A Pilot Randomized Controlled Trial for Feasibility of Enrolling Subjects for Influenza Therapeutic Trials and Administering Influenza Antivirals in the Emergency Department to High Risk Subjects

Background: Although new influenza therapeutics are needed to mediate population level morbidity and mortality associated with both seasonal and pandemic influenza, clinical trials evaluating emerging therapeutics have been challenging. One well-recognized challenge with prior large trials is that they historically have recruited otherwise healthy subjects at clinical sites with low recruitment, resulting in the need to engage with hundreds of recruitment sites, and a relative lack of patients with more severe and/or complicated illness. This has introduced management challenges with trial implementation and evaluation, including high associated costs for subject recruitment and retention.

As the first line of care for many patients with influenza, U.S. emergency departments (EDs) represent an as yet untapped clinical venue for recruiting individuals with influenza into clinical trials. Notably, EDs also have the advantage of caring for patients early in their clinical course, and frequently serve as the initial site of care for those with complicated and/or severe influenza. Taken together this creates opportunities, which could be leveraged for design and implementation of more streamlined influenza therapeutic clinical trial design.

Objectives: This pilot study is designed to demonstrate the feasibility of utilizing EDs as a primary site for subject enrollment in clinical trials evaluating influenza therapeutics, providing pilot data for future clinical trial design and planning.

- Primary Objective: To prospectively enroll at least 50 high-risk subjects with laboratory-confirmed influenza into a randomized, open label study of oral versus IV influenza therapeutic to include symptom evaluation and outcome assessments
- Secondary Objective 1: To identify influenza positive patients utilizing a previously established triage-based assessment and rapid testing algorithm for suspected influenza infection
- Secondary Objective 2: To retrospectively evaluate all potentially eligible patients for potential enrollment biases
- Secondary Objective 3: To create a repository of residual nasopharyngeal samples collected from ED patients with suspected influenza illness

Methods: This is a stage IV, open label randomized controlled trial (RCT) of at least 50 adult subjects, who present to the Johns Hopkins Hospital Emergency Department (JHH ED) during the 2015-2016 influenza season, have laboratory confirmed influenza, and are indicated for antiviral treatment as defined by the CDC. A previously established triage-based influenza assessment and rapid molecular testing algorithm will be utilized to identify influenza positive patients. At least 50 influenza positive patients meeting all inclusion and no exclusion criteria will be prospectively enrolled and randomized to receive either a single intravenous dose of Peramivir or 5 days of oral Oseltamivir. The study drug will be administered in the ED following enrollment and prior to discharge or hospitalization. In addition to baseline data collected during the enrollment visit, patients will complete a daily symptom diary for 14 days as well as a 28 day follow up to identify additional influenza-related complications.