

01-C-0125: A Pilot Study of Non-myeloablative, HLA-matched Allogenic Stem cell Transplantation for Pediatric Hematopoietic Malignancies

Allogenic blood and marrow stem cell transplantation (BMT) plays an important role in the curative treatment of a number of pediatric malignancies. Unfortunately, the success of conventional allogeneic BMT is limited in part by the multiple toxicities associated with myeloablative preparative regimens. Non-myeloablative pre-transplant regimens are associated with less toxic side effects than standard BMT. Recently, a novel immunosuppressive, non-myeloablative pre-transplant chemotherapy regimen has been shown to facilitate complete donor engraftment in an adult trial at the NCI. The primary objective of this protocol is to evaluate the efficacy and safety of this treatment approach in pediatric patients with hematopoietic malignancies.

Eligibility Criteria

- Patients with the following diagnoses are eligible:
- Hodgkin's and Non-Hodgkin's Lymphoma: Refractory disease or relapse after salvage regimen.
- Acute Myelogenous Leukemia: History of bone marrow relapse in remission (CR) #2 or greater.
- Acute Lymphocytic Leukemia: History of bone marrow relapse in CR #2 or greater (CR#1 with Philadelphia chromosome positive or prior induction failure).
- Acute Hybrid Leukemia including mixed lineage, biphenotypic and undifferentiated: History of bone marrow relapse in CR #2 or greater (CR#1 with Philadelphia chromosome positive or prior induction failure).
- Myelodysplastic Syndrome: RAEB or RAEB-t with <10% blasts in marrow and blood.
- Chronic Myelogenous Leukemia: Chronic phase or accelerated phase with <10% blasts in marrow and blood.
- Juvenile Myelomonocytic Leukemia: <10% blasts in marrow and blood.
- Patient age: ≥ 5 years and < 22 years.
- Prior therapy: Chemotherapy to achieve above criteria allowed. Prior BMT allowed as long as at least day 100+ post-prior BMT, no evidence of GVHD, and no detectable residual donor chimerism.
- Donor: First degree related donors, who are HLA matched (single HLA-A or B locus mismatch allowed), weight ≥ 15 kilograms, and who meet standard donation criteria will be considered. The same donor from a prior BMT is allowed.
- ECOG performance status: 0, 1, or 2. and life expectancy: > 3 months.
- Liver function: Serum direct bilirubin < 2.0 mg/dL and serum ALT and AST values $\leq 2.5x$ upper limit of normal. (Values above these levels may be accepted if due to malignancy.)
- Renal function: Age adjusted normal serum creatinine or Cr clearance ≥ 60 mL/min/1.73 m².
- Pulmonary function: DLCO $\geq 50\%$.
- Cardiac function: LVEF $\geq 45\%$ by MUGA or LVSF $\geq 28\%$ by ECHO.

Exclusion Criteria

- Active CNS malignancy: Tumor mass on CT or leptomeningeal disease. (Patients with a history of CNS involvement and no current evidence of CNS disease are allowed.)
- HIV infection, active hepatitis B or C infection: HbSAg or HCV seropositive and elevated liver transaminases.
- Fanconi Anemia.

- Lactating or pregnant females.

General Treatment Plan

- Initial evaluation: Patient and donor will be screened for eligibility. G-CSF mobilized peripheral blood stem cells will be collected from the donor.
- Induction/Consolidation chemotherapy: 1 to 3 cycles will be given every 22 days depending on disease response, CD4 count, and toxicities.
- Lymphoma: fludarabine, etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone, and filgrastim (EPOCH-fludarabine).
- Leukemia and MDS: Fludarabine, cytarabine, and filgrastim (FLAG).
- Transplantation: Fludarabine and cyclophosphamide will be administered over 4 days followed by peripheral blood stem cell transplant. Patients will remain hospitalized until bone marrow recovery. Patients will be monitored closely at the NIH for at least 100 days post-BMT.

Accrual: Open to accrual. Patients can be referred to the NIH, NCI, Pediatric Oncology Branch for evaluation and treatment.