

A major question posed in the decade of the eighties was related to the observation that while the SC erythrocyte contained a 50:50 proportion of HbS to HbC, with no significant difference in the tendency of HbC versus HbA to polymerize with HbS, the SC erythrocyte sickled. This led to a series of crucial studies, which demonstrated that the pathognomic feature of HbSC is the presence of unusually high-density reticulocytes. However, these elegant laboratory studies have not yet been translated into clinical interventions. Based on a series of laboratory investigations at our Center, we have identified two interventions, which may be helpful for this disorder, and are proposing an approach to therapy with the pleotropic drug Hydroxyurea and periodic phlebotomy (HUP Trial). The goal of this clinical trial is to determine whether oral Hydroxyurea (HU) therapy and periodic phlebotomy, compared to HU alone over an 18 month period will decrease self-reported, pain rates in symptomatic patients with HbSC disease, as measured by an increase in the median duration between painful episodes. A secondary aim is to determine whether there will be signs of amelioration of organ damage as a result of these therapies; such as a potential partial return of splenic function, or non-progression of proliferative retinopathy and/or avascular osteonecrosis in previously affected patients. As an ancillary study, we hope to determine whether “responders” will be able to be differentiated from “non-responders” by specific biologic parameters. Such markers will include red cell indices, dense cell formation, blood viscosity, assays and markers for red cell-endothelial adhesion, white cell, endothelial and hemostatic activation, and Nitric Oxide Metabolites. These studies should provide insights into the modes of action of the pleotropic drug Hydroxyurea, as well as initial studies related to the benefits of phlebotomy. The study can be completed within a 21-month period, and will involve a sample size that can be realistically accomplished within the framework of the 10 Comprehensive Sickle Cell Centers.