

NIH ACTIV: Rapidly Advancing Understanding, Prevention, and Treatment of COVID-19- Associated Coagulopathy (CAC)

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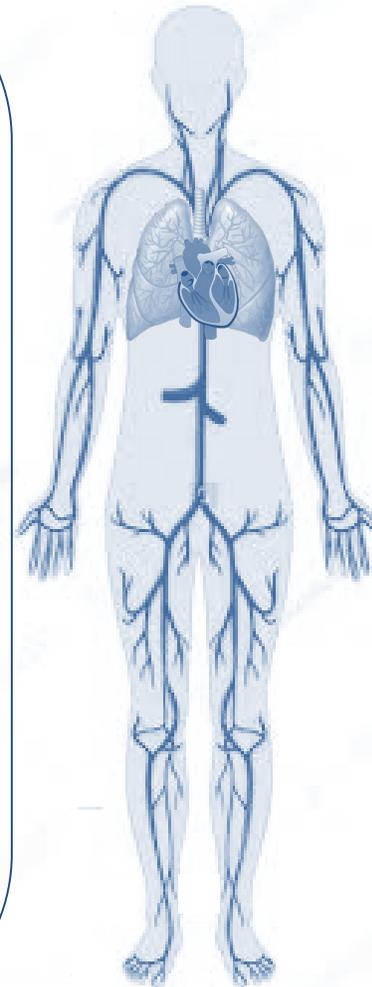
June 11, 2020



COVID-19 Has Severe Effects on the Lung, Heart, Vascular and Blood Coagulation Systems

What We Know About COVID-19-Associated Coagulopathy (CAC)

- **Blood clots in many** critically ill patients
- 71% of COVID-19 patients who died in China had **systemic coagulopathy**
- **Wide range** of affected patients
- Causing **pulmonary embolism, myocardial infarction, stroke, deep-vein thrombosis**
- Unclear if young people have > CAC rate
- **Increased levels of D-dimer*** strongly associated with increased mortality
- Microvascular thrombosis (arterial/venous)
- Compromised oxygenation and **multi-organ failure**



Currently no clear standard-of-care for anticoagulation in hospitalized COVID-19 patients

Urgent need for clinical evidence to guide practice

*biomarker elevated in conditions associated with thrombosis

Understanding, Preventing, and Treating COVID-19 Coagulopathy (CAC): A Collective Path Forward



Identifying the Mechanism:

What is/are the clotting trigger(s) from COVID-19 viral infection (e.g. endothelial dysfunction/injury, inflammatory response)?

Understanding Disease Severity:

What is the role of thrombosis in lung dysfunction, organ failure?

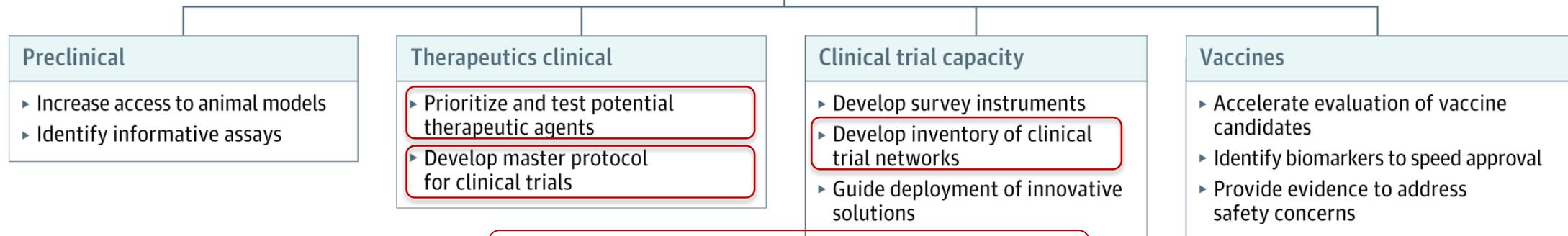
Generating Evidence to Guide Clinical Care:

What is the best treatment of coagulopathy in COVID-19 patients at different stages of illness?

ACTIV Public-Private Partnership: An Integrative Strategy to Advance COVID-19 Therapeutics

ACTIV Public-Private Partnership Accelerating COVID-19 Therapeutic Interventions & Vaccines

Working groups



ACTIV-4 : PROTECT-COVID 19

Federal Partners

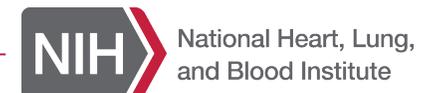


Non-Profit Partners

- Foundation for the National Institutes of Health
- Bill & Melinda Gates Foundation
- Fred Hutchinson Cancer Research Center
- RTI International

Bio/Pharma Industry Partners

- AbbVie
- Amgen
- AstraZeneca
- Bristol Myers Squibb
- Evotec
- GlaxoSmithKline
- Johnson & Johnson
- KSQ Therapeutics
- Eli Lilly and Company
- Merck & Co., Inc.
- Novartis
- Pfizer
- Roche
- Sanofi
- Takeda
- Vir Biotechnology



Understanding, Preventing, and Treating COVID-19 Coagulopathy (CAC): Catalyzing Science and Therapies

ACTIV PPP leverages trans-NIH clinical trial capacity for adaptive clinical trial designs with Master Protocols and conducts cross-disciplinary research with biorepositories for leading-edge natural history studies

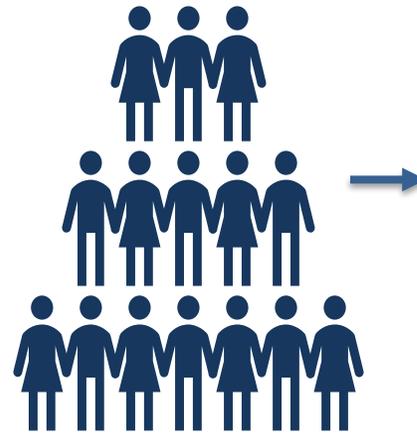


- **Leverage networks' expertise and efficiency**
 - Enhance recruitment speed; facilitate specialized sub-studies
- **Maximize knowledge: Sampling, Imaging, Analysis**
 - **Risk stratification; clinical phenotyping**
 - Stroke and blood-brain barrier
 - Imaging capacities for blood-brain barrier impairment at selected site(s)
 - Interface between inflammation and coagulation
 - Innate immune response
 - Adaptive immune response

ACTIV-4 Master Protocol: Testing Anti-Thrombotic Strategies

Randomized Trial of Anti-Thrombotic Strategies in COVID-19 (PROTECT-COVID 19)

- **First open-label trial** to compare blood-clotting regimens in COVID-19 + patients
- Phase III clinical trial with **focus on low and high doses of heparin**
- **Evolving as an adaptive platform** clinical trial to study other anticoagulants, antiplatelet agents
- Studies will **identify biomarkers to enable patient risk stratification**



- **1,000 COVID-19 + patients**, starting in NY & approximately 15 additional sites
- Includes hospitalized patients with a **D-dimer >500 ng/ml**
- Patients **randomized to higher-dose versus lower-dose heparin** in 1:1 ratio.

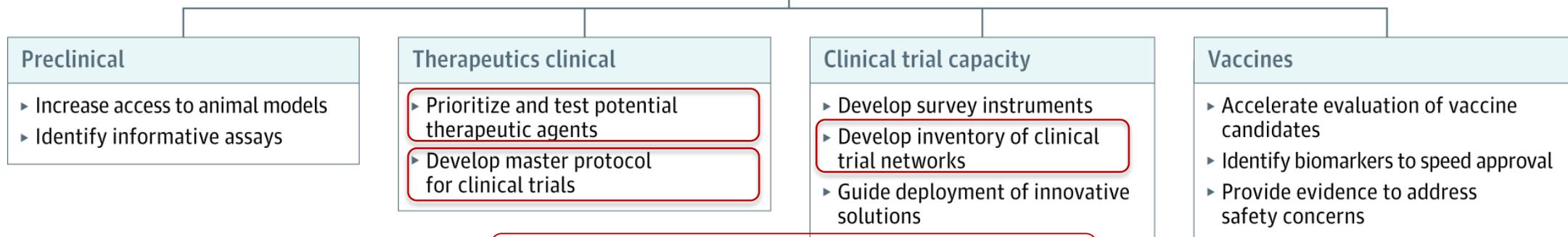


Antithrombotic: Prophylaxis and Treatment

ACTIV Public-Private Partnership: A Rapid Response to Reduce COVID-19 Morbidity and Mortality

ACTIV Public-Private Partnership Accelerating COVID-19 Therapeutic Interventions & Vaccines

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- Eli Lilly and Company
- Merck & Co., Inc.
- Novartis
- Pfizer
- Roche
- Sanofi
- Takeda
- Vir Biotechnology

