MT2014-30R: Analysis of Patients Treated for Chronic Granulomatous Disease Since January 1, 1995 (PIDTC 6903)

Status: Recruiting

Eligibility Criteria

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

Inclusion Criteria:

• Participant Inclusion Criteria (Part 1

•Longitudinal Analysis)

• CGD Patients Undergoing Transplant 1995 to Present with Birth Year In or After 1988 1. CGD Patients will be Defined by both Defective Neutrophil NADPH Oxidase Function and by Clinical History Consistent with CGD Patients must have both of: A functional assay demonstrating abnormal NADPH oxidase function (see A below); AND Clinical history consistent with CGD (see B below). ********** Patients must have both "A" and "B": A. Function: Assays of NADPH Oxidase Function I. Dihydrorhodamine (DHR) Assay:

• Blood sample was obtained at a time when patient was clinically stable and not critically ill, with control samples performed simultaneously indicating a qualified assay; and

• Assay unequivocally demonstrates CGD with an stimulation index (SI) SI < 35 or equivalent. Assay report, including mean fluorescence intensity (MFI) from unstimulated and stimulated samples and gating strategy, must be de-identified and provided. OR II. Nitroblue Tetrazolium Oxidation Test (NBT): o Diagnostic of CGD (reported as reduced granulocyte oxidative response). Report must be de-identified and provided. AND B. Clinical History: One or More of the Following:

• Severe and/or recurrent infection (liver, perirectal or lung abscess; pneumonia; adenitis; or osteomyelitis) due to, for example, Staphylococcus aureus, Burkholderia sp, Serratia marcescens, non-albicans Candida sp, Aspergillus sp or other mold; or Nocardia sp or other deep tissue infection characteristic of CGD

• Sterile granulomatous disease in respiratory, gastrointestinal or urogenital tracts; or Crohn's disease-like colitis

• A family history consistent with either X-linked or autosomal recessive CGD In cases where either functional assay (A) or history (B) is equivocal, one or more of the following may be used to confirm a diagnosis of CGD: C. Absent or significantly reduced in expression or abnormal size of any of the 5 phox components (gp91 phox, p47 phox, p22 phox, p67phox, and p40phox) of NADPH oxidase, by either:

• Western blot

• Northern blot OR D. Mutation in a gene encoding one of the 5 phox components (gp91 phox, p47 phox, p22 phox, p67 phox, and p40 phox) of NADPH oxidase that is predictive of a decreased or absent oxidative burst. (Nonsense, frameshift, or previously described missense mutation associated with CGD). Molecular Diagnosis is Desirable In addition, molecular diagnosis (gene sequencing and expression analysis) of CGD is desirable and should be performed when possible. 2. Further Characterization of Oxidase Level, Longitudinal Study, Prospective Cohort Patients who are to undergo transplantation during the study period must be further characterized as oxidase-null or oxidase positive by level of oxidase production by either:

• DHR assay stimulation Index: where SI â‰¤ 2.5 will be classified as oxidase-null CGD. Those with SI > 2.5 will be classified as oxidase positive CGD. A single validated test that is accepted by the PID-CGD Review Panel is adequate, but testing on two occasions for validation is desirable. OR

• Ferricytochrome C reduction assay of granulocytes with O2 < 2.3 nmoles /106 cells/h classified as oxidase-null CGD. A single validated test that is accepted by the PID-CGD Review Panel is adequate, but testing on two occasions for validation is desirable. OR o Genetic sequencing reporting a mutation that is unequivocally associated to absent oxidase production. (e.g. null mutations) will be classified as oxidase-null CGD (See discussion in Appendix I for how family history, genotype and CGD mutation information will be applied to assigning patients lacking any quantitative oxidase activity measurements to residual oxidase-null or residual oxidase-positive groups). 3. Longitudinal Study, Retrospective Cohort Patients who have already been transplanted will be included regardless of whether further characterization by oxidase level (or genotype/mutation data) is possible or not.

• Non-Transplanted CGD Patients with Birth Year In or After 1988 A non-transplant (conventional therapy) group of CGD subjects will be enrolled in the longitudinal study. The non-transplant subjects will be selected from the potentially eligible (retrospective) patient cohort with diagnosis of CGD treated with conventional non-transplant therapy. Participating sites will enter their entire retrospective cohort of CGD patients having birth year in or after 1988 into the registration cohort for this protocol. Baseline for both non-transplant subjects and HCT subjects for the purpose of comparing survival will be the year of birth. However, for non-transplant subjects, many of the detailed analyses such as infection and autoimmune complication rates will be assessed in the year preceding the date of last contact.

• Participant Inclusion Criteria (Part 2

•Cross-Sectional Analysis) To participate in the Cross-Sectional Analysis, patients must have previously been enrolled into the Longitudinal Analysis of Protocol 6903. All transplanted subjects in the Cross-Sectional Analysis are surviving and shall have at least 3 years of follow-up post-transplant to be included. Non-transplanted CGD subjects will become eligible for consideration for the Cross-Sectional Analysis if they were eligible and enrolled in the retrospective cohort of the Longitudinal Analysis, and if/when they are > 3 years post-diagnosis of CGD. Provision of written informed consent will be required for inclusion in the Cross-Sectional Analysis.

Exclusion Criteria:

• Participant Exclusion Criteria (Longitudinal and Cross- Sectional Analyses)

• Presence of other primary immunodeficiency syndromes that do not meet the clinical and laboratory criteria for CGD.

• Rac2 Deficiency

• Myeloperoxidase Deficiency (MPO Deficiency)

• Glutathione deficiency

• Leukocyte adhesion deficiency syndrome

• Non-transplant subjects:

• The above exclusions pertain.

• In addition, non-transplant subjects will be excluded if the only assessment of oxidase function available is the nitroblue tetrazolium (NBT) test (a non-quantitative test).

Conditions & Interventions

Conditions:
Granulomatous Disease, Chronic
Keywords:
Granulomatous Disease, Chronic, Hematopoietic Stem Cell Transplantation (HSCT), bone marrow transplant (BMT), non-transplant, factors associated with best outcomes of transplant in CGD, Clinics and Surgery Center (CSC)

More Information

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