## PROTOCOL SYNOPSIS - BMT CTN PROTOCOL #1204

**Reduced-Intensity Conditioning for Children and Adults with Hemophagocytic Syndromes or Selected Primary Immune Deficiencies (RICHI)**

**Study Chairpersons:** Carl Allen, MD, PhD and Michael Pulsipher, MD

**Primary Objective:** To prospectively determine the 1-year overall survival in subjects treated for hemophagocytic syndromes or primary immune deficiencies (CGD, HIGM1, IPEX, and severe LAD-I) using a standardized, reduced-intensity conditioning protocol consisting of fludarabine, melphalan and intermediate timing of alemtuzumab (Day -14).

**Secondary Objectives:** Secondary objectives for the study include measurement of sustained engraftment, incidence of HLH and CAEBV reactivation and death from disease, immune reconstitution and functional immune recovery at 1-year, cumulative incidence (CI) of grade II-IV and III-IV acute GVHD and chronic GVHD, transplant-related complications (VOD, CNS toxicity), infectious complications including reactivation of CMV, adenovirus, EBV, invasive fungal infection or bacterial sepsis, and overall survival and rate of sustained engraftment of specific disease subsets.

**Study Design:** This study is designed as a Phase II multi-center trial. The study population includes patients with HLH, HLH-related disorders, and selected primary immune deficiencies: CGD, HyperIgM Syndrome (HIGM1), IPEX Syndrome, or severe LAD-I with indications for HCT receiving a bone marrow transplant from a related or unrelated donor (see HLA typing requirements in eligibility criteria below).

**Accrual Objective:** The trial will accrue a minimum of 35 HLH patients.

**Accrual Period:** The estimated accrual period is 3 years.

**Eligibility Criteria:** Eligible patients are > 3 months and ≤ 45 years of age with Lansky/Karnofsky performance status ≥ 50% who have HLH or related disorders or selected immune deficiencies with an indication for HCT. Patients must have adequate organ function (cardiac, renal, hepatic, pulmonary). Only bone marrow donors are allowed on this study. The donor must be:

- An unaffected sibling donor who is a 6/6 match at HLA–A and –B (intermediate or higher resolution) and –DRB1 (at high resolution using DNA-based typing) *OR*

- An unaffected related donor (other than sibling) who is a 7/8 or 8/8 match for HLA–A, –B, –C (at intermediate or higher resolution), and –DRB1 (at high resolution using DNA-based typing) *OR*
- An unrelated donor who is a 7/8 or 8/8 match at HLA–A, –B, –C, and –DRB1 (at high resolution using DNA-based typing).

**Treatment Description:** All eligible patients undergoing bone marrow HCT will receive reduced-intensity conditioning (RIC) with fludarabine, melphalan and alemtuzumab beginning on Day -14.

**Study Duration:** Patients will be followed for 1 year post-HCT.