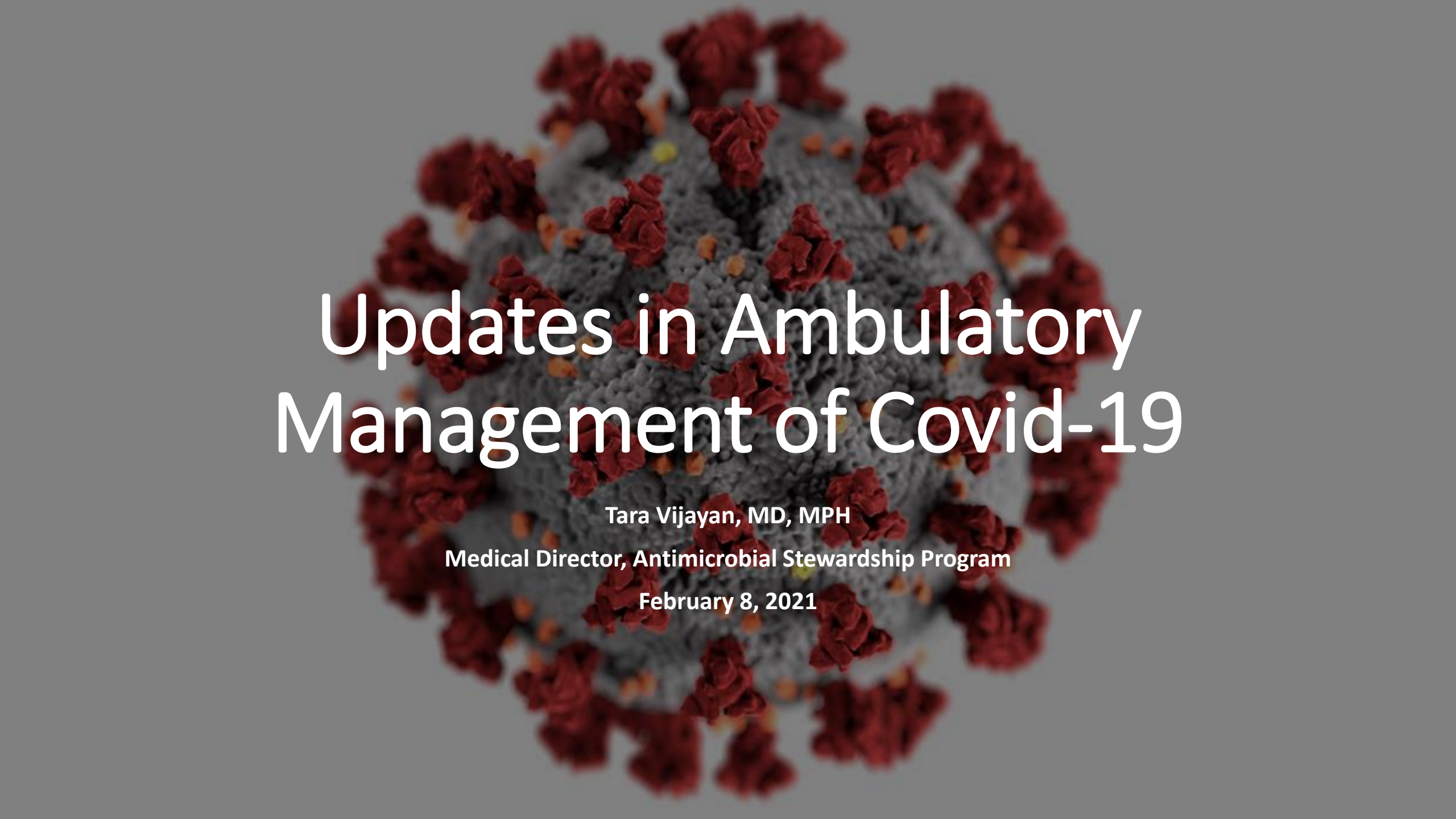


Updates in Ambulatory Management of Covid-19

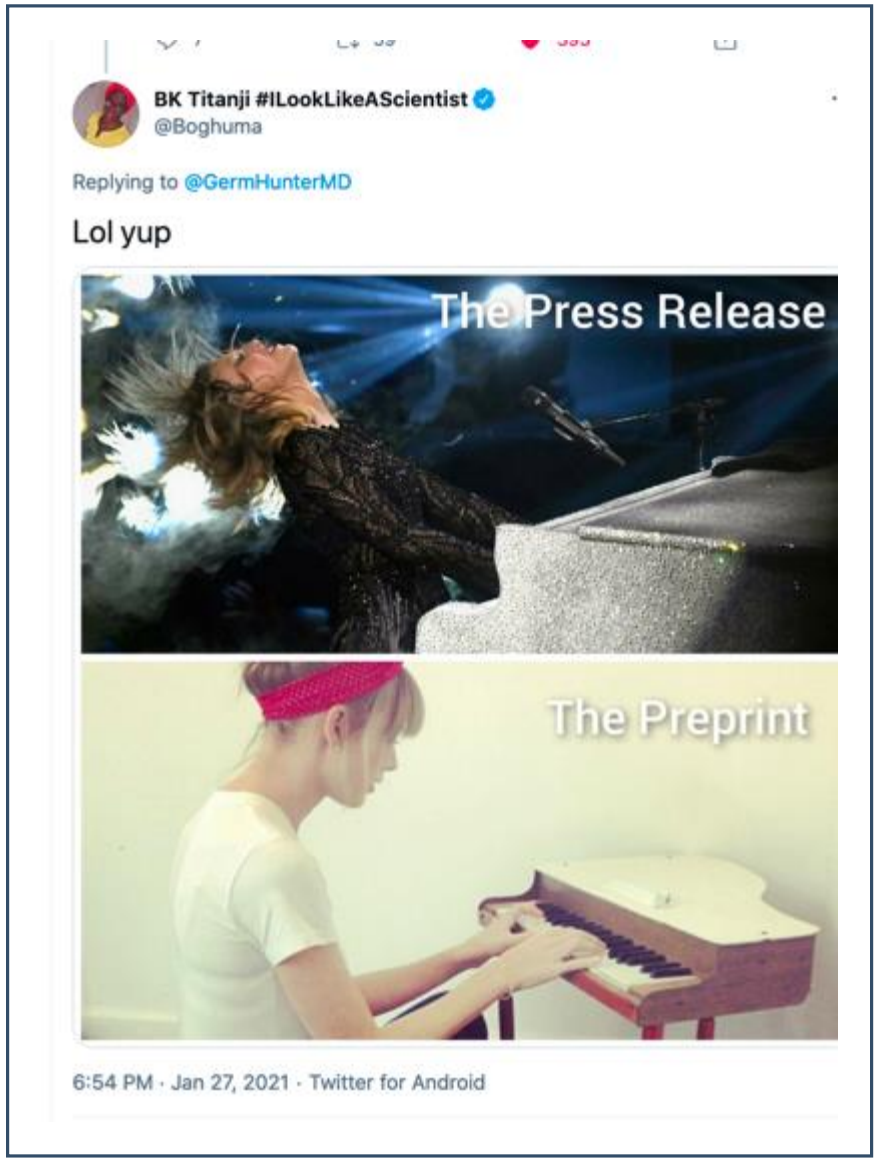
Tara Vijayan, MD, MPH

Medical Director, Antimicrobial Stewardship Program

February 8, 2021

Update on Therapeutics

- Monoclonal Antibodies
- Dexamethasone
- Other outpatient therapeutics: colchicine, fluvoxamine, ivermectin



The data: LyCoV555 and REGN-CoV antibodies

	Bamlanivimab	Casirivimab/Imdevimab
Randomization	452, 1:1:1:1 700mg, 2400mg, 7000mg, placebo	275, 1:1:1 2.4g, 8g, placebo
Inclusion criteria	Symptomatic ≤10d SARS-CoV2 PCR+ ≤3 days from infusion SpO2>93%	Symptomatic ≤7d from randomization SARS-CoV2 PCR+≤3d SpO2>93%
Patient characteristics	70% had at least 1 RF, Age ≥65, BMI ≥35	45% already Ab positive
Primary outcome	VL reduction at d11: no difference seen	VL reduction at d7- demonstrated More significant in Ab negative
Secondary outcome	Reduction in ER visits/hospitalizations: 6.3→1.6% (4.7% absolute reduction) 15%→4% among age ≥65 or BMI ≥35	Medically attended visit: 6→3% 15%→4% if antibody neg (-9, 95%CI -29,11)
Other notes	Reduction in symptoms No difference in any of doses EUA specifies 700mg dose	No difference in doses EUA specifies 2400mg dose

Chen P, Nirula A, Heller B, and colleagues on behalf of the BLAZE-1 Investigators. N Engl J Med. 2020 Oct 28. doi: 10.1056/NEJMoa2029849.
DM Weinreich et al. N Engl J Med 2021;384:238-251.

Adverse Events- not different than placebo

- Infusion reactions
  - We have seen several “delayed” infusion reactions marked by rigors
- Nausea, Vomiting
- Headache
- Pruritis
- Diarrhea

Timeline of roll out at UCLA

Nov 9
- EUA for bamlanivimab
- US Government purchased 300k doses with plans to purchase 650k through June 2021

Nov 11-21
- UCLA Health drafted guidance
- Nov 21 EUA for casirivimab-imdemivab

Dec 10
- UCLA began taking referrals for administration in ETC (2 patients/day Mon-Fri)
- ER able to administer doses to patients who present to ER with illness

Jan 2
- IV league (Culver City) able to administer to 6 more patients (Mon-Sat)

Jan 20
- GOU able to administer to 4 patients a day Sun-Sat

Current capacity: 10-12 a day M-Sat, 4 on Sunday

ETC= Evaluation and Treatment Center
GOU= Gonda Observation Unit

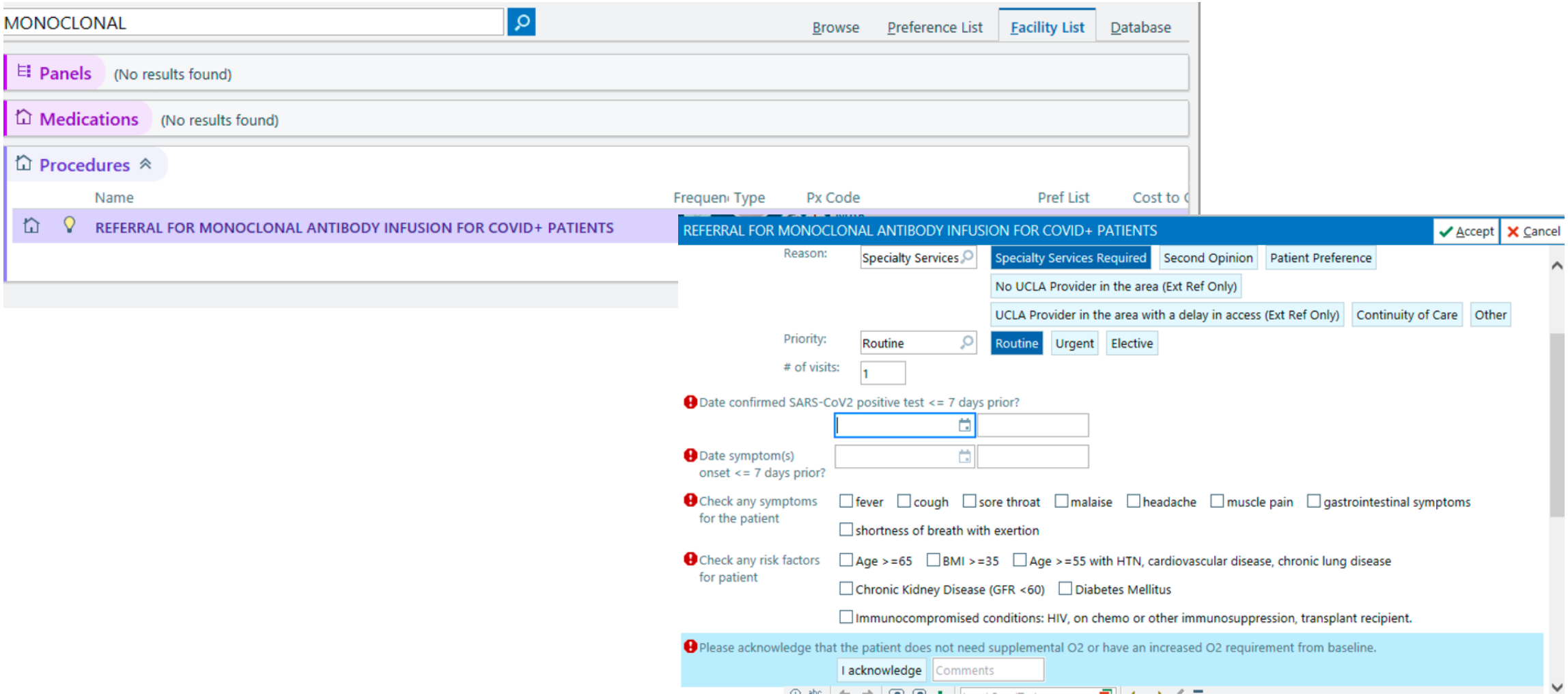
UCLA Criteria

- Not hospitalized
- No new oxygen requirement (SpO2>93%, unless baseline O2)
- Symptom onset ≤ 7 days
- SARS CoV2 PCR positive ≤ 7 days
- Risk Factors for Progression

Risk Factors for Progression: Point System

Point	
3 3	❑ ≥65 years-old ❑ BMI ≥35
2 2 2 2 2	❑ ≥55 years old with cardiovascular disease or HTN or chronic lung disease ❑ Diabetes Mellitus ❑ Chronic Kidney Disease ❑ Immunosuppressed status
1	❑ Medi-Cal recipient (or VFC patient)

Any MD/NP in UCLA Health Can Place Referral in an Ambulatory or ER Context



UCLA Health Monoclonal Antibody Workflow

Referrals reviewed by MAB Team (MD, RN, admin) daily

- Screening note documented for all referrals

Eligible patients offered appointment at Gonda Observation Unit, IV League or Evaluation and Treatment Center

- Patients are given EUA fact sheet to review prior to confirming appointment

If open slots remain, reporting workbench reviewed for all + patients in 48 hours and PCPs emailed

Orders placed for scheduled patients by MAB MD

RN team follows up with patients from 1-2 days prior in ETC or GOU only

- IV League/Accord RN outreaches separately

MD/RN Screening/Triage Notes for Covid-19 monoclonal antibody therapy:

Date of submitted referral: ***
Date of review: @TD@
Date of positive COVID test: ***

@NAME@ was screened for the following:
Date of symptom onset: *** (if >7 days, patient is not eligible)
Check off as many symptoms as apply:

- ☐ Fever
- ☐ Cough
- ☐ Sore throat
- ☐ Malaise
- ☐ Myalgia
- ☐ Headache
- ☐ Gastrointestinal symptoms (Nausea, Vomiting, Diarrhea)
- ☐ Shortness of breath

Is patient pregnant?

- ☐ Yes, ≥20 weeks
- ☐ Yes, <20 weeks
- ☐ No
- ☐ N/A

Oxygenation status:

- ☐ No oxygen
- ☐ Baseline oxygen
- ☐ Requires new oxygen or increase from baseline

Ambulatory Status:

- ☐ No assistance
- ☐ Needs assistance
- ☐ Bed Bound
- ☐ Other: _____

Transportation Status: _____

Please calculate risk stratification points using the following:

Point	
3	☐ ≥65 years-old
3	☐ BMI ≥35
2	☐ ≥55 years old with cardiovascular disease or HTN or chronic lung disease
2	☐ Diabetes Mellitus
2	☐ Chronic Kidney Disease
2	☐ Immunosuppressed status
1	☐ Medi-Cal recipient (or VFC patient if Medicare only)
1	☐ Health Care Worker

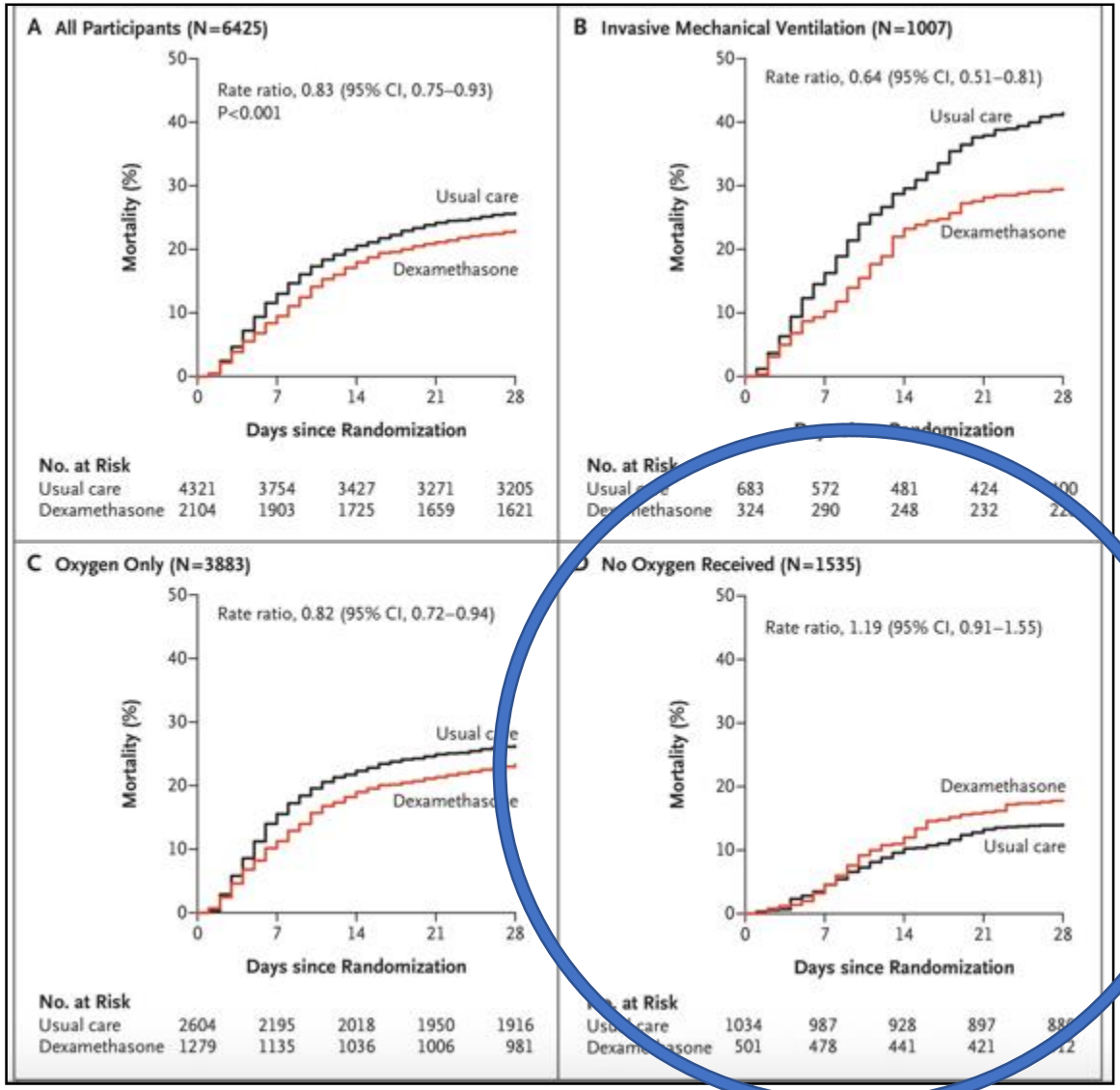
Eligible:

- ☐ Eligible, will call to schedule for IV league for *calendar date*
- ☐ Eligible, will call to schedule for GOU for *calendar date*
- ☐ Eligible, will call to schedule for ETC for *calendar Date*
- ☐ Eligible, not prioritized for this review, will review again next business day
- ☐ Eligible, but needs 24 hour assistance
- ☐ Ineligible due to out of window/no points

Total number of points: ***
Signed by: @ME@
Date of Encounter: @TD@

This patient has been reviewed by MAB Clinical Team.

The data to date: steroids



RECOVERY:

- Dexamethasone
- Tocilizumab
- Colchicine
- Convalescent Plasma
- REGN-CoV2
- Aspirin

Recovery, NEJM, July 17, 2020

Colchicine: Colcorona RCT (Canada, US, Brazil)

- Inhibits tubulin polymerization, targeting NLRP3 inflammasome
- ≥40 years-old+ at least 1 high risk criteria
  - ≥70, obesity (BMI >30), uncontrolled HTN, DM, CAD, lung disease
  - Clinical criteria: fever within 48h, dyspnea, pancytopenia, bicytopenia, ANC high, ALC low
  - Exclusion: IBD, diarrhea, malabsorption, neuromuscular disease, GFR <30, current colchicine use, current chemotherapy
- Target enrollment: 6000
- Colchicine 0.5mg po BID x 3 days, then daily x 27d v placebo x 30d
- Endpoint: death or hospitalization

COLCORONA investigators, https://www.medrxiv.org/content/10.1101/2021.01.26.21250494v1.full.pdf

Results

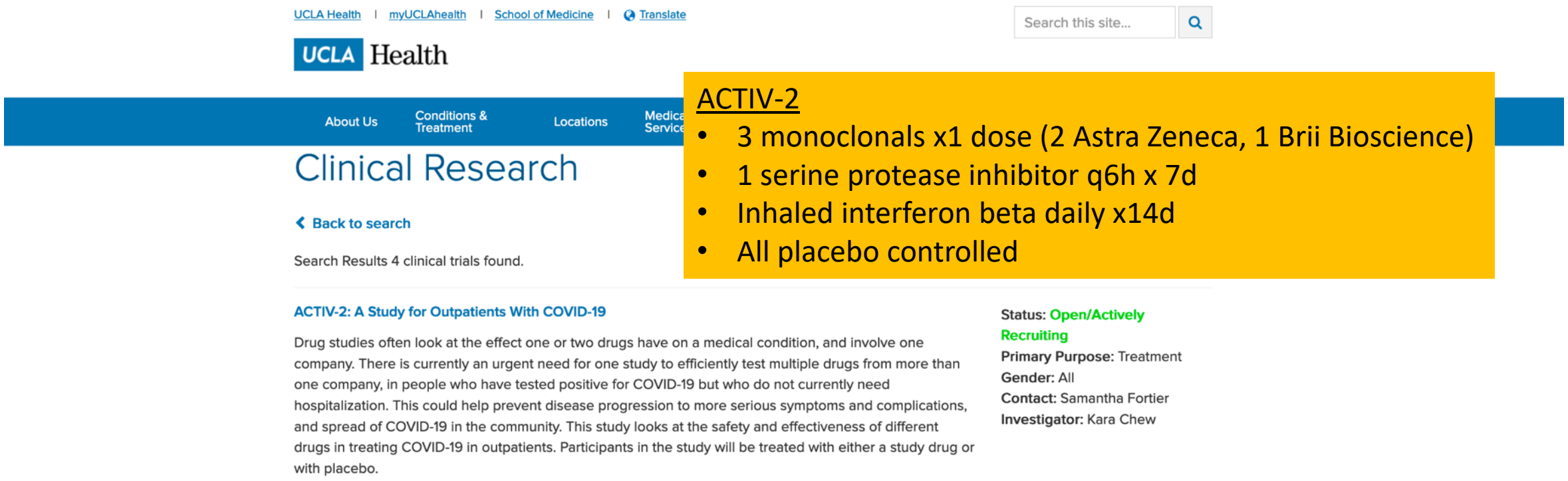
- March 2020- December 2020 (stopped at 75% recruitment)
- 4488 patients enrolled (1:1), 4159 with PCR confirmed
- Primary outcome: 4.7% in Colchicine vs 5.8% in Placebo
  - OR 0.79 (95% CI 0.61, 1.03)
- PCR confirmed: OR 0.75 (95% CI 0.57, 0.99) for hospitalization
  - 0.50 (95% CI 0.23, 1.07) for MV, 0.56 (95% CI 0.19, 1.66) for death
- Adverse events 24.2% v 15.5%, largely diarrhea/GI events
  - fewer serious adverse events (4.9% v 6.3%)
  - PE 0.5% v 0.1% (significant)

Other oral agents

- Fluvoxamine 100mg po daily x 15 days v placebo
  - Sigma-1 receptor agonism
    - modulates cytokine production in endoplasmic reticulum
  - 0 of 80 v 6 of 72 met primary end point of clinical deterioriation (delta 8.7%)
  - STOP COVID trial ongoing (stopcovidtrial.wustl.edu)
- Ivermectin
  - Used extensively in Latin America, Africa
  - Pooled risk ratio for very small studies outside the US 0.17 (95% CI 0.08, 0.35)

Outpatient Trials available at UCLA

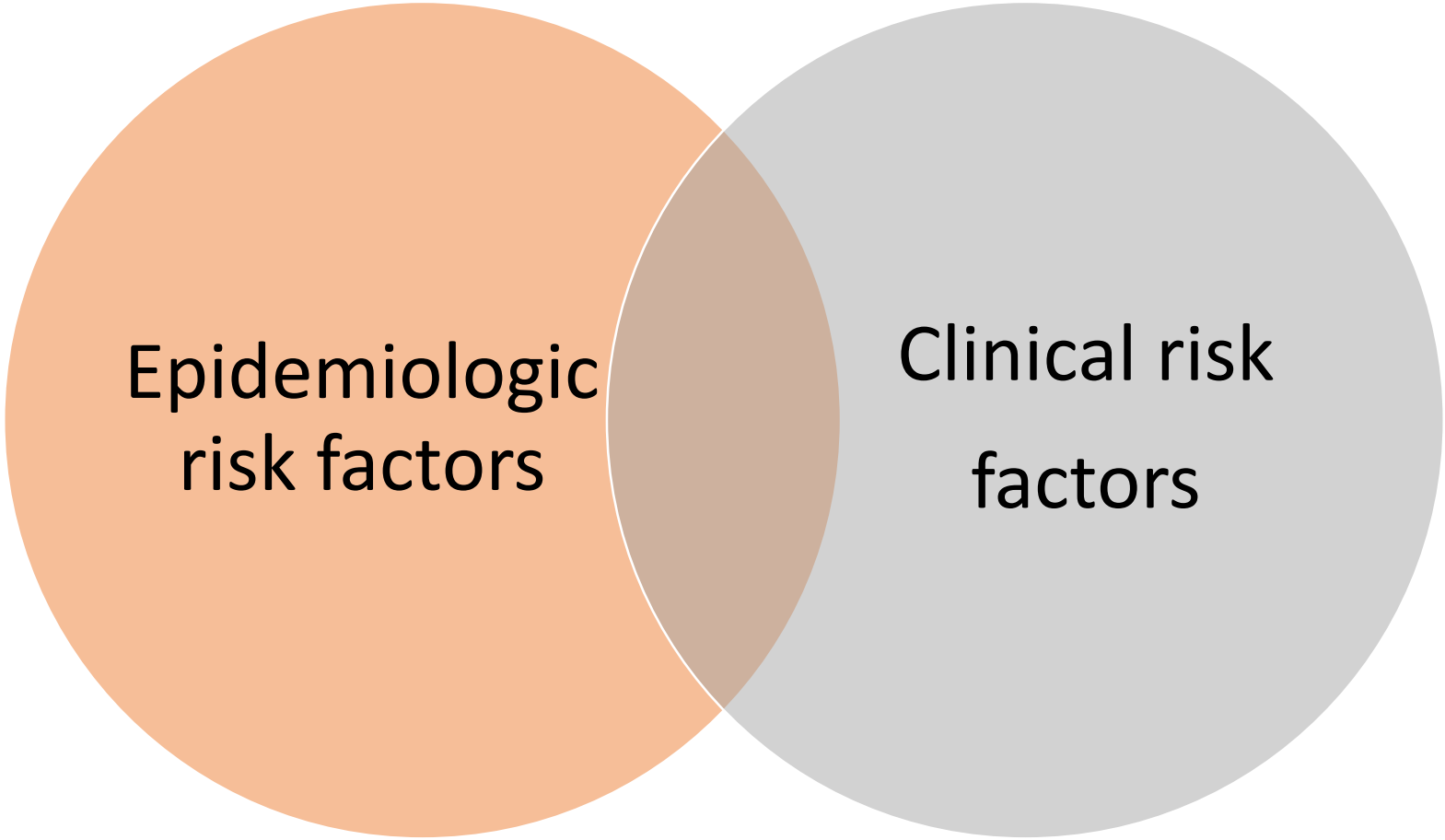
- ACTIV-2, PI Kara Chew, Contact Samantha Fortier
- Convalescent Plasma, PI Judith Currier, Contact Rafael Corona



ACTIV-2

- 3 monoclonals x1 dose (2 Astra Zeneca, 1 Brii Bioscience)
- 1 serine protease inhibitor q6h x 7d
- Inhaled interferon beta daily x14d
- All placebo controlled

We do not understand “high risk”



Summary

- Monoclonal antibodies can be considered for select high-risk patients
  - NIH/DHHS states that these drugs remain investigational
  - >500 referrals to date, >300 high risk patients have received
  - Coram and Premier Home Health are options for home infusions
- Do not use steroids in outpatient setting, trend towards increased mortality for non-hypoxic patients
- Will await peer review, NIH statement, but of all the studies reviewed:
  - Colchicine is interesting, selected high risk population
  - Ivermectin and Fluvoxamine need further studies
- Please consider enrolling your patient in a trial, we need more data