Site and Network Information

NIH/NHLBI ACTIV-4 ACUTE:
COVID-19 Acute Inpatient Antithrombotic Study
Also called the Blood Thinner Study

ACTIV-4
Acute Inpatient Anti-Thrombotic Study

This is a randomized, open label, adaptive platform trial to compare the effectiveness of antithrombotic strategies for prevention of adverse outcomes in patients hospitalized for COVID-19. The flexible adaptive design will allow rapid addition and termination of treatments as the evidence evolves.

We invite you to join as a site for a clinical trial that aims to identify the most appropriate strategy to prevent adverse outcomes in the COVID-19 inpatients. For more information or to join, contact us at: ACTIV4Inpatient@pitt.edu or ACTIV4ACUTE@nyulangone.org

Intervention: Initial 2 Arms:
i. prophylactic dose anticoagulation
ii. therapeutic dose anticoagulation
Additional arms will be added

Inclusion/Exclusion Criteria:
- Hospitalized for COVID-19+, age 18 or over
- Expected to require > 72 hours of hospitalization
- Patients with pregnancy or contraindication to anticoagulation are excluded

Primary Outcome: 21 Day Organ Support Free Days, which is defined as the number of days that a patient is alive and free of organ support through the first 21 days after trial entry. Organ Support is defined as receipt of invasive or non-invasive mechanical ventilation, high flow nasal oxygen, vasopressor therapy, or ECMO, with death at any time (including beyond 21 days) during hospitalization.

Key Secondary Outcome: Composite of death, pulmonary embolism, systemic arterial thromboembolism, myocardial infarction, or ischemic stroke at hospital discharge or 28 days, whichever occurs first.

Primary Safety Endpoint: Major bleeding (as defined by the ISTH)
Secondary Safety Endpoints: Symptomatic intracranial hemorrhage, Confirmed heparin induced thrombocytopenia (HIT).

Expected Enrollment Setting: Inpatient non-ICU level of care and ICU

Other Study Design Features:
- **Co-enrollment in other COVID-19-related trials is permitted**
- These medications (heparins) and doses are approved for preventing and treating blood clots in different situations
- Plans to provide Remdesivir
- Plans to provide rapid COVID testing kits to hospitals (if required)
- Electronic tools will be available to facilitate consent.
- Optional participation in Biobanking blood for studies of biomarkers

Analysis Considerations: 2000 patient target. Modified ITT including only participants who are confirmed to meet eligibility criteria. Adaptive component allows modification of study arms' continuation and duration, subject numbers and eligibility criteria based on safety and efficacy.

Pre-specified subgroups based on disease severity and D-Dimer will be used to identify optimal risk benefit.