NHLBI COVID-19 Clinical Research Framework

COVID-19+ Progression

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

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

Host-Directed Therapeutics Clinical Trials

Cohort of Cohorts for Long-Term Follow up

Screening, Referral and Registries

Community-Engaged Research Consortium
“Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies”

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
CONNETCS Clinical Trial and Registries Platform: Driving Toward COVID-19 Host-directed Interventions Before, During, and After Hospitalization

**COVID-19+ Progression**

- **Prevention**
- **Outpatient Asymptomatic**
- **Outpatient Symptomatic**
- **Emergency Department**
- **Hospitalized Patients (+/- ventilatory support)**
- **Hospital ICU**
- **Convalescence**
- **Recovered**

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

### Patient Populations

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

### Anti-Inflammatory

- **COLOCORONA**
  - Colchicine vs Placebo
- **ORCHID**
  - Hydroxychloroquine vs Placebo

### Passive Immunity

- **C3P0 – Convalescent Plasma vs. Placebo**

### Anti-Thrombotic

- **ACTIV – 4B**
- **ACTIV – 4A**
- **ACTIV – 4C**
Outcomes Related To COVID-19 Treated With Hydroxychloroquine Among In-patients With Symptomatic Disease (ORCHID) Trial

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)

**Prevention**

**Outpatient**

Asymptomatic

Symptomatic

Emergency Department

Hospital Vent/CPAP-free

Hospital ICU

Convalescence

Recovery

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**COVID-19+ Progression**

**Pre-hospital Outpatient**

**C3P0:** 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

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Evaluating the use of *convalescent plasma* to treat non-hospitalized patients with mild COVID-19.
Host-Directed Therapeutics Clinical Trials

Patient Populations

Pre-hospital Outpatient
ACTIV – 4B
- Anticoagulation (apixaban): prophylactic or therapeutic dose
- Antiplatelet agent: low dose aspirin
- Placebo

Hospitalized Patients (+/- ventilatory support)
ACTIV – 4A
- Prophylactic dose of heparin
- Therapeutic dose heparin

Post-hospital Convalescent Patients
ACTIV – 4C
- Prophylactic dose anticoagulant (apixaban)
- Therapeutic dose anticoagulant (apixaban)

Evaluating effectiveness of antithrombotic drugs to reduce life-threatening blood clots.
Cohort of Cohorts for Long-Term Follow up
Community-Engaged Research Consortium
Host-Directed Therapeutics Clinical Trials
Screening, Referral and Registries
Community-Engaged Research Consortium

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Thank you to Patients, NIH Staff, Researchers for your critical role in improving COVID-19 therapies.