AAML05P1: Phase II Pilot Study of Killer Immunoglobulin-Like Receptor-Incompatible Unrelated Donor Hematopoietic Cell Transplantation in Young Patients With Relapsed, Refractory, or Newly Diagnosed Acute Myeloid Leukemia/ Therapy for New Diagnosis High Risk Disease

Basic Study Information

Phase	Type	Status	Age	Sponsor
Phase II	Biomarker/Laboratory Analysis, Treatment	Active	1 month to 21 years of age	COG

Outline

This is a multicenter study.

- Preparative regimen: Patients receive busulfan IV over 2 hours every 6 hours on days -9 to -6, high-dose cyclophosphamide IV over 1 hour on days -5 to -2, anti-thymocyte globulin IV once or twice daily on days -3 to -1, and methylprednisolone IV on days -3 to -1.
- Allogeneic hematopoietic stem cell transplantation (HSCT): Patients undergo allogeneic HSCT on day 0.
- Graft-vs-host disease (GVHD) prophylaxis (for patients undergoing bone marrow transplantation): Patients receive cyclosporine or tacrolimus IV or orally beginning on day -2 and continuing until day 50, followed by a taper until week 24. Patients also receive methotrexate IV on days 1, 3, 6, and 11.

Blood samples will be collected periodically from both patients and donors for pharmacokinetics studies and studies of natural killer cells.

After completion of study treatment, patients are followed every 6 months for 2 years and then annually for 3 years.

Objectives

1. To define the relationship between the status of donor NK-cell receptor and patient outcomes after killer immunoglobulin-like receptor-incompatible unrelated donor (URD) hematopoietic cell transplantation (HCT) in young patients with poor prognosis relapsed or refractory acute myeloid leukemia (AML) or newly diagnosed AML.
2. To assess NK-cell development after URD HCT in these patients.

Projected Accrual

- A total of 400 patients will be accrued for this study.
  Entry Criteria

Disease Characteristics:

- Diagnosis of one of the following:
- Primary refractory acute myeloid leukemia (AML) (> 5% bone marrow blasts after two cycles of induction chemotherapy)
- Newly diagnosed AML with -5/5q- or monosomy 7 in patients who have completed two cycles of induction chemotherapy
- Relapsed AML meeting the customary WHO criteria for AML
- These patients must have undergone re-induction chemotherapy
- No Fanconi anemia
- No CNS disease
- HLA-matched donor available
- Matched at HLA-A, -B, -C, and -DRB1
- Donor with the highest number of KIR-KIR ligand mismatches will be selected

Patient Characteristics:

- Age: 1 month to 21 years of age

Performance Status:

- Karnofsky performance status 50-100% (for patients over 16 years of age
- Lansky PS (for patients 16 and under) 50-100%

Life Expectancy

- Not specified

Hematapoetic

- Not specified

Hepatic

- Total bilirubin ≤ 2 mg/dL
- SGOT (AST) or SGPT (ALT) ≤ 2.5 times upper limit of normal

Renal

- Creatinine clearance or radioisotope glomerular filtration rate at least 60 mL/min OR creatinine adjusted according to age as follows:
- No greater than 0.4 mg/dL (≤ 5 months of age)
- No greater than 0.5 mg/dL (6-11 months)
- No greater than 0.6 mg/dL (1 year-23 months)
- No greater than 0.8 mg/dL (2-5 years)
- No greater than 1.0 mg/dL (6-9 years)
- No greater than 1.2 mg/dL (10-12 years)

- No greater than 1.4 mg/dL (at least 13 years of age [female])
- No greater than 1.5 mg/dL (13-15 years [male])
- No greater than 1.7 mg/dL (at least 16 years of age [male])

Cardiovascular

- DLCO ≥ 50% OR a normal chest x-ray and pulse oximetry in patients who are unable to undergo pulmonary function tests
- Shortening fraction ≥ 27% by ECHO
- Pulmonary: Not specified

Other

- HIV negative
- Not pregnant or nursing
- Negative pregnancy test
- Fertile patients must use effective contraception
- Patients with proven or suspected bacterial sepsis, pneumonia, or meningitis are eligible provided appropriate therapeutic measures have been initiated to control the presumed or proven infection, and systemic signs are not life-threatening
- No evidence or presence of a fungal infection within the past 30 days

Prior/Concurrent Therapy:

- Prior chemotherapy, radiotherapy or any antileukemic therapy allowed provided patients meet 1 of the following criteria:
- Disease has failed induction chemotherapy on another primary treatment trial; these patients may have gone on to have additional therapy
- Received initial treatment for relapsed AML
- No treatment for fungal infection within the past 30 days
  Concurrent radiotherapy to localized painful lesions allowed
- No other concurrent cancer chemotherapy or immunomodulating agents

Who should I contact for more information?

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