrastim as a Treatment Option After Hematopoietic Stem Cell Transplant in Children With High-Risk Acute Myeloid Leukemia

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: Up to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- STEP 0: Patient must be ≤ 21 years of age
    - PLEASE NOTE: Eligibility criteria to enroll onto Step 1 for the treatment trial is ≤ 21 years of age at the time of Step 1 enrollment. Please plan accordingly to ensure that patients who are screened with Step 0 will be at an eligible age at the time of enrollment onto Step 1. Patients who are 21 at the time of screening who turn 22 at the time of enrollment onto Step 1 will not be eligible to enroll onto the study
- STEP 0: Patients with newly diagnosed high risk* de novo AML, newly diagnosed therapy-related AML, relapsed, or refractory AML. in complete remission at the time of transplant. Patients with a history of isolated or combined central nervous system (CNS) or extramedullary disease are eligible if they have no evidence of active CNS or extramedullary disease at the time of trial enrollment (Step 0) and treatment enrollment (Step 1). Eligible patients with histories of isolated or combined CNS or extramedullary disease at time of relapse are required to be in complete remission at time of transplant to be eligible for this study
    - Based on risk criteria adopted by the AAML1831 study
- STEP 0: Patient must plan to have bone marrow sample submitted to Hematologics within 14 days prior to the start of conditioning regimen for HCT.
    - Note: In order to be eligible to enroll onto Step 1 to receive treatment on this study, pre-HCT disease status must be assessed prior to receiving HCT. AML must be in complete remission (Children's Oncology Group [COG]-complete remission [CR], COG-complete remission with partial recovery of platelelt count [CRp], COG-complete remission with incomplete blood count recovery [Cri], with or without detectable minimal residual disease [MRD]); bone marrow CR must be assessed by central flow cytometry performed at Hematologics prior to the start of the conditioning regimen
- STEP 0: Human immunodeficiency virus (HIV)-infected patients are eligible for this trial if the following criteria are met:
    - No history of HIV complications with the exception of CD4 count < 200cells/mm^3
    - No antiretroviral therapy with overlapping toxicity such as myelosuppression
    - CD4 count > 500 cells/mm^3 prior to the diagnosis of newly diagnosed, relapsed, refractory AML.
    - HIV viral loads below the limit of detection within 6 months, as long as the patient is NOT receiving anti-retroviral agents that may interact with ASTX727.
    - No history of highly active antiretroviral therapy (HAART)-resistant HIV
- STEP 0: Patients must be receiving an allogeneic (related, unrelated, and mismatched related, including haploidentical) marrow, peripheral blood, or cord blood transplant for the first time
- STEP 0: HCT conditioning regimen must be planned to begin within 14 days after bone marrow assessment to determine disease status
- STEP 0: Conditioning regimen must be myeloablative and include high dose busulfan, or treosulfan, or total body irradiation
- STEP 0: Patients must not have received prior exposure to ASTX727. Note that patients may have had prior exposure to decitabine
- STEP 1: Patient must be ≤ 21 years of age at the time of study enrollment to step 0 and step 1
- STEP 1: Patients must have a body surface area ≥ 1m^2 at enrollment to step 1
- STEP 1 (PRE-HCT): AML must be in complete remission (COG-CR, COG-CRp, COG-Cri), with or without detectable MRD; bone marrow CR must be assessed by central flow cytometry performed at Hematologics. Disease assessment must be performed within 14 days prior to the start of HCT conditioning regimen
    - Patients with CNS or extramedullary disease within 14 days prior to the start of the HCT condition regimen are not eligible
- STEP 1 (POST-HCT): AML must be in complete remission (COG-CR, COG-CRp, COG-CRi). Bone marrow evaluation must show CR with no detectable minimal residual disease (MRD negative by central flow cytometry at Hematologics)
    - Note: Disease assessment is required to be performed within 14 days prior to enrollment onto Step 1
    - Patients with CNS or extramedullary disease post-HCT are not eligible
- STEP 1: Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients ≤ 16 years of age. Patients must have Karnofsky performance score ≥ 50 or Lansky play-performance scale score ≥ 50
- STEP 1: Patients must have fully recovered from the acute toxicities related to the conditioning regimen and the transplant. If, after 42-100 days post-transplant, the eligibility criteria are met, the patient is considered to have recovered adequately

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- STEP 1: Platelet count ≥ 50,000 µL (without requirement for platelet transfusion within the last 7 days)
- STEP 1: Hemoglobin ≥ 8.0 g/dL at baseline (may receive red blood cell [RBC] transfusions)
- STEP 1: Absolute neutrophil count ≥ 1,000 µL with no myeloid growth factor support within the last 3 days
- Estimated glomerular filtration rate (GFR) (eGFR) ≥ 60 mL/min/1.73 m^2 "Bedside" Schwartz formula (2009) OR
    - OR- A 24 hour urine creatinine clearance ≥ 60 mL/min/1.73 m^2
    - A GFR ≥ 60 mL/min/1.73 m^2. GFR must be performed using direct measurement with a nuclear blood sampling method OR direct small molecule clearance method (iothalamate or other molecule per institutional standard)
    - Note: Estimated GFR (eGFR) from cystatin C or other estimates not listed above are not acceptable for determining eligibility
- STEP 1: Bilirubin (total or sum of conjugated + unconjugated) ≤ 1.5 x upper limit of normal (ULN) for age
- STEP 1: Alanine aminotransferase (ALT) ≤ 3 x ULN
- STEP 1: Aspartate aminotransferase (AST) ≤ 3 x ULN
- STEP 1: Albumin ≥ 2 g/dL

Exclusion Criteria:

- STEP 0: Patients with known inherited marrow failure syndromes, including, but not limited to Fanconi Anemia, Dyskeratosis congenita, and Shwachman-Diamond syndrome
- STEP 0: Known or suspected hypersensitivity to filgrastim, decitabine or cedazuridine (ASTX727)
- STEP 0: Patients who have received a prior solid organ transplantation are not eligible
- STEP 1: ASTX727 can cause fetal harm when administered to pregnant women. Pregnancy tests must be obtained in girls who are post-menarchal. Males or females of reproductive potential may not participate unless they have agreed to use two effective methods of birth control, including a medically accepted barrier or contraceptive method (eg, male or female condom) for the duration of the study. Abstinence is an acceptable method of birth control. Women of childbearing potential must use highly effective contraception during treatment with ASTX727 and for at least 6 months after the last dose. Men with female partners of childbearing potential should be advised to practice highly effective contraceptive measures of birth control and not to father a child while receiving treatment with decitabine and for 3 months after the last dose. Breastfeeding is not allowed during the study and for at least 2 weeks after the last dose of study drug
- STEP 1: Patients who are currently receiving another investigational drug are not eligible
- STEP 1: Patients who are currently receiving other anti-cancer agents are not eligible. Patients receiving intrathecal chemotherapy in the prior 14 days are eligible
- STEP 1: Patients receiving or for whom there is a plan to administer anticancer non-protocol therapy, radiation therapy or immunotherapy during the study period are not eligible (note that prophylactic use of chemotherapeutic agents for graft versus host disease [GVHD] is allowed, e.g. methotrexate for GVHD prophylaxis). Intrathecal cytarabine administered at the discretion of the treating physician throughout maintenance therapy is allowed
- STEP 1: Drugs known to be metabolized by cytidine deaminase (CDA) should not be given (such drugs include cytarabine, gemcitabine, azacitidine, vidarabine, zalcitabine, zidovudine, telbivudine, didanosine, stavudine, lamivudine, abacavir, emtricitabine, entecavir, trifluridine, tenofovir and adefovir) on days when ASTX727 is administered and for 24 hours thereafter
- STEP 1: Patients is not able to swallow intact tablets. Nasogastric or G tube administration is not allowed
- STEP 1: Patient is not able to start ASTX727 and filgrastim (rh-GCSF) between day 42 and day 100 following completion of allo-HCT. If, after enrollment, protocol therapy is started more than 100 days following allo-HCT, the patient will be removed from protocol therapy
- STEP 1: Patients with graft loss are not eligible
- STEP 1: Patients with steroid refractory or dependent acute GVHD are not eligible. Patients must be on < 1 mg/kg/day of methylprednisolone (or equivalent prednisone/prednisolone dose) that is being tapered. Patients must not be on any second line systemic therapies. Continued GVHD prophylaxis with calcineurin inhibitors, sirolimus, abatacept or mycophenolate mofetil is acceptable
- STEP 1: Patients who have an uncontrolled viral, bacterial, fungal, or protozoal infection are not eligible
- STEP 1: Patients with active transplant associated thrombotic microangiopathy with ongoing hemolysis and need treatment (e.g. eculizumab) are not eligible
- STEP 1: Patients with sinusoidal obstruction syndrome with ongoing need for treatment (e.g. defibrotide, diuresis, supplemental oxygen) are not eligible
- STEP 1: Idiopathic pneumonitis syndrome or other non-infectious lung injury requiring ongoing treatment (corticosteroids, tumor necrosis factor [TNF] inhibitors, or other biologics) or supplemental oxygen are not eligible
- STEP 1: Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study are not eligible

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, DRUG: Decitabine, DRUG: Decitabine and Cedazuridine, BIOLOGICAL: Filgrastim, PROCEDURE: Imaging Procedure, PROCEDURE: Lumbar Puncture
Conditions:
Acute Myeloid Leukemia Post Cytotoxic Therapy, Recurrent Acute Myeloid Leukemia, Refractory Acute Myeloid Leukemia

More Information

Description:
This phase I trial tests the safety, side effects, and best dose of ASTX727 and filgrastim for the treatment of children with high risk acute myeloid leukemia that has come back after a period of improvement (recurrent) or that does not respond to treatment (refractory) who have undergone allogenic hematopoietic stem cell transplantation. ASTX727 is a combination of cedazuridine and decitabine. Cedazuridine is in a class of medications called cytidine deaminase inhibitors. It prevents the breakdown of decitabine when taken by mouth, making it more available in the body so that decitabine will have a greater effect. Decitabine is in a class of medications called hypomethylation agents. It works by helping the

bone marrow produce normal blood cells and by killing abnormal cells in the bone marrow. Filgrastim works in synergy with decitabine and enhances its activity. Giving ATSX727 and filgrastim may be safe and tolerable in treating children with high risk, recurrent or refractory acute myeloid leukemia who have undergone allogenic hematopoietic stem cell transplantation.

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