Study of Rezafungin Compared to Standard Antimicrobial Regimen for Prevention of Invasive Fungal Diseases in Adults Undergoing Allogeneic Blood and Marrow Transplantation

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Willing and able to provide written informed consent. 2. Males or females ≥18 years of age. 3. Receiving a human leukocyte antigen (HLA) matched allogeneic peripheral BMT from a family or unrelated donor, HLA-mismatched related or unrelated donor, or haploidentical donor. 4. Diagnosed with 1 of the following underlying diseases: 1. Acute myeloid leukemia (AML), with or without a history of myelodysplastic syndrome, in first or second complete remission. 2. Acute lymphoblastic leukemia, in first or second complete remission. 3. Acute undifferentiated leukemia in first or second remission. 4. Acute biphenotypic leukemia in first or second complete remission. 5. Chronic myelogenous leukemia in either chronic or accelerated phase. 6. One of the following myelodysplastic syndrome(s) defined by the following: i. Refractory anemia. ii. Refractory anemia with ringed sideroblasts. iii. Refractory cytopenia with multilineage dysplasia. iv. Refractory cytopenia with multilineage dysplasia and ringed sideroblasts. v. Refractory anemia with excess blasts

•1 (5-10% blasts). vi. Refractory anemia with excess blasts

•2 (10-20% blasts). vii. Myelodysplastic syndrome, unclassified. viii. Myelodysplastic syndrome associated with isolated del (5q). g. Lymphoma (including Hodgkin's) with chemosensitive disease (i.e., response to chemotherapy) and receiving a related or unrelated donor transplant. h. Aplastic anemia. i. Primary or secondary myelofibrosis. j. Chronic myelomonocytic leukemia. k. Chronic lymphocytic leukemia. l. Drepanocytosis (sickle cell anemia). m. Red blood cell aplasia. n. Myeloproliferative disorder, unclassified. o. Multiple myeloma (plasma cell myeloma). 5. Receiving myeloablative or reduced-intensity conditioning regimens. 6. Adequate renal and hepatic function prior to initiation of conditioning regimen, therefore between 40 days prior and 10 days prior to BMT, documented as follows: 1. Hepatic: alanine aminotransferase less than or equal to (≤) 2.5 × upper limit of normal (ULN) and total serum bilirubin ≤1.5 × ULN (excluding Gilbert's Syndrome). 2. Renal: serum creatinine ≤2 milligrams (mg)/deciliter (dL) and with creatinine clearance (CrCl) greater than or equal to (≥) 30 milliliters (mL)/minute (min) without a history of renal transplant, or undergoing weekly dialysis within 4 weeks of the BMT. 7. Baseline blood samples drawn for Platelia galactomannan enzyme immunoassay (GM EIA) and β-D glucan levels within 15 days before randomization, with results available prior to randomization. 8. Baseline Toxoplasma serologies available within 6 weeks prior to randomization. Subjects with a positive toxoplasma IgG serology at any time prior to randomization do not need to repeat the toxoplasma serologies (IgG and IgM) and will be considered to have a prior history of toxoplasmosis. 9. Baseline glucose-6-phosphate dehydrogenase (G6PD) deficiency determination by the investigator prior to randomization with no known evidence of G6PD deficiency performed any time prior to randomization. If the Investigator assesses the subject as G6PD sufficient, the G6PD test result does not need to be entered into the EDC system. 10. Female subjects of child-bearing potential \<2 years post-menopausal (unless surgically sterile) must agree to and comply with using 1 barrier method (e.g., female condom with spermicide) plus one other highly effective method of birth control (e.g., oral contraceptive, implant, injectable, indwelling intrauterine device, vasectomized partner), or sexual abstinence (only possible if it corresponds to the subject's usual lifestyle) while participating in this study, and for 30 days after the last dose of study drug. Male subjects must be vasectomized, abstain from sexual intercourse, or agree to use barrier contraception (condom with spermicide), and agree not to donate sperm while participating in the study and for 120 days from the last IV dose of study drug.

Exclusion Criteria:

1. Diagnosis of AML not in morphological remission. 2. Diagnosis of chemotherapy-resistant lymphoma: a first relapse can occur provided that a second complete remission has occurred. 3. Suspected or diagnosed invasive fungal disease (IFD) within 4 weeks of randomisation. 4. Diagnosed symptomatic heart failure with left ventricular ejection fraction (LVEF) at rest ≤50%, or shortening fraction ≤26%. 5. Personal or family history of Long QT interval on electrocardiogram (ECG) (QT) syndrome or a prolonged QT interval corrected for heart rate by Fridericia's formula (QTcF) (\>470 milliseconds \[msec\] in males and \>480 msec in females); or concurrent administration of terfenadine, cisapride, astemizole, erythromycin, pimozide, quinidine, or halofantrine. 6. Diagnosed reduced lung function with either diffusion capacity (corrected for hemoglobin) or forced expiratory volume in 1 second (FEV1) ≤65% of predicted value, or O2 saturation ≤82% on room air. 7. Suspected or documented PCP within 2 years of screening. 8. Positive baseline serum Platelia GM EIA (≥ 0.5) and/or β-D glucan assay (Fungitell ≥80 picograms \[pg\]/mL or Fujifilm Wako \>11 pg/mL) within 15 days prior to the transplant. 9. Receipt of previous allogeneic BMT. 10. Planned receipt of cord blood for transplantation. 11. Planned peripheral blood or marrow autograft. 12. Not applicable to protocol Amendment 6. 13. Grade 2 or higher ataxia, tremor, motor neuropathy, or sensory neuropathy, per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. 14. History of severe (Grade ≥3) ataxia, neuropathy or tremors; or a diagnosis of multiple sclerosis or a movement disorder (including Parkinson's disease or Huntington's disease). 15. . . 1. Planned or ongoing intake at screening of a known severe neurotoxic medication or with a known moderate neurotoxic medication in a patient with ataxia, tremor, motor neuropathy, or sensory neuropathy of CTCAE version 5.0 Grade 1 or higher. 2. Any contraindication or a medication or supplement known to severely interact with the standard antimicrobial regimen (SAR) as detailed in the US Prescribing Information (USPI) or Summary of Product Characteristics (SmPC) of fluconazole, posaconazole, or TMP/SMX. 16. Known hypersensitivity to Rezafungin for Injection, any echinocandin, fluconazole, posaconazole, other azole antifungal, or to any of their excipients. 17. Known hypersensitivity or inability to receive TMP/SMX or any of its excipients, including but not limited to anaphylaxis, exfoliative skin disorders, or acute porphyria. 18. Recent use of an investigational medicinal product within 28 days or 5 half-lives of the investigational medicinal product, whichever is greater, to prevent overlapping toxicities when this study's investigational product is dosed, or presence of an investigational device at the time of screening. In some cases, use of investigational products may be acceptable in consultation with the Sponsor's Medical Monitor. 19. Known infection with HIV. Subjects with unknown HIV status should be tested for HIV antibodies per standard of care. 20. Pregnant or lactating females. 21. The Principal Investigator (PI) determines that the subject should not participate in the study. 22. Considered unlikely to follow up for 90 days after receipt of the BMT due to logistic concerns (i.e., location relative to transplant center). 23. Known liver cirrhosis, diagnosed according to country or Medical Society specific guidelines and documented in the medical records prior to initiating conditioning regimen.

Conditions & Interventions

Interventions:

DRUG: Rezafungin for Injection, DRUG: Posaconazole, DRUG: Fluconazole, DRUG: Trimethoprim-sulfamethoxazole (TMP/SMX), DRUG: Intravenous Placebo, DRUG: Oral Placebo

Conditions:

Candidemia, Mycoses, Fungal Infection, Fungemia, Invasive Candidiasis, Pneumocystis, Mold Infection, Invasive Fungal Disease, Prophylaxis of Invasive Fungal Infections, Aspergillus

Keywords:

Mycoses, Prophylaxis of Invasive Fungal Infections, Aspergillus, Candidiasis, Candidemia, Candidiasis, Invasive, Fungemia, Sepsis, Blood and Marrow Transplant (BMT), Infection, Invasive Fungal Infections, Systemic Inflammatory Response Syndrome, Inflammation, Pathologic Processes, Fluconazole, Posaconazole,

Caspofungin, Trimethoprim-sulfamethoxazole (TMP/SMX), Echinocandins, Antifungal Agents, 14-alpha Demethylase Inhibitors, Cytochrome P-450 Enzyme Inhibitors, Enzyme Inhibitors, Molecular Mechanisms of Pharmacological Action, Steroid Synthesis Inhibitors, Physiological Effects of Drugs, Cytochrome P-450 CYP2C9 Inhibitors, Cytochrome P-450 CYP2C19 Inhibitors, Pneumocystis, Mold Infection, Rezafungin, Anti-Infective Agents

More Information

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