Extended vs Short-term Abatacept Dosing for Graft Versus Host Disease Prophylaxis

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 2 years and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

1. Must be at least 2 years old and weigh 10 kg.
2. Must have a willing unrelated adult donor (bone marrow or peripheral blood). Donors may have a single mismatch (i.e. be a 7/8) and this mismatch may be at the allele or antigen level; however, donors with allele level disparity should be given preference over those with antigen level disparity. Patients for whom a donor is available with disparity only in the host versus graft direction (because of recipient homozygosity), will not be eligible, since this mismatching does not increase the risk for GVHD. Centers may perform extended typing (e.g. DQB1 and DPB1) according to institutional practices and use these results in selecting donors; however, it is recommended that this extending typing be used only to select between donors who are equally well matched with the recipient at the A, B, C and DRB1.
3. All patients and/or their parents or legal guardians must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines.
4. Must have a hematologic malignancy treatable by HCT (except for those stipulated below under study Exclusion Criteria), which is in remission by standard testing (no patients in relapse will be included).
5. Patients with an inherited predisposition to leukemia or otherwise hematologic malignancies that have not been associated with predisposition to transplant morbidities or non-hematologic cancers.
6. Karnofsky performance score or Lanskey Play-Performance Scale score >/= 80.

- If the patient does not meet defined eligibility requirements, the PI/study committee must be contacted to determine eligibility.

Exclusion Criteria:

1. Patients with the following hematologic malignancies will be excluded: Chronic Lymphocytic Leukemia, Myeloma and Primary Myelofibrosis.
2. Active Relapse (>5% blasts) of their primary malignancy.
3. For patients with Acute Lymphocytic Leukemia (ALL) with pre-transplant MRD testing performed as standard practice at the treating institution, patients with MRD >0.01% will be ineligible.
4. For patients with Acute Myeloid Leukemia (AML) with pre-transplant MRD testing as standard of practice at the treating institution, patients with any MRD status are eligible and should be enrolled at the discretion of provider.
5. For patients with MDS, those with >5% blasts will be excluded.
6. Prior allogeneic HCT.
7. Uncontrolled viral, bacterial, fungal or protozoal infection at the time of study enrollment.
8. HIV infection.
9. Serious psychiatric disease including schizophrenia, bipolar disorder and severe depression.
10. Prisoners or others who are compulsorily detained.
11. Any patient with a known or suspected inherited predisposition to cancer should be discussed with the study team prior to screening for eligibility.
    1. Patients with a known inherited or constitutional predisposition to transplant morbidities, including, but not limited to Fanconi Anemia, Dyskeratosis Congenita, Shwachman-Diamond Syndrome and Down Syndrome will be excluded.
    2. Patients with known inherited or constitutional predisposition to non-hematologic cancers including, but not limited to Li-Fraumeni syndrome, BRCA1 and BRCA2 mutations will be excluded.
12. Patients with active non-hematological malignancies (except non-melanoma skin cancers) or those with non-hematological malignancies (except non-melanoma skin cancers) who have been rendered with no evidence of disease, and are disease free for <2 years.
13. Incompletely treated active tuberculosis Infection.
14. Pregnancy (positive serum b-HCG) or breastfeeding.
15. Estimated GFR of < 50 mL/min/1.73m2.
16. Cardiac ejection fraction < 50 (using M-Mode if assessment is done by ECHO)
17. T.bilirubin > 2 × upper limit of normal or ALT > 4 × upper limit of normal or unresolved veno-occlusive disease.
18. Pulmonary disease with FVC, FEV1 or DLCO parameters <45% predicted (corrected for hemoglobin) or requiring supplemental oxygen. Children who are developmentally unable to perform pulmonary function testing will be assessed solely on their need for supplemental oxygen.
19. Presence of antibodies to a mismatched donor HLA antigen (please refer to Section 3.4.g).
20. Patients who have developed severe AGVHD, severe CGVHD or relapse will be excluded at the time of randomization.
21. Exclusion Criteria Prior to Randomization (prior to 5th dose of abatacept/placebo):

1. Severe allergic reaction during the first 4 doses of abatacept
2. If any clinical events occur that preclude further dosing of abatacept, those patients will be deemed ineligible for randomization

Conditions & Interventions

Interventions:
DRUG: Placebo, DRUG: Abatacept
Conditions:
Graft Vs Host Disease

More Information

Description:
This is a multicenter randomized, double blind, Phase 2 trial for patients receiving transplants from 7 of 8 HLA matched donors, in which an extended dosing regimen of abatacept, and a short-term dosing regimen + placebo, when added to standard calcineurin inhibitor + methotrexate-based prophylaxis, will be compared for their ability to improve outcomes in patients with a minimum follow-up of one year post-transplant. All patients will receive 4 doses of abatacept (Days -1, +5, +14, +28). Prior to the fifth dose, patients will be randomly assigned to the 4-dose abatacept arm and receive 4 doses of placebo or 8-dose abatacept arm and receive 4 more doses of abatacept. The primary endpoint of the study will be severe AGVHD-free, severe CGVHD-free, relapse-free survival (SGRFS). The study will end when the last patient has reached 2 years after transplant. Results will first be calculated and the study unblinded when the last patient has reached one year post-transplant.

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