MT2015-29 : Myeloablative Allogeneic Hematopoietic Cell Transplantation Using a Related or Adult Unrelated Donor for the Treatment of Hematological Disorders

Status: Recruiting

Eligibility Criteria

Sex: All
Age: up to 60 Years old
This study is NOT accepting healthy volunteers
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Inclusion Criteria:

• Age: â‰¤ 60 years of age

• Performance Status: Karnofsky â‰¥ 70%, Lansky play score â‰¥ 70

• Consent: Voluntary written consent (adult or legally authorized representative; or parental/guardian)

• Adequate Organ Function:

• Renal: Creatinine <2x upper limit of normal. Patients above this limit must have creatinine clearance â‰¥ 40 ml/min/1.73m2 as determined by an age-appropriate method, such as cystatin C GFR.

• Hepatic: Bilirubin, AST, alkaline phosphatase <4 times the upper limit of institutional normal

• Pulmonary: Diffusion capacity of oxygen, corrected for hemoglobin, > 50% of predicted. For pediatric patients not able to undergo PFTs or diffusion testing: O2 sat of >95% on room air

• Cardiac: Absence of decompensated congestive heart failure, or uncontrolled arrhythmia and left ventricular ejection fraction > 45%. For children not able to cooperate with MUGA or echocardiography, such should be clearly stated in the physician's documentation

• HIV Status: HIV infection with undetectable viral load. All HIV+ patients must be evaluated by Infectious Disease (ID) and a HIV management plan establish prior to transplantation Other

Inclusion Criteria:

• Women of child bearing potential and sexually active males with partners of child bearing potential must agree to use adequate birth control for the duration of treatment.

• Donor Availability: Patients considered for transplantation must have a sufficient graft as based on current criteria of the University of Minnesota Blood and Marrow Transplantation Program

• Eligible Diseases and Status: Patients are eligible unless their treatment is to be guided by a higher priority protocol.

• Acute Leukemias: Must be in remission by morphology (â‰¤5% blasts). Also a small percentage of blasts that is equivocal between marrow regeneration vs. early relapse are acceptable provided there are no associated cytogenetic markers consistent with relapse.

• Acute Myeloid Leukemia (AML) and related precursor neoplasms: 2nd or greater complete remission (CR); first complete remission (CR1) in patients > 60 years old; CR1 in â‰¤ 60 years old that is NOT considered as favorable-risk.

• Favorable risk AML is defined as having one of the following:

• t(8,21) without cKIT mutation

• inv(16) or t(16;16) without cKIT mutation

• Normal karyotype with mutated NPM1 and wild type FLT-ITD

• Normal karyotype with double mutated CEBPA

• Acute prolymphocytic leukemia (APL) in first molecular remission at the end of consolidation

• Very high risk pediatric patients with AML: Patients <21 years, however, are eligible with (M2 marrow) with < 25% blasts in marrow after having failed one or more cycles of chemotherapy.

• Acute lymphoblastic leukemia (ALL)/lymphoma: second or greater CR; CR1 unable to tolerate consolidation chemotherapy due to chemotherapy-related toxicities; CR1 high-risk ALL.

• High risk ALL is defined as having one of the following:

• Evidence of high risk cytogenetics, e.g. t(9;22), t(1;19), t(4;11), other MLL rearrangements, IKZF1

• 30 years of age or older at diagnosis

• White blood cell counts of greater than 30,000/mcL (B-ALL) or greater than 100,000/mcL (T-ALL) at diagnosis

• CNS leukemia involvement during the course of disease

• Slow cytologic response (>10% lymphoblasts in bone marrow on Day 14 of induction therapy)

• Evidence of persistent immonophenotypic or molecular minimal residual disease (MRD) at the end of induction and consolidation therapy

• Very high risk pediatric patients with ALL: patients <21 years are also considered high risk CR1 if they had M2 or M3 marrow at day 42 from the initiation of induction or M3 marrow at the end of induction. They are eligible once they achieve a complete remission.

• Chronic Myelogenous Leukemia excluding refractory blast crisis: To be eligible in first chronic phase (CP1) patient must have failed or be intolerant to one or more tyrosine kinase inhibitors.

• Plasma Cell Leukemia after initial therapy, in patients who have achieved at least a partial remission

• Myeloproliferative Neoplasms/Myelofibrosis, either primary as a result of polycythemia vera or essential thrombocythemia, with disease risk of intermediate or high-risk according to DIPSS criteria. Blasts must be <10% by bone marrow aspirate morphology.

• Myelodysplasia (MDS) IPSS INT-2 or High Risk (i.e. RAEB, RAEBt) or Refractory Anemia with severe pancytopenia, transfusion dependence, or high risk cytogenetics or molecular features. Blasts must be < 10% by a representative bone marrow aspirate morphology.

• Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL), Marginal Zone B-Cell Lymphoma or Follicular Lymphoma are eligible if there was disease progression/relapse within 12 of achieving a partial or complete remission. Patients who had remissions lasting > 12 months, are eligible after at least two prior therapies. Patients with bulky disease (nodal mass greater than 5 cm) should be considered for debulking chemotherapy before transplant.

• Lymphoplasmacytic Lymphoma, Mantle-Cell Lymphoma, Prolymphocytic Leukemia are eligible after initial therapy in CR1+ or PR1+.

• Diffuse large Cell NHL > CR/> PR: Patients in CR/PR with initial short remission (<6 months) are eligible, or those who have failed/or are not eligible for autologous transplant.

• Lymphoblastic Lymphoma, Burkitt's Lymphoma, and other high-grade NHL after initial therapy if stage III/IV in CR1/PR1 or after progression if stage I/II < 1 year.

• Multiple Myeloma beyond PR2: Patients with chromosome 13 abnormalities, first response lasting less than 6 months, or Î²-2 microglobulin > 3 mg/L, may be considered for this protocol after initial therapy.

• Juvenile myelomonocytic leukemia

• Biphenotypic/Undifferentiated/Prolymphocytic Leukemias in first or subsequent CR.

• MRD positive leukemia (AML, ALL or accelerated/blast phase CML). Selected patients in morphologic CR, but with positive immunophenotypic (flow cytometry) or molecular evidence of MRD may be eligible if recent chemotherapy has not resulted in MRD negative status.

• Natural Killer Cell Malignancies

• Acquired Bone Marrow Failure Syndromes except for Fanconi Anemia or Dyskeratosis Congenita

• Other Leukemia Subtypes: A major effort in the field of hematology is to identify patients who are of high risk for treatment failure so that patients can be appropriately stratified to either more (or less) intensive therapy. This effort is continually ongoing and retrospective studies identify new disease features or characteristics that are associated with treatment outcomes. Therefore, if new features are identified after the writing of this protocol, patients can be enrolled with the approval of two members of the study committee.

Exclusion Criteria:

• Chemotherapy refractory large cell and high grade NHL (i.e., progressive disease after > 2 salvage regimens)

• CML in blast crisis

• Large cell lymphoma, mantle cell lymphoma and Hodgkin disease that is progressing on salvage therapy.

• Evidence of progressive disease by imaging modalities or biopsy

•persistent PET activity, though possibly related to lymphoma, is not an exclusion criterion in the absence of CT changes indicating progression.

• Active central nervous system malignancy

• if â‰¤ 18 years old, prior myeloablative transplant within the last 6 months. If >18 years old prior myeloablative allotransplant or autologous transplant

• Active HIV infection or known HIV positive serology

• active uncontrolled infection

• Pregnant or breastfeeding. The agents used in this study include Pregnancy Category D: known to cause harm to a fetus. Females of childbearing potential must have a negative pregnancy test prior to starting therapy.

Conditions & Interventions

Interventions:
Biological: HSCT with TBI Regimen, Biological: HSCT with Non-TBI Regimen
Conditions:
Acute Leukemia, Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, Lymphoma, Chronic Myelogenous Leukemia, Plasma Cell Leukemia, Myeloproliferative Neoplasms, Myelofibrosis, Myelodysplasia, Refractory Anemia, High Risk Anemia, Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma, Marginal Zone B-Cell Lymphoma, Follicular Lymphoma, Lymphoplasmacytic Lymphoma, Mantle-Cell Lymphoma, Prolymphocytic Leukemia, Diffuse Large Cell Non Hodgkins Lymphoma, Lymphoblastic Lymphoma, Burkitt Lymphoma, High Grade Non-Hodgkin's Lymphoma, Adult, Multiple Myeloma, Juvenile Myelomonocytic Leukemia, Biphenotypic/Undifferentiated/Prolymphocytic Leukemias, MRD Positive Leukemia, Natural Killer Cell Malignancies, Acquired Bone Marrow Failure Syndromes
Keywords:
AML, ALL, MDS, NHL, CLL, CML, SLL, Clinics and Surgery Center (CSC)

More Information

Description: The primary research element is to determine whether a graft-versus-host disease (GVHD) prophylaxis regimen of post-transplant cyclophosphamide, tacrolimus and MMF will reduce the likelihood of chronic GVHD in patients receiving a standard hematopoietic myeloablative stem cell transplant. The treatment related components of this protocol are established clinical practices and are considered non-investigational. The primary endpoint is cumulative incidence of chronic GVHD requiring systemic immunosuppressive treatment at 1 year post-transplant.
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