PROTOCOL SYNOPSIS - BMT CTN PROTOCOL #0903

Allogeneic Hematopoietic Cell Transplant for Hematological Cancers and Myelodysplastic Syndromes in HIV-Infected Individuals

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Primary Objective: The primary objective is to assess the feasibility and safety of allogeneic hematopoietic cell transplantation (HCT) in HIV-infected patients. The primary endpoint is 100-Day Non-Relapse Mortality (NRM).

Secondary Objectives: Patients will be assessed for the following endpoints:

1. Disease status at Day 100 post-HCT
2. Time to hematopoietic recovery
3. Chimerism at 4 weeks, 100 days, and 6 months
4. Hematologic function at 100 days and 6 months
5. Infections
6. Six-month overall survival
7. Acute graft-vs-host disease
8. Chronic graft-vs-host disease
9. Immunologic reconstitution at 8 weeks, 6, 12 and 24 months
10. Impact of HCT on the HIV reservoir at Day 100, 6,12 and 24 months post-HCT

Study Design: This study is designed as a Phase II multi-center trial.

Accrual Objective: The trial will accrue 15 patients.

Accrual Period: The estimated accrual period is 2 years.

Eligibility Criteria: Patients ≥ 15 years old, HIV-infected and diagnosed with acute myeloid leukemia (AML) or acute lymphocytic leukemia (ALL) in first or second complete remission (CR); Int-2 or high-risk myelodysplastic syndrome (MDS) with < 10% marrow blasts and no circulating myeloblasts after their most recent therapy; or Hodgkin or non-Hodgkin lymphoma beyond first CR with at least a partial response to last treatment. Patients must have either an 8/8 matched related donor at HLA-A, -B, -C, (serologic typing or higher resolution) and –DRB1 (at high resolution using DNA based typing), or at least a 7/8 matched unrelated donor at HLA-A, -B, -C and DRB1 (at high resolution using DNA based typing). A 7/8 matched related donor match is permitted only if an 8/8 unrelated donor cannot be identified. A secondary matching

criterion is the presence of homozygosity for the CCR5delta32 mutation. Allogeneic transplantation using cord blood, T-cell depletion or prior allogeneic HCT are not allowed for this study.

Patients must have adequate organ function defined as 1) left ventricular ejection fraction at rest $\geq$ 40%; 2) DLCO, FEV_1, FVC $\geq$ 45% predicted; 3) total bilirubin $\leq$ 2.0 mg/dL, and ALT and AST $\leq$ 5 x upper limit of normal (ULN); 4) creatinine clearance > 40mL/min (measured or calculated). Karnofsky/Lansky performance status $\geq$ 70%.

Treatment Description: Patients with HIV infection and hematological malignancies or myelodysplastic syndromes (MDS) will be treated with either reduced-intensity or fully ablative allogeneic hematopoietic cell transplantation (HCT). Where feasible, an attempt will be made to identify hematopoietic cell donors who are homozygotes for the CCR5delta32 mutation. Patients will receive standard immunosuppressive therapy post-transplant that will be tapered as per the institutional standard of care. Graft-versus-host disease will be treated per the institutional standard of care.

Study Duration: Patients will be followed for two years following allogeneic HCT.