Phase I/II Trial of Lentiviral Gene Transfer for SCID-X1 With Low Dose Targeted Busulfan Conditioning

Status: RECRUITING

Eligibility Criteria

Sex: MALE
Age: 0 years to 5 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- 1. Diagnosis of SCID-X1 based on immunophenotype and lack of T cell function (proliferation to PHA <10% of the lower limit of normal for the laboratory) AND confirmed by a mutation in IL2RG 2. Lack of an HLA identical (A, B, C, DR, DQ) related donor 3. Age 5 years old or younger 4. Signed informed consent 5. Documentation of willingness to follow up for 15 years post-infusion as currently required by the FDA 6. If the patient has previously undergone allogeneic transplant, lack of donor T cell engraftment must be documented.

7. Age at least 8 weeks by the time of busulfan administration

Exclusion Criteria:

1. Patients with an active, therapy-resistant infection. Infections that are known to be highly morbid in SCID patients will be considered active and therapy-resistant if the infectious agent is repeatedly isolated despite a minimum of 2 weeks of appropriate therapy and is associated with significant organ dysfunction (including but not limited to abnormalities listed below).
    1. Mechanical ventilation including continuous positive airway pressure
    2. Abnormal liver function defined by AST and ALT >10 times the upper range of normal OR Bilirubin >2 mg/dL
    3. Shortening fraction on echocardiogram <25% or ejection fraction <50%
    4. Renal failure defined as glomerular filtration rate <30 ml/min/1.73 m2 or dialysis dependence
2. Uncontrolled seizure disorder
3. Encephalopathy
4. Documented coexistence of any disorder known to affect DNA repair
5. Diagnosis of active malignant disease other than EBV-associated lymphoproliferative disease
6. Patients with evidence of infection with HIV-1
7. Major (life-threatening) congenital anomalies. Examples of "major (life-threatening) congenital anomalies" include, but are not limited to: unrepaired cyanotic heart disease, hypoplastic lungs, anencephaly or other major central nervous system malformations, other severe non-repairable malformations of the gastrointestinal or genitourinary tracts that significantly impair organ function.
8. Other conditions which in the opinion of the P.I. or co-investigators, contra-indicate collection and/or infusion of transduced cells or indicate patient's inability to follow the protocol. These may include for example clinical ineligibility to receive anesthesia, severe deterioriation of clinical condition of the patient after collection of bone marrow but before infusion of transduced cells, or documented refusal or inability of the family to return for scheduled visits. There may be other unforeseen rare circumstances that would result in exclusion of the patient, such as sudden loss of legal guardianship

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Conditions & Interventions

Interventions:
BIOLOGICAL: autologous CD34+ cell transduced with G2SCID vector
Conditions:
Severe Combined Immunodeficiency, X Linked, Gene Therapy
Keywords:
lentiviral, Gene therapy, busulfan

More Information

Description:
This is a phase I/II open label multi-center study in which patients will receive low dose targeted busulfan followed by infusion of autologous CD34+ selected bone marrow or mobilized peripheral blood cells transduced with the G2SCID vector. Subjects will be enrolled over 3 years and be followed for 2 years post-infusion on this protocol, then followed long-term on a separate long-term follow-up protocol. Enrollment of subjects will be agreed upon by representatives of both sites. Data will be collected uniformly from both sites through an electronic capture system and key laboratory studies will be centralized. Harvest, cellular manufacturing and infusion will occur at each site using the same SOPs. Key aspects of cellular product characterization will be centralized

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