NHLBI COVID-19 Clinical Research Framework

**Goals**

- **Reduce case severity/fatality, speed recovery**
- **Understand short- and long-term trajectory**
- **Enable risk stratification, precision interventions**
- **Identify biomarkers and therapeutic targets**
- **Target populations most severely affected**

**COVID-19+ Progression**

1. Prevention
2. Outpatient Asymptomatic
3. Outpatient Symptomatic
4. Emergency Department
5. Hospital Vent/CPAP-free
6. Hospital ICU
7. Convalescence
8. Recovered

**Host-Directed Therapeutics Clinical Trials**

- Understand short- and long-term trajectory
- Enable risk stratification, precision interventions
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- Target populations most severely affected

**Cohort of Cohorts for Long-Term Follow-Up**

**Screening, Referral, and Registries**

**Community-Engaged Research Consortium**
Goal: Leverage and expand NHLBI’s national clinical research networks to rapidly and nimbly respond to emerging research and clinical needs for COVID-19

- Leveraging existing assets, data, and studies
- Comprehensive, expandable platform linking trial network, registries, and cohorts
- Facilitating case finding, clinical trial accrual, longitudinal studies, and community engagement
CONNECTS Clinical Trial and Registries Platform: Driving Toward COVID-19 Host-Directed Interventions Before, During, and After Hospitalization

**COVID-19+ Progression**
- COVID-19: Prevention
- COVID-19+ Asymptomatic Outpatient
- COVID-19+ Symptomatic Outpatient
- COVID-19+ Emergency Department
- COVID-19+ Hospital Vent/CPAP-Free
- COVID-19+ ICU
- COVID-19+ Convalescence
- COVID-19+ Recovered

### Host-Directed Therapeutics Clinical Trials & Case Registries

#### Patient Populations
- **Pre-hospital Outpatient**
  - COLOCORONA: Colchicine vs. Placebo
- **Hospitalized Patients (+/- ventilatory support)**
  - ORCHID: Hydroxychloroquine vs. Placebo
- **Post-hospital Convalescent Patients**
  - C3P0 – Convalescent Plasma vs. Placebo

#### Passive Immunity
- **ACTIV – 4B**

#### Anti-Inflammatory
- **ACTIV – 4A**

#### Anti-Thrombotic
- **ACTIV – 4C**
Outcomes Related To COVID-19 Treated With Hydroxychloroquine Among Inpatients With Symptomatic Disease (ORCHID) Trial

Prevention - Outpatient Asymptomatic - Outpatient Symptomatic - Emergency Department - Hospital Vent/CPAP-free - Hospital ICU - Convalescence - Recovered

Hospitalized Patients (+/- ventilatory support)

Patient Demographics

- Asian: 11
- Other: 41
- Non-Hispanic White: 137
- Hispanic: 178
- Non-Hispanic Black: 112

Addressed early question about Hydroxychloroquine effectiveness. Study was stopped on June 19 because there was no benefit or harm.
The Clinical Trial of COVID-19 Convalescent Plasma of Outpatients (C3PO)

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- Convalescence
- Recovered

**Patient Populations**

- Pre-hospital Outpatient

**Passive Immunity**

**C3PO: Convalescent Plasma vs. Placebo**

- **Population**: Adults presenting to the ED:
  - Mild, symptomatic, lab confirmed COVID-19
  - High risk for progression to severe/critical illness
  - Clinically stable for outpatient management at randomization
- **Planned Enrollment**: 600 in total (300 per arm)
- **Intervention**: A single dose of convalescent plasma (CP) or saline placebo

Evaluating the use of convalescent plasma to treat non-hospitalized patients with mild COVID-19.
Accelerating COVID-19 Therapeutic Interventions and Vaccines 4 (ACTIV-4)

Host-Directed Therapeutics Clinical Trials

**Patient Populations**
- Pre-hospital Outpatient
- Hospitalized Patients (+/- ventilatory support)
- Post-hospital Convalescent Patients

**Anti-Thrombotic**
- **ACTIV – 4B**
  - Anticoagulation (apixaban): prophylactic or therapeutic dose
  - Antiplatelet agent: low dose aspirin
  - Placebo

- **ACTIV – 4A**
  - Prophylactic dose heparin
  - Therapeutic dose heparin

- **ACTIV – 4C**
  - Prophylactic dose anticoagulant (apixaban)
  - Therapeutic dose anticoagulant (apixaban)

Evaluating effectiveness of antithrombotic drugs to reduce life-threatening blood clots.
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**Community-Engaged Research Consortium**
Thank you to Patients, NIH Staff, Researchers for your critical role in improving COVID-19 therapies.

C3PO Clinical Trial of COVID-19 Covalescent Plasma in Outpatients

ORCHID Trial