MT2010-09 Primary Immune Deficiency Treatment Consortium (PIDTC). PROJECT 1: A Prospective Natural History Study of Diagnosis, Treatment and Outcomes of Children with SCID Disorders (RDCRN PIDTC #6901)

Status: Recruiting

Eligibility Criteria

Sex: All
Age: Not specified
This study is NOT accepting healthy volunteers

Inclusion Criteria:

Stratum A: Typical SCID (formerly referred to as Classic SCID)- -Subjects who meet the following inclusion criteria and the intention is to treat with allogeneic hematopoietic cell transplant (HCT) are eligible for enrollment into Stratum A (Typical SCID) of the study:

• 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 (PHA) OR

• T cells of maternal origin present. Stratum B: Leaky SCID, Omenn Syndrome, Reticular Dysgenesis- -Subjects who meet the following criteria and the intention is to treat with HCT are eligible for enrollment into Stratum B: Leaky SCID:

• Maternal lymphocytes tested for and not detected AND

• Either one or both of the following (a,b) :

• a.) <50% of lower limit of normal T cell function as measured by response to PHA, OR response to anti-CD3/CD28 antibody

• b.) Absent or <30% of lower limit of normal proliferative responses to candida and tetanus toxoid antigens

• AND at least two of the following (a through e):

• a.) Reduced number of CD3 T cells

• age â‰¤2 years: <1500/microliter

• age >2 years and â‰¤4 years: <800/microliter

• age >4 years: <600/microliter

• b.) â‰¥80% of CD3+ or CD4+ T cells that 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 cells

• c.) Hypomorphic mutation in IL2RG in a male, or homozygous hypomorphic mutation or compound heterozygosity with â‰¥1 hypomorphic mutation in an autosomal SCID-causing gene

• d.) Low T Cell Receptor Excision Circles (TRECs) and/or the percentage of CD4+/45RA+/CD31+ or CD4+/45RA+/CD62L+ cells is below the lower limit of normal.

• e.) Functional testing in vitro supporting impaired, but not absent, activity of the mutant protein, AND

• Does not meet criteria for Omenn Syndrome. Omenn Syndrome:

• Generalized skin rash

• Maternal lymphocytes tested for and not detected; --Note: If maternal engraftment was not assessed and ruled out, the subject is not eligible as Omenn Syndrome.

• â‰¥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 <2 years of age);

• Absent or low (< 30% lower limit of normal) T cell proliferation response to antigens (Candida, tetanus) to which the subject has been exposed NOTE: If proliferation to antigen was not performed, but at least 4 of the following 9 supportive criteria, at least one of which must be among those marked with an asterisk (*) below are present, the subject is eligible as Omenn Syndrome:

• Hepatomegaly

• Splenomegaly

• Lymphadenopathy

• Elevated IgE

• Elevated absolute eosinophil count

• *Oligoclonal T cells measured by CDR3 length or flow cytometry

• *Proliferation to PHA is reduced <50% of lower limit of normal or SI <30

• *Hypomorphic mutation in a SCID causing gene

• Low TRECS and/or the percentage of CD4+/45RA+/CD31+ or CD4+/45RA+/CD62L+ cells is below the lower limit of normal. Reticular Dysgenesis:

• Absence or very low number of T cells (CD3 <300/ÂµL

• No or very low (<10% lower limit of normal) T cell response to PHA

• Severe neutropenia (absolute neutrophil count < 200 /ÂµL) AND

• â‰¥2 of the following (a,b,c):

• a.) Sensori-neural deafness

• b.) Deficiency of marrow granulopoiesis on bone marrow examination

• c.) A pathogenic mutation in the adenylate kinase 2 (AK2) gene identified. Stratum C: Subjects who meet the following criteria and the intention is to treat with therapy other than allogeneic HCT, primarily PEG-ADA ERT or gene therapy with autologous modified (gene transduced) cells, are eligible for enrollment into Stratum C:

• ADA Deficient SCID with intention to treat with PEG-ADA ERT

• ADA Deficient SCID with intention to treat with gene therapy

• X-linked SCID with intention to treat with gene therapy

• Any SCID patient previously treated with a thymus transplant (includes intention to treat with HCT, as well as PEG-ADA ERT or gene therapy)

• Any SCID patient who received therapy for SCID deemed "non-standard" or "investigational", including in utero procedures.

Exclusion Criteria:

-Subjects who meet any of the following exclusion criteria are disqualified from enrollment in Strata A, B, or C of the study:

• Presence of an Human Immunodeficiency Virus (HIV) infection (by PCR) or other cause of secondary immunodeficiency

• Presence of DiGeorge syndrome

• MHC Class I and MHC Class II antigen deficiency, and

• Metabolic conditions that imitate SCID or related disorders such as folate transporter deficiency, severe zinc deficiency or transcobalamin deficiency.

Conditions & Interventions

Conditions:
Severe Combined Immunodeficiency (SCID), Leaky SCID, Omenn Syndrome, Reticular Dysgenesis, ADA SCID, XSCID
Keywords:
Severe Combined Immunodeficiency (SCID), natural history study, SCID treatment

More Information

Contact(s): Kim Nelson - knelso62@fairview.org
Principal Investigator: Christen Ebens
Phase: N/A
IRB Number: 1011M93312
System ID: NCT01186913