Conditioning SCID Infants Diagnosed Early

Status: RECRUITING

Eligibility Criteria

Age: 0 years to 2 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1\. Infants with SCID, either typical or leaky or Omenn syndrome. 1. Typical SCID is defined as either of the following * Absence or very low number of T cells (CD3+ T cells \<300/microliter AND no or very low T cell function (\<10% of lower limit of normal) as measured by response to phytohemagglutinin OR * Presence of maternally derived T cells 2. Leaky SCID is defined as the following • Absence of maternally derived T cells • AND either one or both of the following (i, ii): i) \<50% of lower limit of normal T cell function as measured by response to PHA OR \<30% of lower limit of normal T cell function as measured by response to CD3 ii) Absent or \<10% of lower limit of normal proliferative responses to candida and tetanus toxoid antigens (must document post vaccination or exposure for this criterion to apply) • AND at least two of the following (i through iii): i) CD3 T cells \< 1500/microliter ii) \>80% of CD3+ or CD4+ T cells are CD45RO+ AND/OR \>80% of CD3+ or CD4+ T cells are CD62L negative AND/OR \>50% of CD3+ or CD4+ T cells express HLA-DR (at \< 4 years of age) AND/OR are oligoclonal T iii) Low TRECs and/or the percentage of CD4+/45RA+/CD31+ or CD4+/45RA+/CD62L+ cells is below the lower level of normal. 3. Omenn syndrome • Generalized skin rash * Maternal lymphocytes tested for and not detected. * \>80% of CD3+ or CD4+ T cells are CD45RO+ AND/OR \>80% of CD3+ or CD4+ T cells are CD62L negative AND/OR \>50% of CD3+ or CD4+ T cells express HLA-DR (\<2 years of age) * Absent or low (up to 30% lower limit of normal (LLN)) T cell proliferation to antigens (Candida, tetanus) to which the patient has been exposed IF: Proliferation to antigen was not performed, but at least 4 of the following 8 supportive criteria, at least one of which must be among those marked with an asterisk (*) below are present, the patient is eligible as Omenn Syndrome. 1. Hepatomegaly 2. Splenomegaly 3. Lymphadenopathy 4. Elevated IgE 5. Elevated absolute eosinophil count 6. *Oligoclonal T cells measured by CDR3 length or flow cytometry (upload report) 7. *Proliferation to PHA is reduced to \< 50% of lower limit of normal (LLN) or SI \< 30 8. *Low TRECs and/or percentage of CD4+/RA+ CD31+ or CD4+/RA+ CD62L+ cells below the lower level of normal 2\. Documented mutation in one of the following SCID-related genes a. Cytokine receptor defects (IL2RG, JAK3) b. T cell receptor rearrangement defects (RAG1, RAG2) 3. No available genotypically matched related donor (sibling) 4. Availability of a suitable donor and graft source 1. Haploidentical related mobilized peripheral blood cells 2. 9/10 or 10/10 allele matched (HLA-A, -B, -C, -DRB1, -DQB1) volunteer unrelated donor mobilized peripheral blood cells 5. Age 0 to 2 years at enrollment Note: to ensure appropriate hepatic metabolism, age at time of busulfan start: For IL2RG/JAK3: 8 weeks For RAG1/RAG2: 12 weeks 6\. Adequate organ function defined as: 1. Cardiac: Left ventricular ejection fraction (LVEF) at rest ≥ 40% or, shortening fraction (SF) ≥ 26% by echocardiogram. 2. Hepatic: Total bilirubin \< 3.0 x the upper limit of normal (ULN) for age (patients who have been diagnosed with Gilbert's Disease are allowed to exceed this limit) and AST and ALT \< 5.0 x ULN for age. 3. Renal: GFR estimated by the updated Schwartz formula ≥ 90 mL/min/1.73 m2. If the estimated GFR is \< 90 mL/min/1.73 m2, then renal function must be measured by 24-hour creatinine clearance or nuclear GFR, and must be \> 50 mL/min/1.73 m2. 4. Pulmonary No need for supplemental oxygen and O2 saturation \> 92% on room air at sea level (with lower levels allowed at higher elevations per established center standard of care).

Exclusion Criteria:

1. Presence of any serious life-threatening or opportunistic infection at time of enrollment and prior to the initiation of the preparative regimen. Serious infections as defined below that occur after enrollment must be reported immediately to the Study Coordinating Center, and enrollment will be put on hold until the infection resolves. Ideally enrolled subjects will not have had any infection. If patients have experienced infections, these must have resolved by the following definitions: a. Bacterial i. Positive culture from a sterile site (e.g. blood, CSF, etc.): Repeat culture(s) from same site must be negative and patient has completed appropriate course of antibacterial therapy (typically at least 10 days). ii. Tissue-based clinical infection (e.g. cellulitis): Complete resolution of clinical signs (e.g. erythema, tenderness, etc.) and patient has completed appropriate course of antibacterial therapy (typically at least 10 days). iii. Pneumonia, organism not identified by bronchoalveolar lavage: Complete resolution of clinical signs (e.g. tachypnea, oxygen requirement, etc.) and patient has completed appropriate course of antibacterial therapy (typically at least 10 days). If possible, radiographic resolution should also be demonstrated. b. Fungal i. Positive culture from a sterile site (e.g. blood, CSF, etc.): Repeat culture(s) from same site is negative and patient has completed appropriate course of antifungal therapy (typically at least 14 days). The patient may be continued on antifungal prophylaxis following completion of the treatment course. c. Pneumocystis i. Complete resolution of clinical signs (e.g. tachypnea, oxygen requirement, etc.) and patient has completed appropriate course of therapy (typically at least 21 days). If possible, radiographic resolution should also be demonstrated. The patient may be continued on prophylaxis following completion of the treatment course. d. Viral i. Viral PCRs from previously documented sites (blood, nasopharynx, CSF) must be re-tested and are negative. ii. If re-sampling a site is not clinically feasible (i.e. BAL fluid): Complete resolution of clinical signs (e.g. tachypnea, oxygen requirement, etc.). If possible, radiographic resolution should also be demonstrated. 2. Patients with HIV or HTLV I/II infection will be excluded.

Conditions & Interventions

Interventions:
DRUG: Busulfan, DEVICE: Cell processing for TCRαβ+/CD19+ depletion
Conditions:
SCID

More Information

Contact(s): Allison Neutzling - aweiss@nmdp.org
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT03619551
