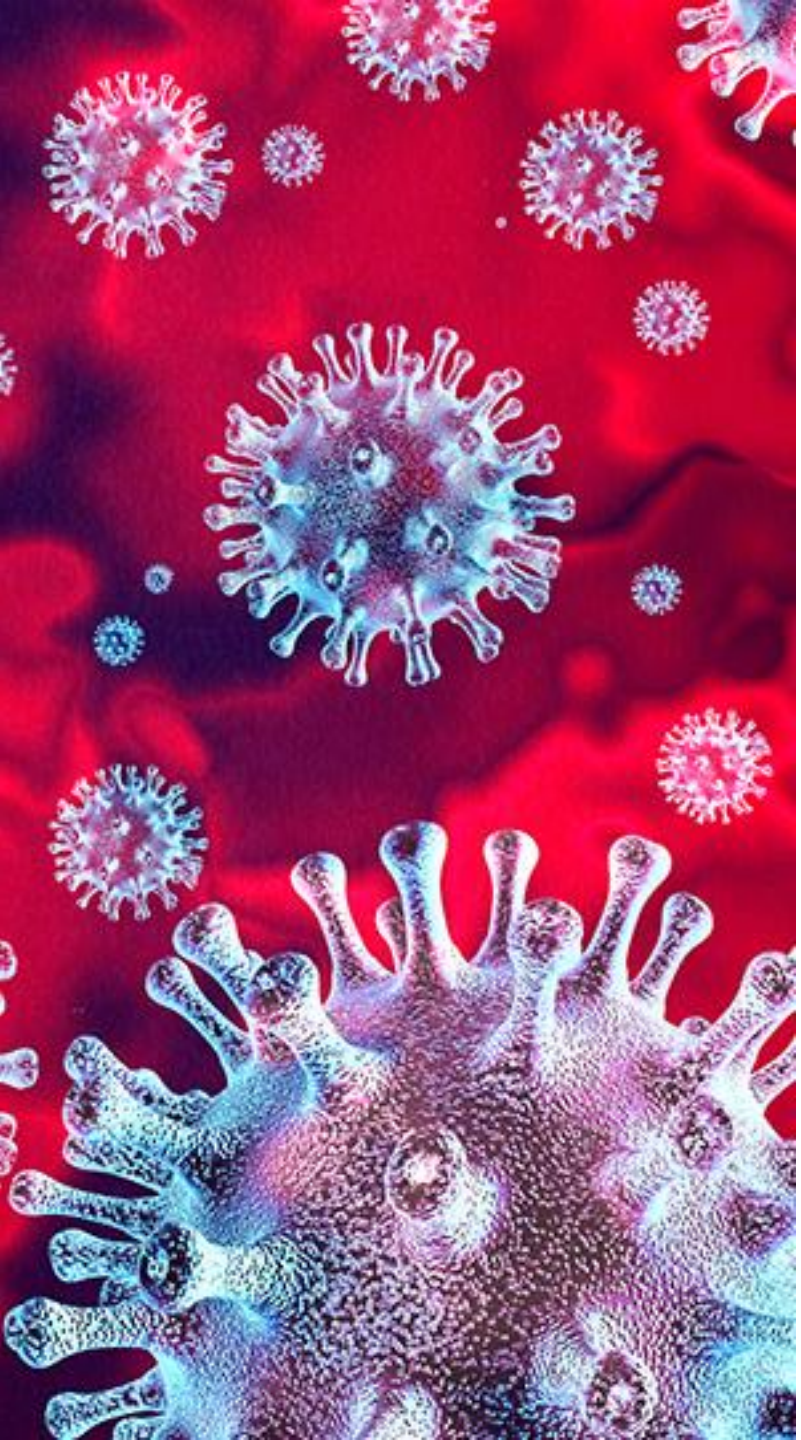

What's the Buzz Around Various Clinical Trials for COVID-19?

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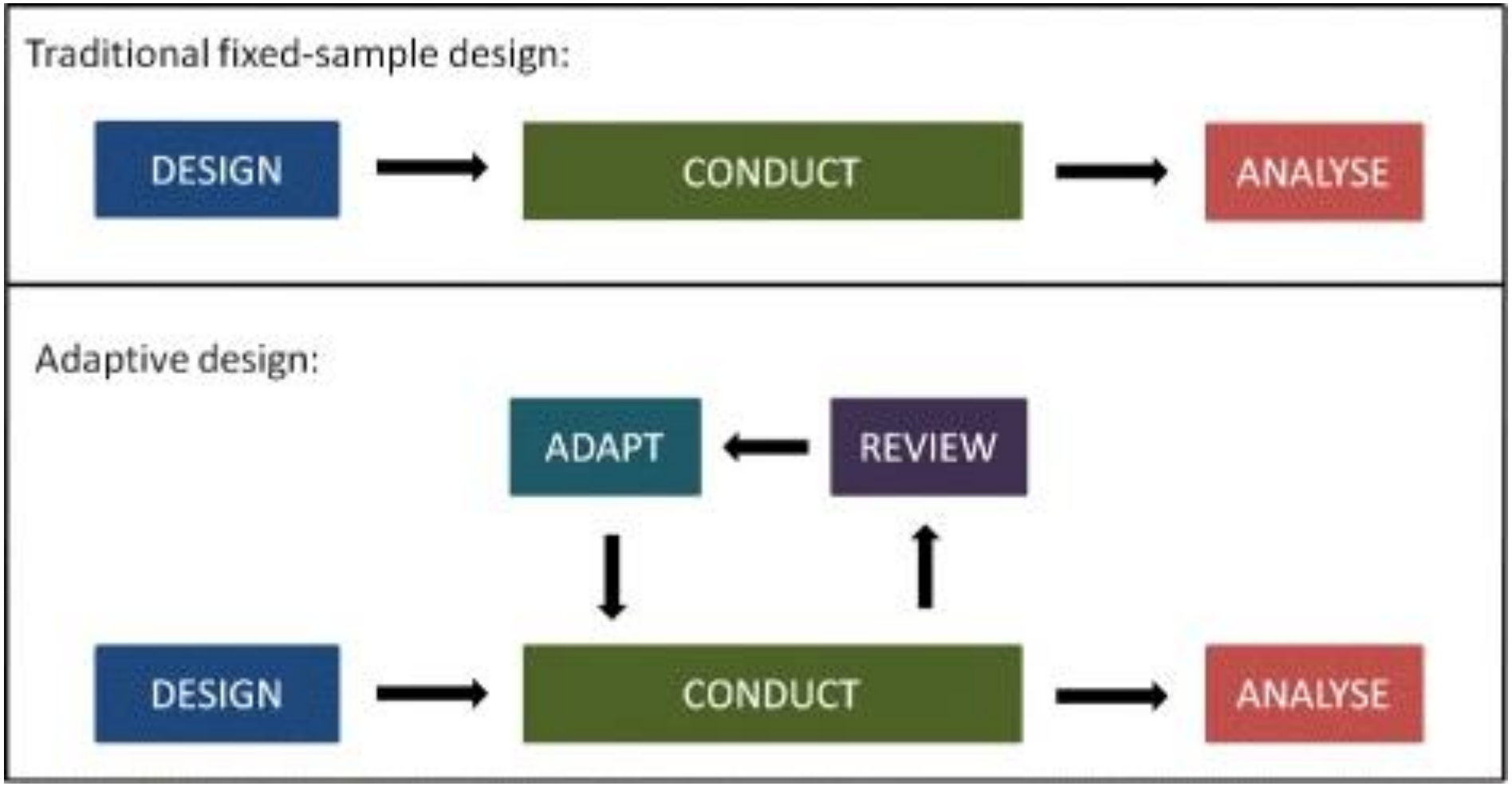
Disclosures

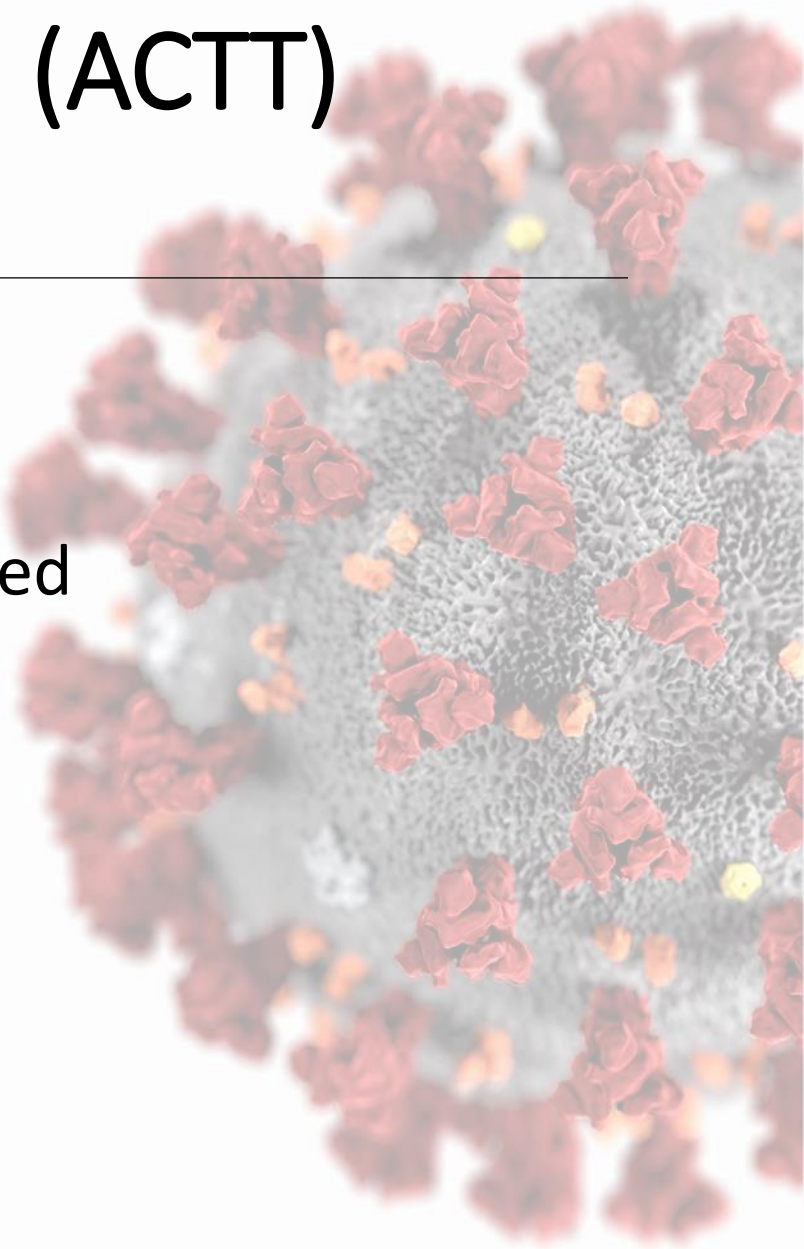
- I was a co-investigator for ACTT trial
- I do not personally endorse any therapy for COVID-19 other than high quality medical care

What is an adaptive design trial?



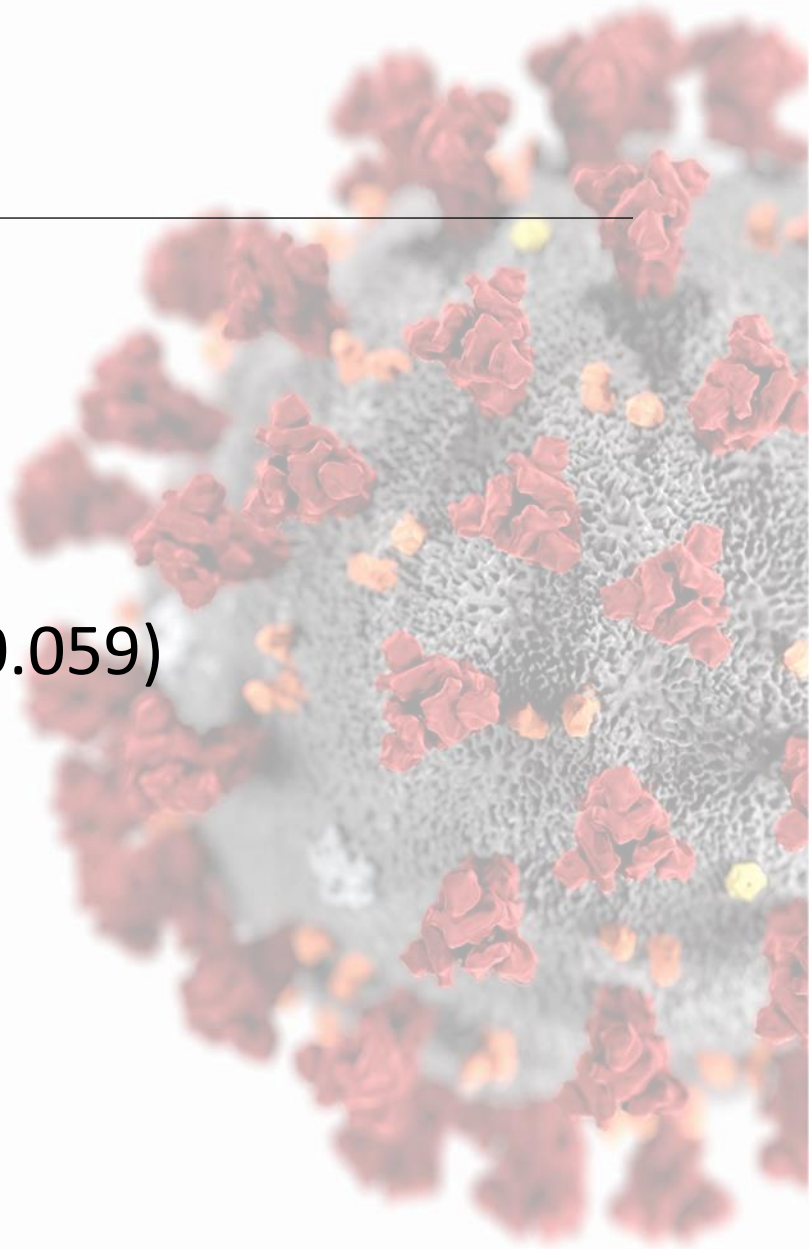
Adaptive Covid-19 Treatment Trial (ACTT) (NCT04280705)

- NIH/NIAID sponsored
- Adaptive design
- 1:1 Randomized, Placebo-controlled, double blinded
- Multicenter trial
- ACTT1
  - Remdesivir 200mg d1
  - 100mg d2-10
- Primary outcome: time to recovery



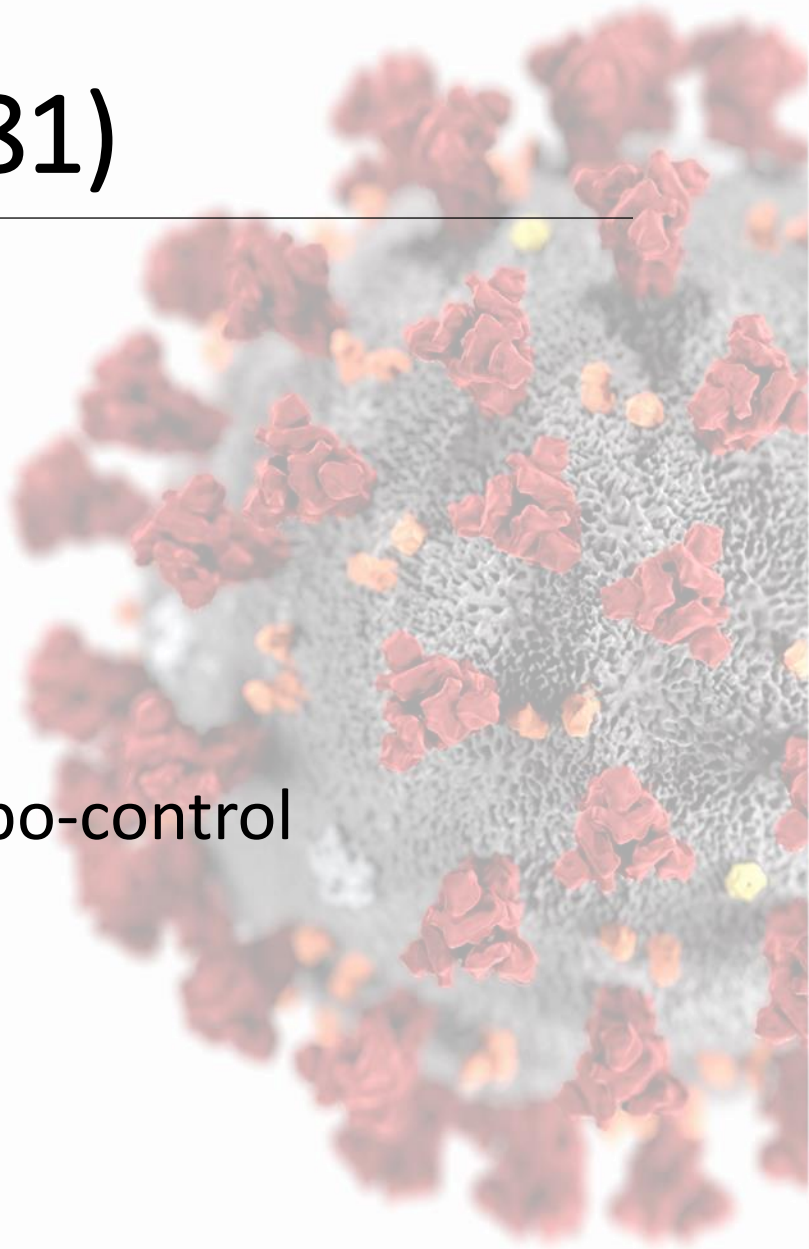
ACTT, Preliminary Findings

- 1063 patients enrolled
- Placebo 15d to recovery, 11d with Remdesivir
  - 31% faster time to recovery (p=0.001)
- Placebo 11.6% mortality, 8% with Remdesivir (p=0.059)
- Not actively enrolling for the first adaptation
- Trial will adapt based on findings



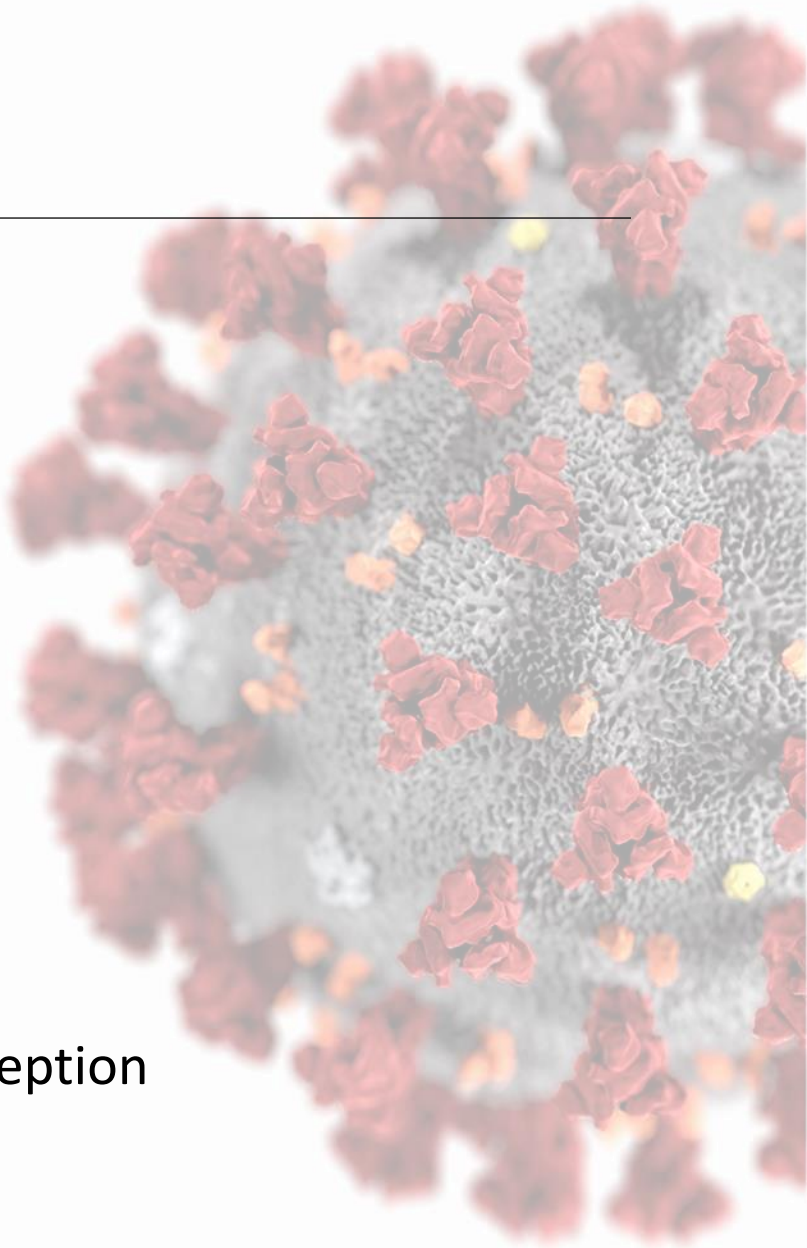
HCQ + Azithromycin (NCT04358081)

- Novartis sponsored study
- Three arms:
  - HCQ 600mg D1, 200mg tid thereafter
  - HCQ + AZT 500mg d1, 25mg d2-5
  - Placebo
- Multi-center, Randomized, Double-blinded, placebo-control
- Planned 444 patient enrollment



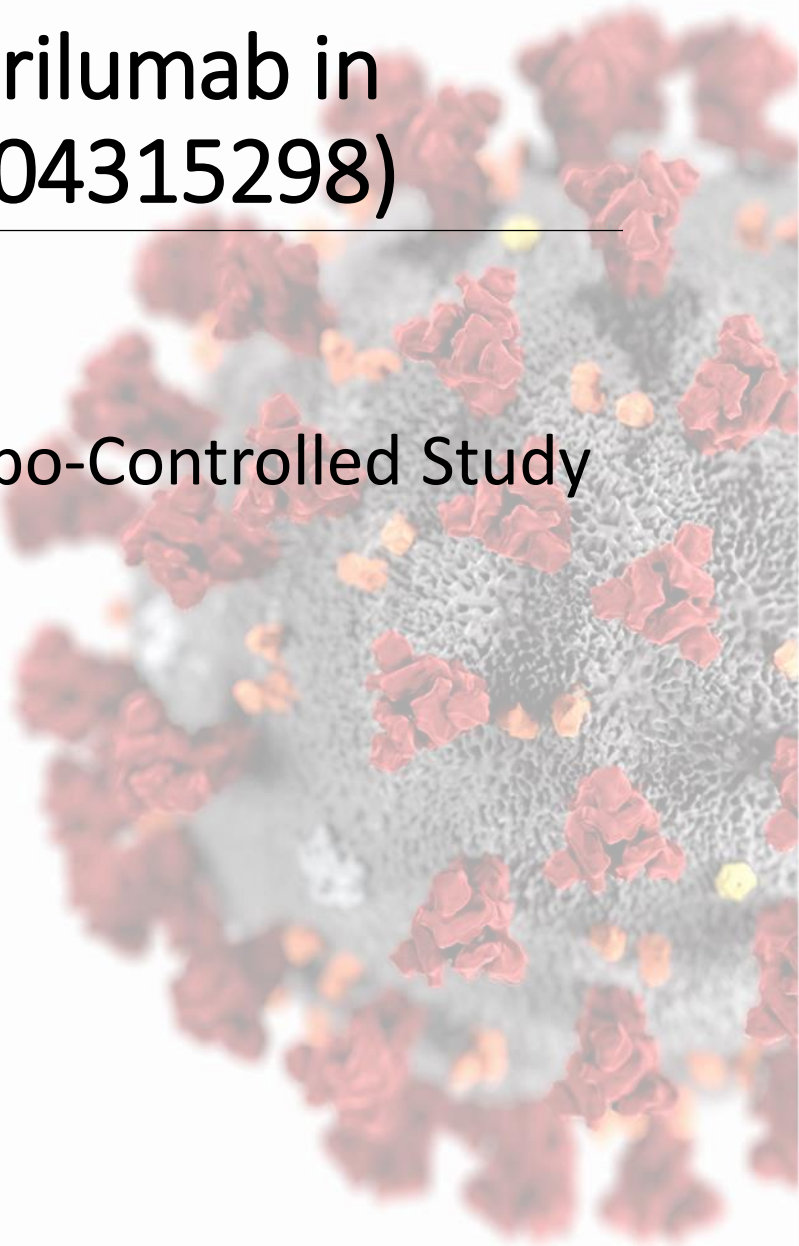
HCQ + Azithromycin

- Primary outcome:
  - % of participants to achieve clinical response
- Enrollment criteria:
  - Adult patient
  - Signs/symptoms less than 7d prior to randomization
- Exclusion Criteria
  - Cytokine storm
  - Concurrent treatment with other SARS-2 therapies
  - CrCl <45
  - EKG abnormalities (historical or present)
  - Pregnancy or women of childbearing age must take contraception
- Not yet recruiting



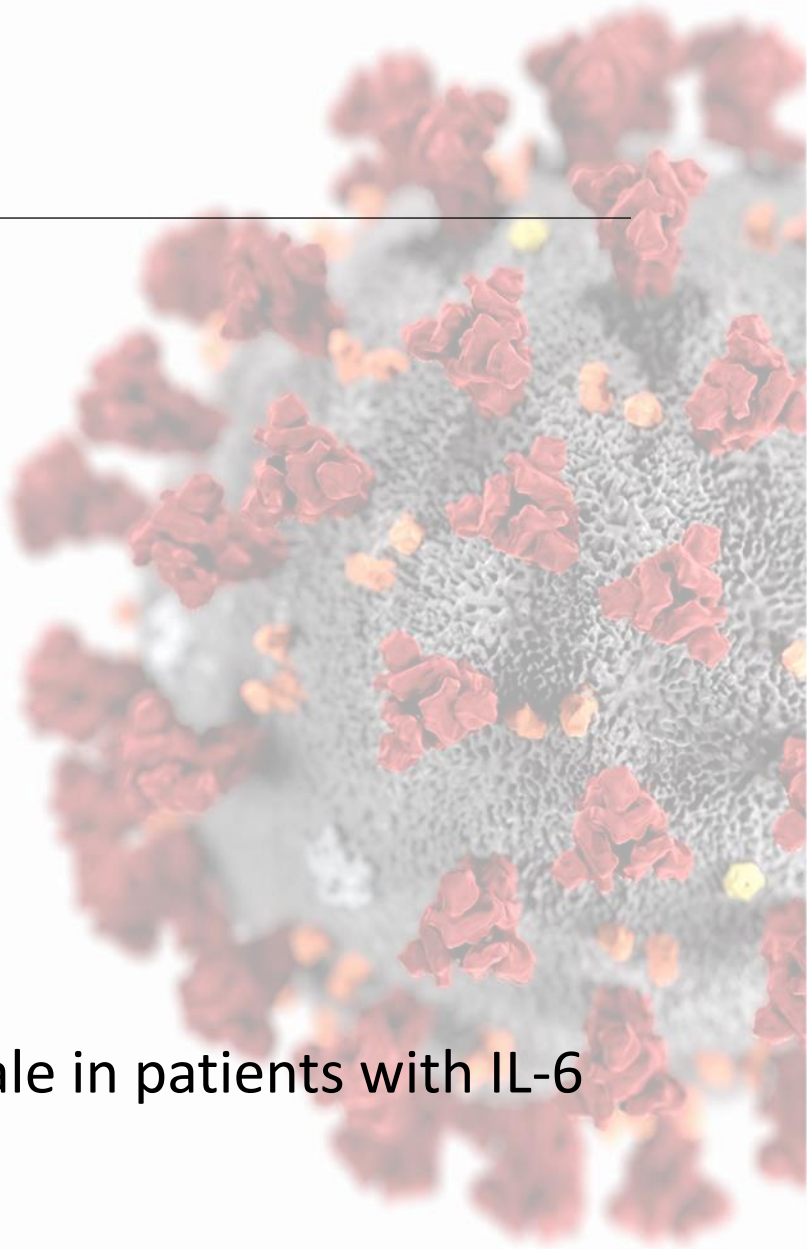
Evaluation of the Efficacy and Safety of Sarilumab in Hospitalized Patients with Covid-19 (NCT04315298)

- Regeneron Pharmaceuticals sponsored
- Adaptive Phase, Randomized, Double-Blind, Placebo-Controlled Study
- 3 arms:
  - Sarilumab high dose (400mg)
  - Sarilumab low dose (200mg)
  - Placebo
- Phase II/III Clinical Trial



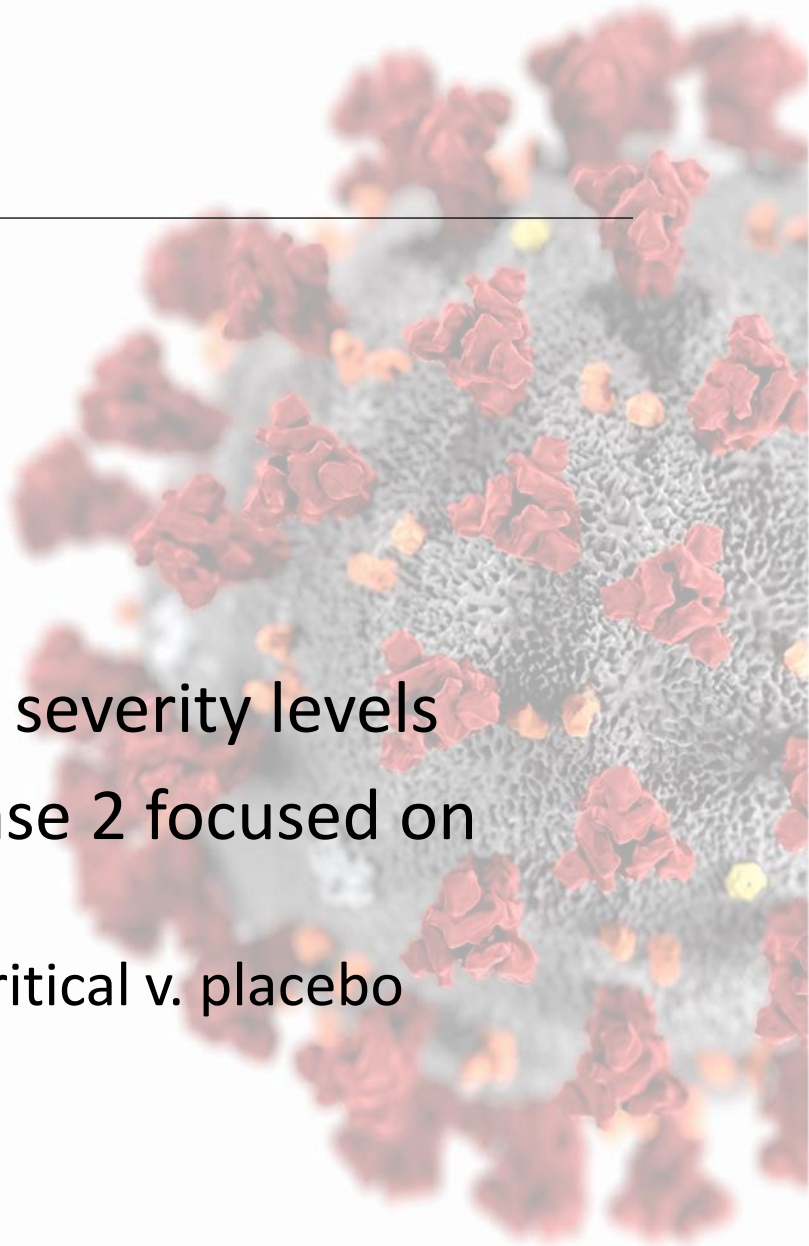
Sarilumab

- Inclusion Criteria:
  - Covid test + w/i 2 weeks
  - Hospitalized with severe disease
- Exclusion Criteria:
  - Low ANC
  - Elevated AST/ALT
  - Treated with IL-6 or Janus Kinas inhibitor
- Primary Outcome:
  - Phase 2: Percent change in CRP in 4 days
  - Phase 3: Time to improvement using –point ordinal scale in patients with IL-6 levels greater than the upper limit of normal



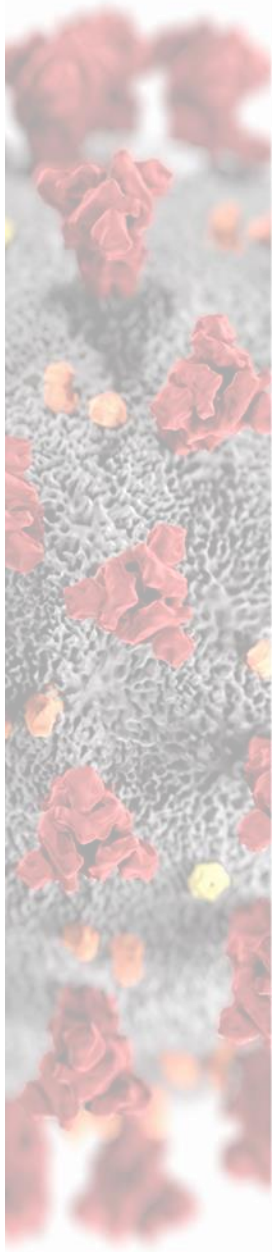
Sarilumab, Preliminary Data

- Phase 2 study: Enrolled 457 patients
  - 28% severe (oxygen requirement)
  - 49% critical (mechanical ventilation, high flow, ICU)
  - 23% MSOD
- Primary Outcome: Drug rapidly lowered CRP at all severity levels
- Exploratory analysis of clinical outcomes from phase 2 focused on severe and critical groups
  - No notable clinical benefit when combining severe + critical v. placebo



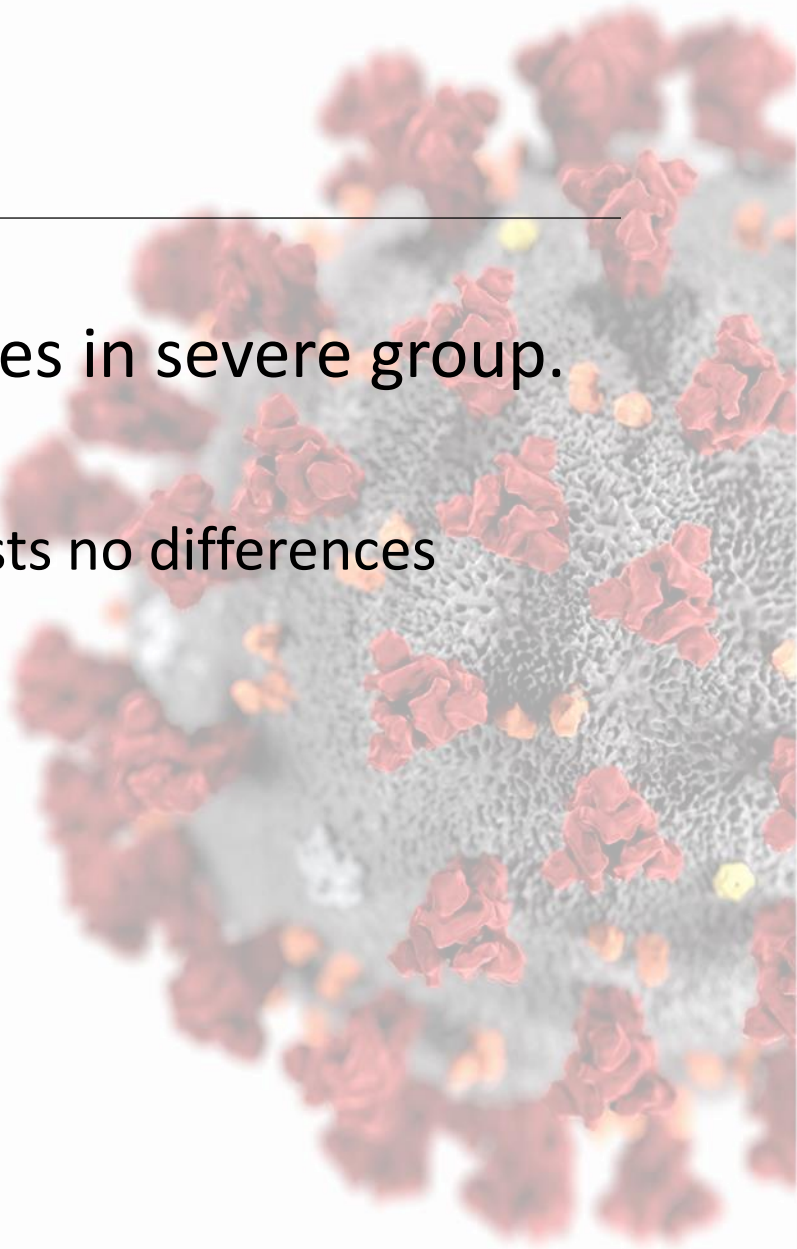
U.S. Kevzara Trial – Phase 2 Efficacy Results

	Placebo	Kevzara 200 mg	Kevzara 400 mg
PRIMARY ENDPOINT (REDUCTION IN C-REACTIVE PROTEIN)			
	(n=77)	*(n=136)*	*(n=145)*
% change from baseline in CRP (Patients with high baseline IL-6, where data was available)	-21%	-77%	-79%
EXPLORATORY CLINICAL ENDPOINTS IN "CRITICAL" GROUP			
	(n=44)	*(n=94)*	*(n=88)*
Died or "On a ventilator"	24 (55%)	43 (46%)	28 (32%)
Died	*12 (27%)*	*34 (36%)*	*20 (23%)*
On a ventilator	*12 (27%)*	*9 (10%)*	*8 (9%)*
Clinical improvement (Achieved ³2 point improvement on 7-point scale)[1]	18 (41%)	48 (51%)	52 (59%)
Off oxygenation	18 (41%)	40 (43%)	51 (58%)
Discharged	18 (41%)	37 (39%)	47 (53%)



Sarilumab, Preliminary Data

- Phase 2 data suggested negative trends in outcomes in severe group.
- Discontinued severe group
  - Although further analysis from the phase 3 data suggests no differences between severe v. critical
- Discontinued 200mg group



REMAP-COVID (NCT02735707)

- Sub-platform of REMAP-CAP
- Sponsor: MJM Bonten
- Randomized, embedded, multicenter, multifactorial, adaptive trial for community acquired PNA, repurposed for COVID-19

REMAP-COVID

- Simultaneous evaluation of several domains
- Broad inclusion criteria and then more specific inclusion for each platform

D1: Steroids

1. Fixed dependent
2. Shock dependent

D2: ABX

1. Ceftriaxone
2. Moxi/Levo
3. Pip/Tazo
4. Ceftaroline
5. Amoxicillin-Clavulanate

D3: Immunoglobulin

1. No immunoglobulin
2. Convalescent plasma

D4: Antiviral

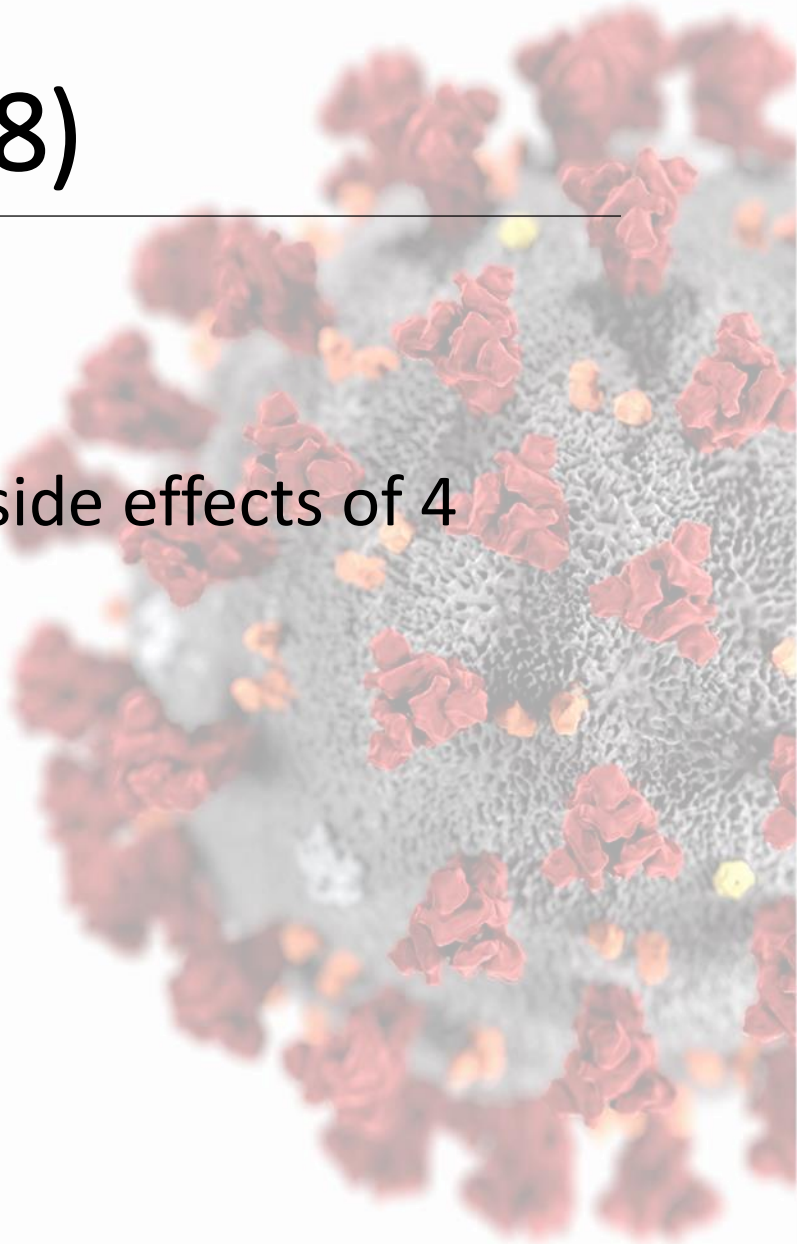
1. No antiviral
2. Lopinavir-ritonavir
3. HCQ
4. HCQ + Lopinavir/ritonavir

D5: Immune Modulation

1. No Immune modulation
2. Interferon-B1a
3. Anakinra
4. Tocilizumab
5. Sarilumab

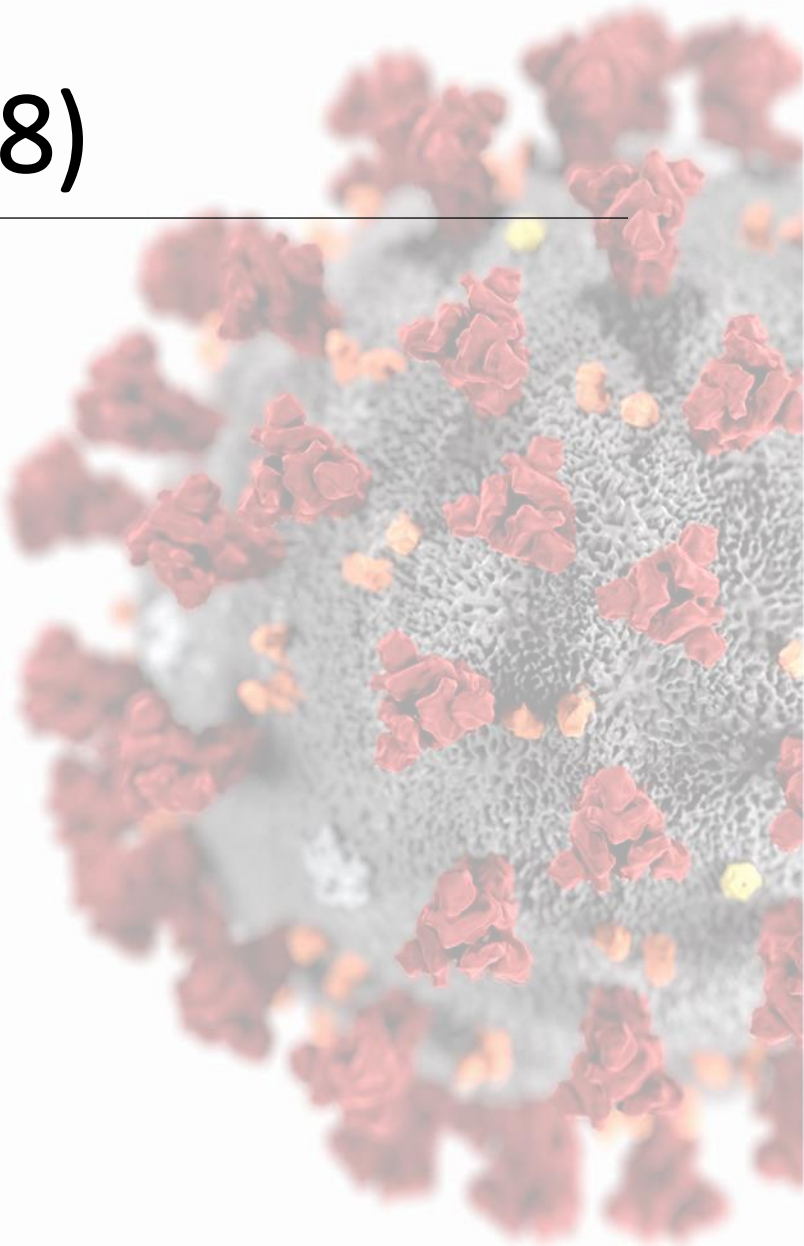
COVID-19 Vaccines (NCT 04368728)

- Biontech SE/Pfizer
- Randomized, placebo-controlled
- Safety, tolerability, immunogenicity and potential side effects of 4 different vaccine candidates against COVID-19
- 21 arms
  - Low/medium/high dose vaccines
  - 1 or 2 doses
  - 18-55yo, 65-85yo, 18-55yo
  - 3 placebo arms



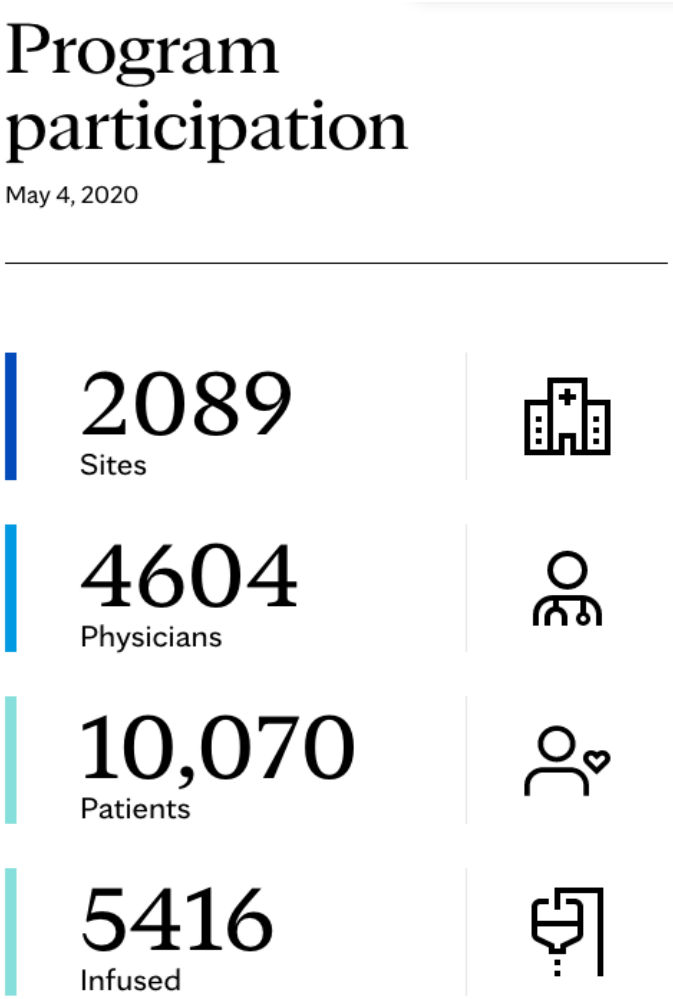
COVID-19 Vaccines (NCT 04368728)

- Primary Outcomes (10):
  - Local/systemic events
  - Hematology and chemistry changes
- Secondary outcomes:
  - Immunogenicity
- Planned enrollment:
  - 8640 participants
  - Not yet enrolling participants



Expanded Access to Convalescent Plasma (NCT04338360)

- Led by Mayo Clinic
- Supported by US Government
- More information at uscovidplasma.org
- Study Population: severe or life-threatening manifestations of COVID-19



Expanded Access to Convalescent Plasma

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
Provide access to COVID-19 convalescent plasma	Availability of convalescent plasma	Expanded access protocol
Secondary		
Safety	Serious adverse events	Required as part of expanded access protocol under IND
Tertiary/Exploratory		
Health care utilization	1. Acute care facility length of stay 2. Days spent in intensive care unit 3. Survival to acute care facility discharge	Evaluation of potential for efficacy