A Study of Tacrolimus/Methotrexate/Ruxolitinib Versus Post-Transplant Cyclophosphamide/Tacrolimus/Mycophenolate Mofetil in Non-Myeloablative/Reduced Intensity Conditioning Allogeneic Peripheral Blood Stem Cell Transplantation (BMT CTN 2203)

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Age 18.0 years or older at the time of enrollment. * Participants undergoing allogeneic HCT for one of the following indications: * Acute leukemia or chronic myelogenous leukemia with no circulating blasts and with less than 5% blasts in the bone marrow. Therapy related myeloid neoplasms are allowed. * Myelodysplasia/chronic myelomonocytic leukemia with no circulating blasts and with less than 10% blasts in the bone marrow (higher blast percentage allowed in MDS due to lack of differences in outcomes with \< 5% versus 5-10% blasts in this disease). Therapy related myeloid neoplasms are allowed. * Lymphoma \[follicular lymphoma, Hodgkin lymphoma, diffuse large B cell lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma, angioimmunoblastic T-cell lymphoma and anaplastic large cell lymphoma\]. * Planned NMA/reduced intensity conditioning regimen. * Participants must have a related or unrelated PBSC donor as follows: * Sibling donor must be a 6/6 match for HLA-A and -B at intermediate (or higher) resolution, and -DRB1 at high resolution using DNA-based typing and must be willing to donate peripheral blood stem cells and meet institutional criteria for donation. HLA-matched parents and children may be used as donors. * Unrelated donor must be a 7/8 or 8/8 match at HLA-A, -B, -C and -DRB1 at high resolution using DNA-based typing. Unrelated donor must be willing to donate peripheral blood stem cells and meet NMDP criteria for donation. * Donor selection must comply with 21 CFR 1271. * Cardiac function: Left ventricular ejection fraction at least 45%. * Estimated creatinine clearance greater than 60 ml/min using the 2021 CKD-EPI formula or 24-hour urine creatinine clearance. * Pulmonary function: DLCO corrected for hemoglobin at least 40% and FEV1 predicted at least 50%. * Liver function: AST/ALT \< 3x ULN; Total bilirubin \< 2 mg/dL excluding Gilbert's syndrome or hemolysis. * Karnofsky Performance Score of at least 60%. * Female participants (unless postmenopausal for at least one year before the screening visit, or surgically sterilized), agree to practice two effective methods of contraception at the same time, or agree to completely abstain from heterosexual intercourse, from the time of signing the informed consent through 15 months post-transplant. Fertility preservation methods will be left to institutional standards. * Male participants (even if surgically sterilized), of partners of women of childbearing potential must agree to one of the following: practice effective barrier contraception or abstain from heterosexual intercourse from the time of signing the informed consent through 15 months post-transplant. * Plans for the use of targeted small molecule inhibitor post-transplant maintenance therapy must be disclosed upon enrollment and must be used irrespective of the outcome of the randomization. Planned use of investigational maintenance agents is not permitted. Planned hypomethylating agents as maintenance therapy is not permitted. * Voluntary written consent obtained prior to the performance of any study-related procedure that is not a part of standard medical care, with the understanding that consent may be withdrawn by the participant at any time without prejudice to future medical care.

Exclusion Criteria:

* Prior allogeneic transplant. * Active CNS involvement by malignant cells. * Participants with secondary AML arising from myeloproliferative neoplasms or overlap syndromes, including CMML and MDS/MPN syndromes; participants with secondary AML arising from myelodysplastic neoplasm are eligible. * Participants with primary myelofibrosis. * Participants with uncontrolled bacterial, viral, or fungal infections (currently taking medication and with progression or no clinical improvement) at time of enrollment. * Active or inadequately treated latent infection with Mycobacterium tuberculosis (i.e., TB). * Presence of clinically significant fluid collection (ascites, pleural or pericardial effusion) that interferes with methotrexate clearance or makes methotrexate use contraindicated. * Participants seropositive for human immunodeficiency virus (HIV) with detectable viral load. HIV+ participants with an undetectable viral load on antiviral therapy are eligible. * Evidence of uncontrolled hepatitis B virus (HBV) or hepatitis C virus (HCV). The study allows: * Positive HBV serology with undetectable viral load and ongoing antiviral prophylaxis to prevent potential HBV reactivation. * Positive HCV serology with quantitative PCR for plasma HCV RNA below the lower limit of detection, with or without concurrent antiviral HCV treatment. * Arterial or venous thrombosis including DVT, PE, stroke, and myocardial infarction within six (6) months prior to enrollment or New York Heart Association (NYHA) Class III or IV heart failure, uncontrolled angina, severe uncontrolled ventricular arrhythmias, or electrocardiographic evidence of acute ischemia. Catheter-associated DVT is not exclusionary. * Female participants who are pregnant (as per institutional practice) or lactating. * Participants with a serious medical or psychiatric illness likely to interfere with participation in this clinical study. * Participants with prior malignancies except resected non-melanoma skin cancer or treated cervical carcinoma in situ. Cancer treated with curative intent ≥ 5 years previously will be allowed. Cancer treated with curative intent \< 5 years previously must be reviewed and approved by the Protocol Officer or Chairs. * Planned use of ATG or alemtuzumab in conditioning regimen. * Planned use of prophylactic donor leukocyte infusions. * Prior use of ruxolitinib. * Prior use of immune checkpoint inhibitors (i.e., PD1, PDL1, CTLA4 modulators) within six (6) months prior to conditioning. * For participants with 7/8 HLA-matched donors: * Donor specific antibodies (DSAs) directed at the mismatched donor allele. * Any use of desensitization protocols. * Treatment with any other Investigational Medicinal Product (IMP) is not allowed while on study treatment. An IMP is defined as medications without any known FDA or EMA approved indications.

Conditions & Interventions

Interventions:
DRUG: Tacrolimus (Tac), DRUG: Methotrexate (MTX), DRUG: Ruxolitinib (Rux), DRUG: Cyclophosphamide, DRUG: Mycophenolate mofetil (MMF)
Conditions:
Graft-versus-host Disease (GVHD)
Keywords:
Graft-versus-host Disease (GVHD), Chronic GvHD (cGvHD), steroid-refractory, ruxolitinib, Janus kinase inhibitor

More Information

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