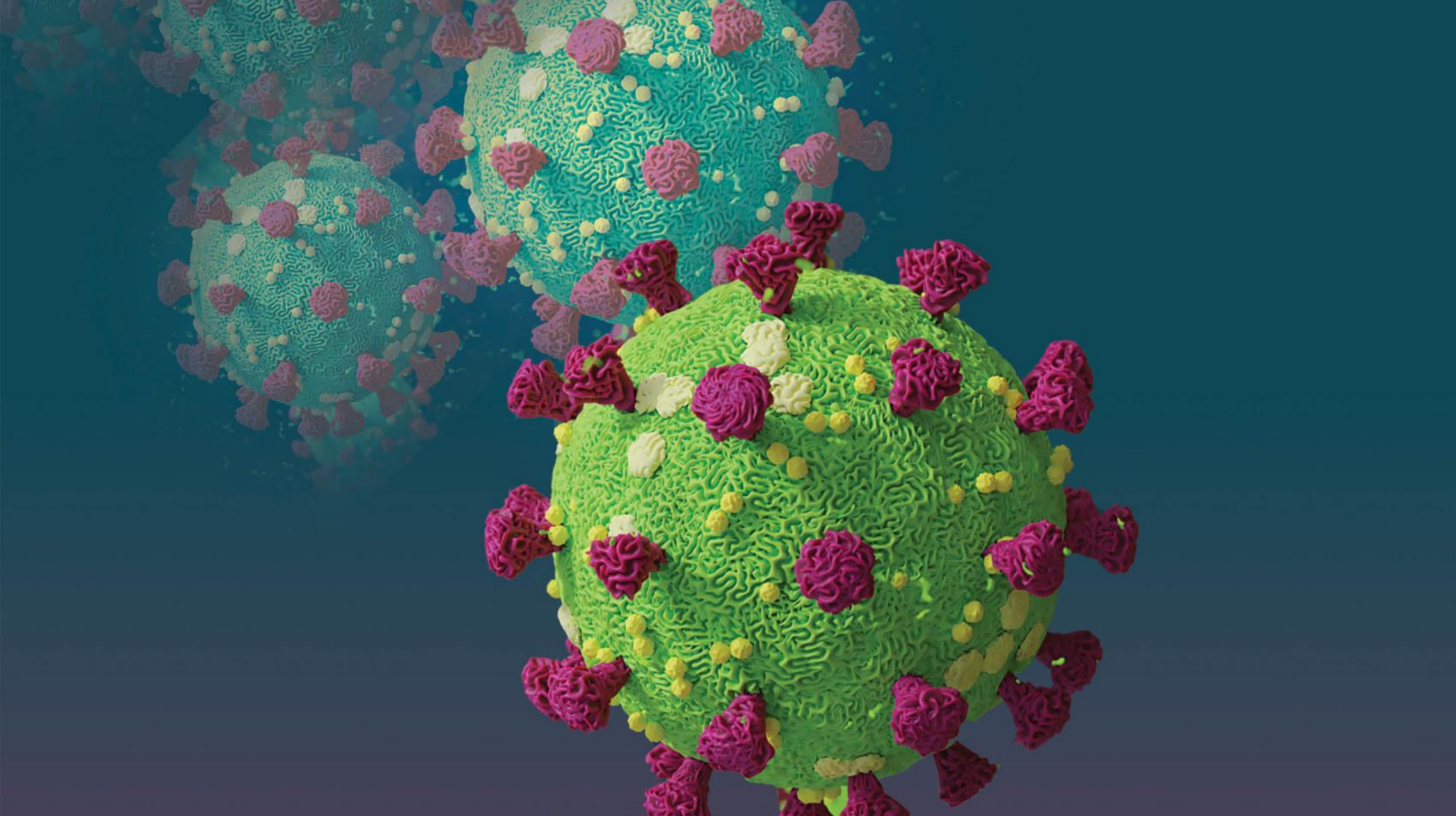


Project ECHO®

Med Learning Group - COVID-19 Frontline

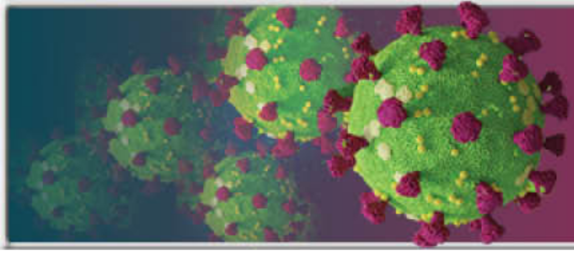
A NEW LIGHT IN THE DARKNESS:

New Virus-neutralizing Monoclonal Antibodies and Other Point-of-Care Therapies Recently Granted Emergency Use Authorizations for Patients with COVID-19

MEETING INFO
Tuesday, April 6, 2021

FACULTY
Shyam Kottilil, MD, PhD
Professor of Medicine Chief,
Division of Infectious Diseases
Institute of Human Virology
University of Maryland Baltimore, MD

This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
This activity is supported by an educational grant from Lilly.



AGENDA

1. **Rationale for the Use of New Virus-neutralizing Monoclonal Antibodies**
    a. High mutation rate of RNA viruses
    b. The risk of viral mutations leading to therapy resistance ***(Whiteboard theme: depiction of viral mutations leading to therapy resistance)***
    c. Mechanism of action of new virus-neutralizing monoclonal antibodies in mitigating the risk of viral resistance to therapy

2. **Therapies Granted Emergency Use Authorization for Patients with COVID-19**
    a. What is emergency use authorization?
    b. Clinical trial data on the efficacy and safety of new virus-neutralizing monoclonal antibodies and other therapies approved for emergency use in all patients who test positive for COVID-19 ***(Whiteboard theme: MOA of new virus-neutralizing monoclonal antibodies approved for emergency use in all patients who test positive for COVID-19)***
    c. Guidance of the development of in-clinic infusion capability to deliver new virus-neutralizing monoclonal antibodies at the point-of-care

3. **COVID-19 Vaccine Development**
    a. Efficacy and safety of the first FDA-granted emergency use authorization vaccine for the prevention of COVID-19
    b. Updates on vaccines in development

4. **Case studies**

5. **Conclusions**

A Light in the Darkness: New Virus-neutralizing Monoclonal Antibodies and Other Point-of-Care Therapies Recently Granted Emergency Use Authorization for Patients with COVID-19

FACULTY

PROGRAM CHAIR

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Baltimore, MD

Christopher Palma, MD, ScM
Assistant Professor of Medicine
University of Rochester
Rochester, NY

PROGRAM OVERVIEW

The COVID-19 FRONTLINE TeleECHO series provides a comprehensive and up-to-date perspective on the ever-changing management of patients with COVID-19. Each TeleECHO session features in-depth case studies to encourage retention of the lessons and provide new perspectives on the management of patients during the COVID-19 pandemic. The case studies will focus on different issues facing clinicians, such as identifying patients who would benefit from monoclonal antibody therapy and best practices for incorporating agents authorized for emergency use into the care of hospitalized and non-hospitalized patients with COVID-19. Strategies for administering neutralizing monoclonal antibodies, such as referral to local infusion centers or developing in-clinic infusion capabilities, will also be discussed.

TARGET AUDIENCE

This CME initiative is designed for HCPs who are involved in the care and treatment of patients with COVID-19 in an outpatient setting, including physicians, NPs, PAs, nurses, pharmacists and paramedics.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Assess the rationale for the use of neutralizing monoclonal antibody therapies in recently diagnosed COVID-19 patients to prevent the development of severe disease
- Critique the efficacy and safety of new virus-neutralizing monoclonal antibody therapies and other therapies approved for emergency use in all patients who test positive for COVID-19
- Develop in-clinic infusion capability in order to administer new virus-neutralizing monoclonal antibodies to patients with COVID-19 at the point-of-care

ACCREDITATION STATEMENT

Med Learning Group is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.
This CME activity was planned and produced in accordance with the ACCME Essentials.

CREDIT DESIGNATION STATEMENT

Med Learning Group designates this live virtual activity for a maximum of 1.0 *AMA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the live virtual activity.

NURSING CREDIT INFORMATION

Purpose: This program would be beneficial for nurses involved in the treatment of patients with COVID-19.
Credits: 1.0 ANCC Contact Hour.

CNE Accreditation Statement: Ultimate Medical Academy/CCM is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Awarded 1.0 contact hour of continuing nursing education of RNs and APNs.

ABIM Maintenance of Certification

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.0 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

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DISCLOSURE OF CONFLICTS OF INTEREST

Faculty Member	Disclosures
Shyama Kottilil, MD, PhD	Discloses that the University of Maryland has received funds to participate in trials, as well he has received research funds paid to the university from Merck Inc, Gilead Sciences and Arbutus Pharmaceuticals. He has also provided contracted research for Regeneron, Eli Lilly, and air Pharmaceuticals, as well as serving on the advisory board for hepatitis b functional cure program at Merck Inc.
Roger Bedimo, MD, MS	Discloses that he has worked as a Consultant for Merck & Co, Viiv Healthcare and Theratechnologies.
William A. Fischer II, MD	Discloses that he has been contracted for research for Ridgeback Biopharmaceuticals for COVID-19 research, as well as worked as Consulted for Merck and Roche. He also worked for Syneos and Janssen for adjudication of AE in RSV and Influenza studies respectively, and served as the site PI for the Phase I Lilly study of - Bamlanivimab and for the Phase II study of Casirivimab/Imdevimab at University of North Carolina.
Shivakumar Narayanan, MBBS, MD	Discloses that has received contracted research funding from Regeneron Pharmaceuticals. Dr. Narayanan has been an investigator in clinical studies sponsored by Regeneron Pharmaceuticals. He is a principal investigator and a recipient of contracted research funding from Gilead Sciences.
Christopher Palma, MD, ScM	Discloses that he has been contracted for research for Regeneron.

CME Content Review

The content of this activity was independently peer reviewed.
The reviewer of this activity has nothing to disclose.

CNE Content Review

The content of this activity was peer reviewed by a nurse reviewer.
The reviewer of this activity has nothing to disclose.

Staff Planners and Managers

The staff, planners, and managers reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME/CE activity:

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Christina Gallo, SVP, Educational Development for Med Learning Group, has nothing to disclose.

Diana Tommasi, PharmD, Medical Director for Med Learning Group, has nothing to disclose.

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Russie Allen, Accreditation and Outcomes Coordinator for Med Learning Group, has nothing to disclose.

Morgan Kravarik, Program Coordinator for Med Learning Group, has nothing to disclose.

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METHOD OF PARTICIPATION

There are no fees for participating and receiving CME credit for this live virtual activity. To receive CME/CNE credit participants must:

1. Read the CME/CNE information and faculty disclosures.
2. Participate in the web-based live activity.
3. Submit the evaluation form to Med Learning Group.

You will receive your certificate upon completion.

DISCLAIMER

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This activity is designed for educational purposes. Participants have a responsibility to use this information to enhance their professional development in an effort to improve patient outcomes. Conclusions drawn by the participants should be derived from careful consideration of all available scientific information. The participant should use his/her clinical judgment, knowledge, experience, and diagnostic decision making before applying any information, whether provided here or by others, for any professional use.

For CME questions, please contact Med Learning Group at info@medlearninggroup.com

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COVID-19 FRONTLINE

A Light in the Darkness: New Virus-neutralizing Monoclonal Antibodies and Other Point-of-Care Therapies Recently Granted Emergency Use Authorizations for Patients with COVID-19

Shyam Kottilil MD, PhD
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University of Maryland
Baltimore, MD

1

Disclosures

- Dr. Kottilil discloses that the University of Maryland has received funds to participate in trials. He has received research funds paid to the university from Merck Inc, Gilead Sciences, and Arbutus Pharmaceuticals. He has also provided contracted research for Regeneron, Eli Lilly, and air Pharmaceuticals, and served on the advisory board for Hepatitis B Functional Cure Program at Merck Inc.
- During this lecture, Dr. Kottilil may mention the use of medications for both FDA-approved and nonapproved indications.

This activity is supported by an independent medical education grant from Lilly.

2

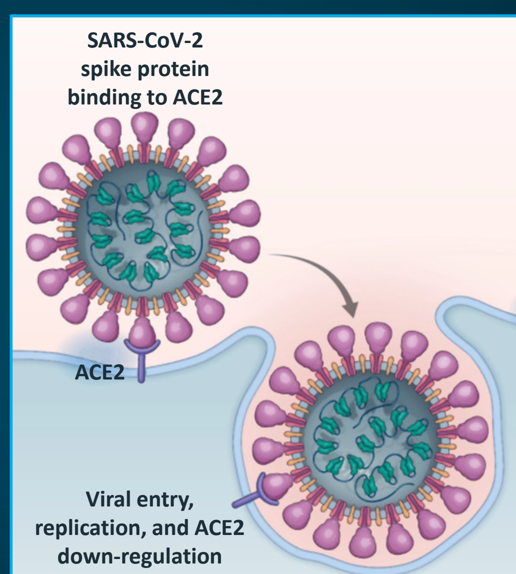
Learning Objectives

- Assess the rationale for the use of neutralizing monoclonal antibody therapies in recently diagnosed COVID-19 patients to prevent the development of severe disease
- Critique the efficacy and safety of new virus-neutralizing monoclonal antibody therapies and other therapies approved for emergency use in all patients who test positive for COVID-19
- Develop in-clinic infusion capability in order to administer new virus-neutralizing monoclonal antibodies to patients with COVID-19 at the point-of-care

3

SARS-CoV-2

- COVID-19 is caused by the SARS-CoV-2 virus[1–3]
- The virus is spread primarily via respiratory droplets during face-to-face contact[2]
- Spike protein on viral surface binds to ACE2 receptor on target cells, facilitating viral entry into host cells[2,3]



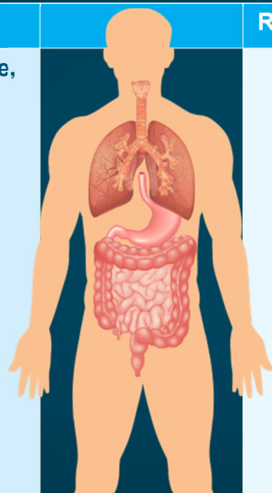
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; COVID-19 = coronavirus disease 2019; ACE = angiotensin-converting enzyme.

1. Adapted from Vaduganathan M, et al. *N Engl J Med*. 2020;382:1653-1659. 2. Wiersinga WJ, et al. *JAMA*. 324:782-793. 3. Baum A, et al. *Science*. 2020;369:1014-1018.

4

Clinical Presentation of COVID-19

Systemic and respiratory disorders caused by COVID-19



Systemic Disorders	Respiratory Disorders
Fever, cough, fatigue, sputum production, headache	Rhinorrhea, sneezing, sore throat
Hemoptysis, acute cardiac injury	Pneumonia
Hypoxemia	Ground-glass opacities
Dyspnea, Lymphopenia	RNAemia, acute respiratory distress syndrome
Diarrhea	

Most common symptoms of COVID-19 at presentation

Symptom	Patients Presenting with Symptom (N = 1420)
Headache	70.3%
Loss of smell	70.2%
Nasal obstruction	67.8%
Asthenia	63.3%
Cough	63.2%
Myalgia	62.5%
Rhinorrhea	60.1%
Taste dysfunction	54.2%
Sore throat	52.9%
Fever (>38°C)	45.4%

RNA = ribonucleic acid; C = Celsius.

Guan WJ, et al. *N Engl J Med*. 2020;382:1708-1720. Rothan HA, et al. *J Autoimmun*. 2020;109:102433. Lechien JR , et al. *J Intern Med*. 2020;288:335-344. Wang WW, et al. *J Med Virol*. 2020;92:441-447.

5

COVID-19 Disease Severity

A large study of 44,672 confirmed COVID-19 cases identified by the Chinese Centers for Disease Control and Prevention found that 81% of cases were mild-to-moderate, 13.8% were severe, and 6.1% were critical

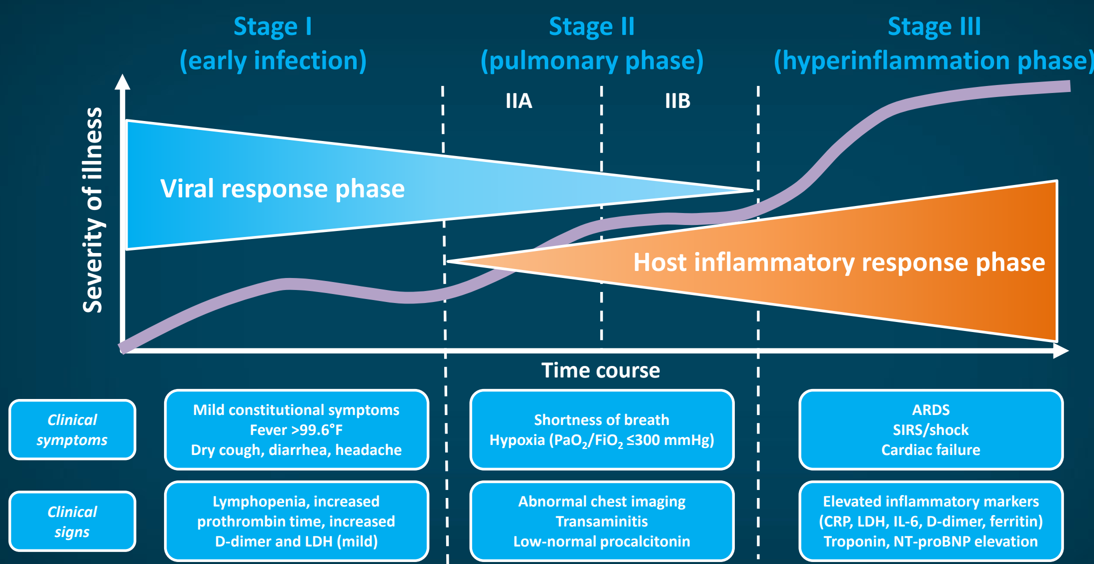
	Disease Characteristics—NIH
Mild illness	Various symptoms (eg, fever, cough, sore throat, headache, malaise, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging
Moderate illness	SpO_2 ≥94% on room air and lower respiratory disease evidenced by clinical assessment or imaging
Severe illness	SpO_2 <94% on room air, PaO_2/FiO_2 <300, respiratory rate >30 breaths/min, or lung infiltrates >50%
Critical illness	Respiratory failure, septic shock, and/or multiorgan dysfunction

SpO_2 = oxygen saturation; PaO_2 = arterial partial pressure of oxygen; FiO_2 = fraction of inspired oxygen; NIH = National Institutes of Health.

Wu Z, McGoogan JM. *JAMA*. 2020;323:1239-1242. NIH. COVID-19 treatment guidelines (https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf). Accessed 12/2/2020.

6

Phases of COVID-19



ARDS = acute respiratory distress syndrome; CRP = C-reactive protein; IL-6 = interleukin 6; LDH = lactate dehydrogenase; NT-proBNP = N-terminal pro B-type natriuretic peptide; SIRS = systemic inflammatory response syndrome.

Adapted from Siddiqi HK, Mehra MR. *J Heart Lung Transplant.* 2020;39:405-407.

7

Association Between Pre-existing Characteristics and COVID-19 Survival

- Prospective cohort study of 20,133 patients in UK hospitalized with COVID-19
- Increasing age, male sex, and chronic comorbidities, including obesity, were identified as independent risk factors for mortality

		HR (95% CI)	*P*- value
Age on admission (years)	<50		
	50–59	2.63 (2.06–3.35)	<.001
	60–69	4.99 (3.99–6.25)	<.001
	70–79	8.51 (6.85–10.57)	<.001
	≥80	11.09 (8.93–13.77)	<.001
Sex at birth	Female	0.81 (0.75–0.86)	<.001
Chronic cardiac disease	Yes	1.16 (1.08–1.24)	<.001
Chronic pulmonary disease	Yes	1.17 (1.09–1.27)	<.001
Chronic kidney disease	Yes	1.28 (1.18–1.39)	<.001
Diabetes	Yes	1.06 (0.99–1.14)	.087
Obesity	Yes	1.33 (1.19–1.49)	<.001
Chronic neurological disorder	Yes	1.17 (1.06–1.29)	.001
Dementia	Yes	1.40 (1.28–1.52)	<.001
Malignancy	Yes	1.13 (1.02–1.24)	.017
Moderate/severe liver disease	Yes	1.51 (1.21–1.88)	<.001

1 2 5 10

UK = United Kingdom; HR = hazard ratio; CI = confidence interval.

Docherty AB, et al. *BMJ.* 2020;369:m1985.

8

Risk Factors for Severe Disease

Case series of 5700 hospitalized patients in NYC, Long Island, and Westchester County, NY found:

- Median number of total comorbidities at admission: 4 (IQR: 2–8)
- 88% of patients had more than one comorbidity
- Most common comorbidities were hypertension (56.6%), obesity (41.7%), and diabetes (33.8%)

Risk Factors for Severe COVID-19

- **Older age**
- **Chronic obstructive pulmonary disease**
- **Cardiovascular disease (eg, heart failure, coronary artery disease, or cardiomyopathy)**
- **Type 2 diabetes mellitus**
- **Obesity (body-mass index >30)**
- **Sickle cell disease**
- **Chronic kidney disease**
- **Immunocompromised state from solid-organ transplantation**
- **Cancer**

IQR = interquartile range.

Richardson S, et al. *JAMA*. 2020;323:2052-2059. NIH. COVID-19 treatment guidelines (https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf). Accessed 12/2/2020.

9

Antibody Therapies for the Management of COVID-19

10

Antibody Therapy in Mild-to-Moderate COVID-19

	Asymptomatic or presymptomatic	Mild illness	Moderate illness	Severe illness	Critical illness
Features	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (eg, fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94%	Oxygen saturation <94% respiratory rate ≥30 breaths/min; lung infiltrates >50%	Respiratory failure, shock, and multiorgan dysfunction or failure
Testing	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
Isolation	Yes	Yes	Yes	Yes	Yes
Proposed disease pathogenesis	Viral replication		Inflammation		
Potential treatment	Antiviral therapy	Antibody therapy		Anti-inflammatory therapy	
Management considerations	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)

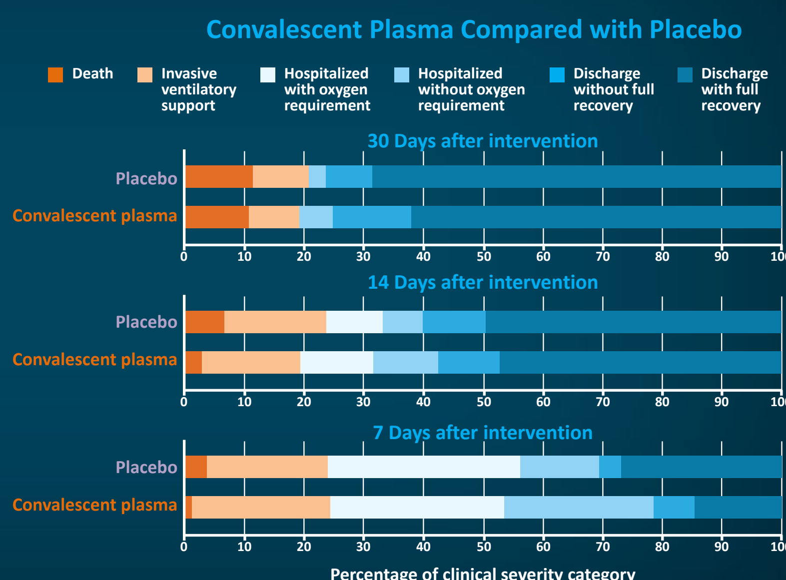
According to the Centers for Disease Control and Prevention (CDC), diagnostic testing for SARS-CoV-2 is intended to identify current infection in individuals and is performed when a person has signs or symptoms consistent with Covid-19 or when a person is asymptomatic but has recent known or suspected exposure to SARS-CoV-2. Screening testing for SARS-CoV-2 is intended to identify infected persons who are asymptomatic and without known or suspected exposure to SARS-CoV-2. Screening testing is performed to identify persons who may be contagious so that measures can be taken to prevent further transmission.

Adapted from Gandhi RT, et al. *N Engl J Med.* 2020;383:1757-1766

11

Convalescent Plasma in Severe COVID: Not Highly Effective

- Convalescent plasma had no impact on survival at 30 days in severe COVID-19 in 333 hospitalized patients
  - >98% on convalescent plasma and 95% on placebo with oxygen saturation <93% on room air at baseline
  - 29% on convalescent plasma and 24% on placebo in ICU at baseline
  - 92% on convalescent plasma and 96% on placebo given steroids during trial



ICU = intensive care unit.

Simonovich VA, et al. *N Engl J Med.* 2020;Nov 24: Epub ahead of print.

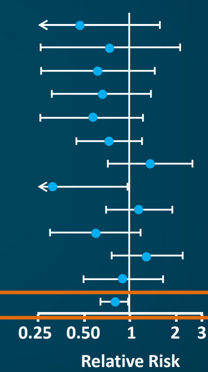
12

Effect of Anti-SARS-CoV-2 Antibody Level on 30-Day Mortality

- Death within 30 days after plasma transfusion in 3 titer groups
  - High-titer: 22.3% (115/515)
  - Medium-titer: 27.4% (549/2006)
  - Low-titer: 29.6% (166/561)
- Significantly lower risk of death within 30 days among patients who had not received mechanical ventilation before transfusion in high-titer group compared with low-titer group (RR = 0.66; 95% CI, 0.48–0.91)

High vs Low Antibody Levels

Subgroup	No. of patients	Mortality at 30 days
Before May 15, no mechanical ventilation, 18–59 yr	109	0.47 (0.14–1.57)
May 15 or later, no mechanical ventilation, 18–59 yr	196	0.74 (0.26–2.13)
Before May 15, no mechanical ventilation, 60–69 yr	93	0.62 (0.26–1.47)
May 15 or later, no mechanical ventilation, 60–69 yr	117	0.66 (0.31–1.38)
Before May 15, no mechanical ventilation, ≥70 yr	74	0.57 (0.26–1.22)
May 15 or later, no mechanical ventilation, ≥70 yr	128	0.73 (0.45–1.20)
Before May 15, mechanical ventilation, 18–59 yr	81	1.35 (0.72–2.54)
May 15 or later, mechanical ventilation, 18–59 yr	47	0.31 (0.10–0.97)
Before May 15, mechanical ventilation, 60–69 yr	75	1.14 (0.70–1.88)
May 15 or later, mechanical ventilation, 60–69 yr	44	0.60 (0.30–1.19)
Before May 15, mechanical ventilation, ≥70 yr	48	1.29 (0.76–2.21)
May 15 or later, mechanical ventilation, ≥70 yr	46	0.91 (0.50– 1.66)
All subgroups	1058	0.80 (0.65–0.97)



RR = relative risk; yr = year(s).

Joyner MJ, et al. *N Engl J Med.* 2021;Jan 13: Epub ahead of print.

13

Emergence Use Authorization (EUA) for Convalescent Plasma

- EUA issued for **high-titer** convalescent plasma
- Authorized for the treatment of hospitalized patients with COVID-19 early in the disease course and for hospitalized patients with impaired humoral immunity
- Early disease generally means prior to respiratory failure requiring intubation and mechanical ventilation

US Food and Drug Administration (FDA). Convalescent plasma fact sheet (www.fda.gov/media/141478/download). Accessed 2/25/2021.

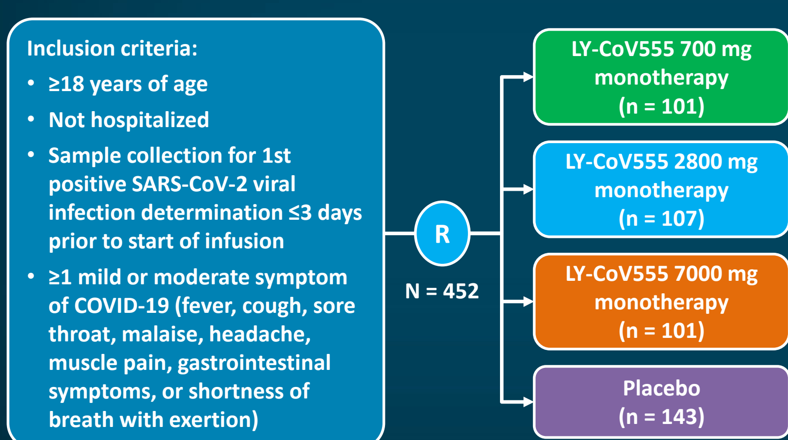
14

Monoclonal Antibody Therapies

15

BLAZE-1: Phase 2 Trial of Bamlanivimab (LY-CoV555)

- Interim results from phase 2 trial of bamlanivimab in patients with mild-to-moderate COVID-19
- Risk factors for severe COVID-19 in 70% of bamlanivimab and 66% of placebo patients at baseline



Interim analysis

- Positive SARS-CoV-2 test ≤3 days before infusion
- Mild or moderate COVID-19 symptoms
- Primary endpoint: change from baseline to day 11 (±4 days) in SARS CoV-2 viral load
- Secondary endpoints include safety, symptom severity, hospitalization, and time points for viral clearance

Chen P, et al. *N Engl J Med*. 2020;Oct 28: Epub ahead of print.

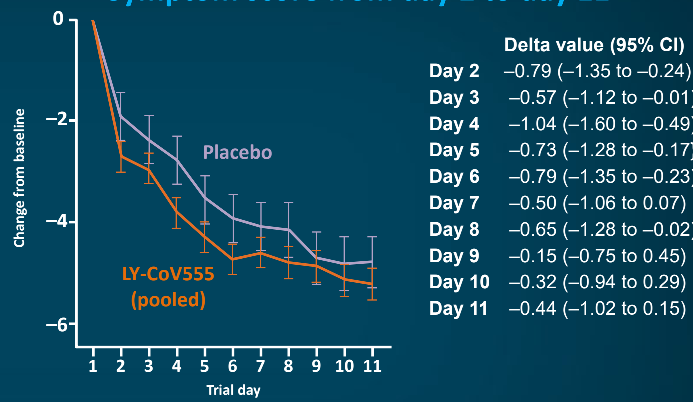
16

BLAZE-1 Interim Results

Treatment	Patients Hospitalized/ Total No.	Incidence of Hospitalization (%)
Placebo	9/143	6.3
Bamlanivimab 700 mg	1/101	1.0
Bamlanivimab 2800 mg	2/107	1.9
Bamlanivimab 7000 mg	2/101	2.0
Bamlanivimab pooled doses	5/309	1.6

- In subjects ≥65 years and/or with a BMI ≥35, day 29 hospitalization was 4% in treated patients and 15% in those receiving placebo

Symptom score from day 2 to day 11



- Symptom scores ranged from 0 to 24 and included eight domains, each of **which** was graded on a scale of 0 (no symptoms) to 3 (severe symptoms)

BMI = body-mass index.

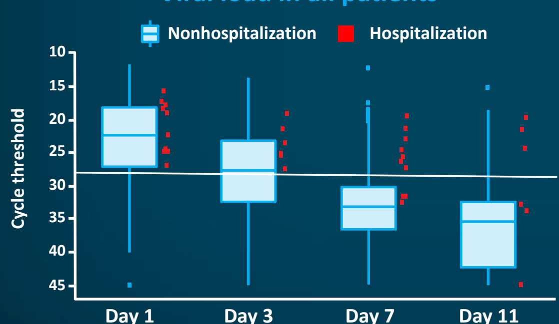
Chen P, et al. *N Engl J Med*. 2020;Oct 28: Epub ahead of print.

17

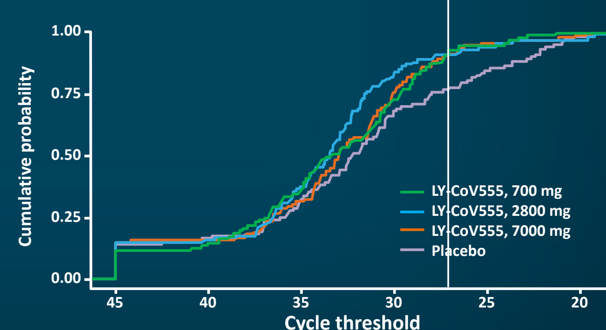
BLAZE-1: Viral Loads Over Time

- Correlation between high viral load and hospitalization
- At day 7, the frequency of hospitalization was 12% (7 of 56 patients) among those who had a Ct value of less than 27.5, as compared with a frequency of 0.9% (3 of 340 patients) among those with a lower viral load.

Viral load in all patients



Viral load on day 7 in each trial group



Ct = PCR (polymerase-chain reaction) cycle threshold (higher viral load = lower Ct value).

Chen P, et al. *N Engl J Med*. 2020;Oct 28: Epub ahead of print.

18

BLAZE-1: Bamlanivimab Safety

- No serious AEs reported with bamlanivimab use

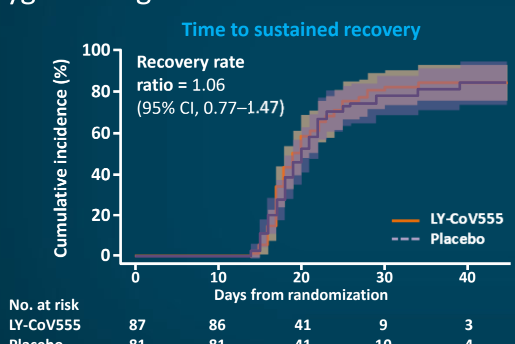
Adverse Event	LY-CoV555 (N=309) 700 mg (n = 101)	LY-CoV555 (N=309) 2800 mg (n = 107)	LY-CoV555 (N=309) 7000 mg (n = 101)	LY-CoV555 (N=309) Pooled Doses (n = 309)	Placebo (n = 143)
	Number of patients (%)				
Serious adverse event	0	0	0	0	1 (0.7)
Adverse events					
Any	24 (23.8)	23 (21.5)	22 (21.8)	69 (22.3)	35 (24.5)
Mild	16 (15.8)	18 (16.8)	10 (9.9)	44 (14.2)	18 (12.6)
Moderate	7 (6.9)	3 (2.8)	8 (7.9)	18 (5.8)	16 (11.2)
Severe	0	2 (1.9)	3 (3.0)	5 (1.6)	1 (0.7)
Missing data	1 (1.0)	0	1 (1.0)	2 (0.6)	0

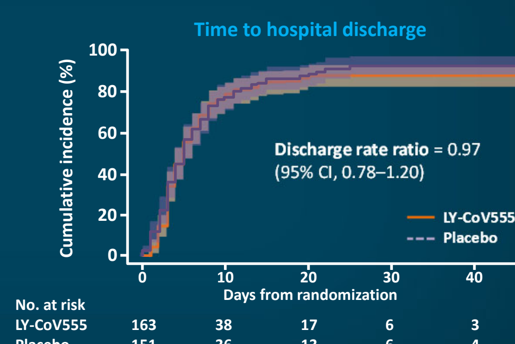
- Infusion-related reactions were reported in 2.3% of patients receiving bamlanivimab and 1.4% of patients in the placebo group
  - Most reactions were mild and occurred during the infusion

Chen P, et al. *N Engl J Med*. 2020;Oct 28: Epub ahead of print.

ACTIV-3 Trial: Bamlanivimab in Hospitalized Patients

- Hospitalized patients were randomized to receive bamlanivimab or placebo in addition to high-quality supportive care, including remdesivir and, when indicated, supplemental oxygen and glucocorticoids



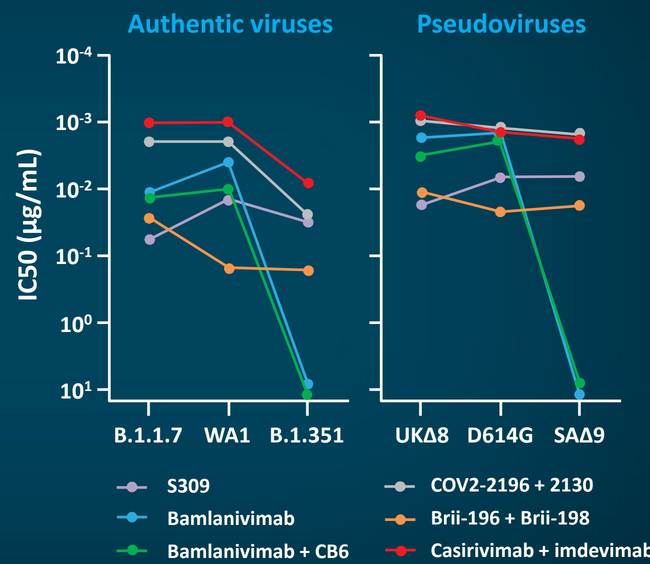


- Trial was paused when bamlanivimab was not shown to improve outcomes in hospitalized patients with COVID-19 who did not have end-organ failure

ACTIV-3/TICO LY-CoV555 Study Group. *N Engl J Med*. 2020;Dec 22: Epub ahead of print.

Emergence of SARS-CoV-2 Variants

- Several SARS-CoV-2 variants with enhanced transmissibility have emerged
  - B.1.1.7 contains 8 spike mutations and emerged in the UK
  - B.1.351 from South Africa has 9 spike mutations
- Activity against the B.1.351 variant is:
  - Reduced with casirivimab
  - Absent with bamlanivimab

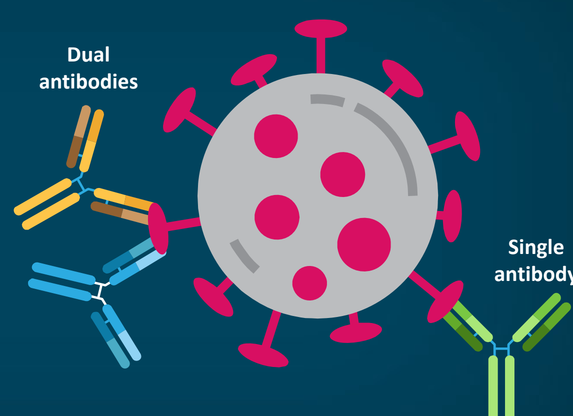


WA1 = wild-type strain; UKΔ8 = pseudovirus with 8 B.1.1.7 mutations; SAΔ9 = pseudovirus with 9 B.1.351 mutations; IC50 = half maximal inhibitory concentration.
Wang P, et al. *Nature.* 2021;Epub ahead of print.

21

Mechanism of Action of mAb Therapies Against SARS-CoV-2

- Neutralizing monoclonal antibodies against SARS-CoV-2 bind to the receptor-binding domain (RBD) of the spike protein and prevent host-cell entry
- Dual monoclonal antibody cocktail contains 2 potent antibodies that simultaneously and noncompetitively bind to different regions of the RBD
  - Use of 2 individual antibodies prevents generation of escape mutants and therapy failure

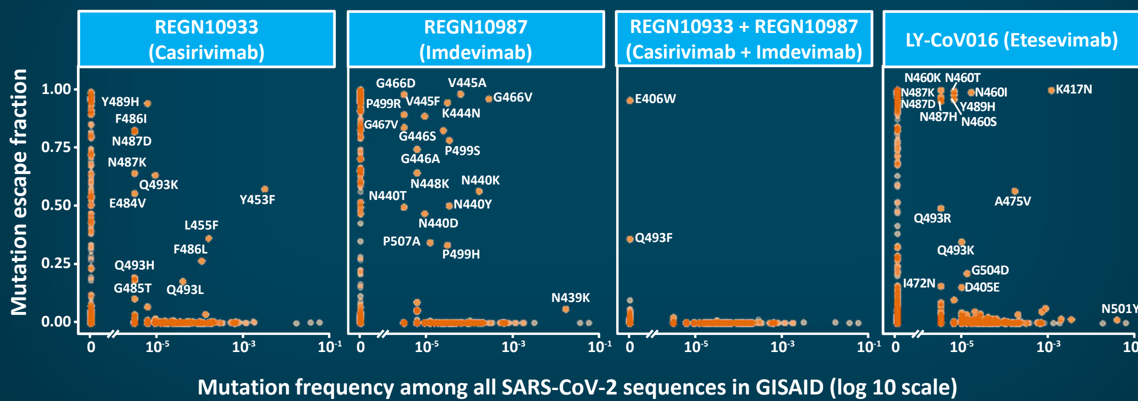


Hansen J, et al. *Science.* 2020;369:1010-1014.

22

Antibody Escape Mutations in Circulating SARS-CoV-2

- Many variants that can escape a single monoclonal antibody are currently in circulation
- Very few variants are capable of escaping dual monoclonal-antibody therapies



GISAID = Global Initiative on Sharing Avian Influenza Data.

Starr TN, et al. *Science.* 2021;371:850-854.

23

Bamlanivimab Plus Etesevimab

- Etesevimab is a neutralizing monoclonal antibody that binds to a different epitope on the spike protein than bamlanivimab
- 577 nonhospitalized patients with mild-to-moderate COVID-19 were randomized to bamlanivimab (700 mg, 2800 mg, or 7000 mg), combination therapy (bamlanivimab 2800 mg + etesevimab 2800 mg), or placebo

	Bamlanivimab 700 mg	Bamlanivimab 2800 mg	Bamlanivimab 7000 mg	Bamlanivimab 2800 mg + Etesevimab 2800 mg	Placebo
Change in log viral load from baseline to day 11	–3.72 *P* = 0.69	–4.08 *P* = 0.21	–3.49 *P* = 0.16	–4.37 *P* = 0.01	–3.80
COVID-19-related hospitalizations or ED visits	1.0%	1.9%	2.0%	0.9%	5.8%

ED = emergency department.

Gottlieb RL, et al. *JAMA.* 2021;Jan 21: Epub ahead of print.

24

Casirivimab and Imdevimab (REGN-COV2)

Ongoing phase 1–3 trial of casirivimab and imdevimab in nonhospitalized adults with mild-to-moderate COVID-19

Inclusion criteria:
- ≥18 years
- ≥1 symptom of COVID-19
- Positive SARS-CoV-2 test <72 hours prior to randomization
- Symptoms consistent with COVID-19 with onset <7 days before randomization
- No hospitalization due to COVID-19

R

- 2.4 g casirivimab and imdevimab (1.2 g each)
- 8.0 g casirivimab and imdevimab (4.0 g each)
- Placebo

Casirivimab and imdevimab EUA. (www.fda.gov/media/143892/download). Accessed 1/7/2021.

25

Casirivimab and Imdevimab: Interim Results

Interim analysis of 275 nonhospitalized patients with mild-to-moderate COVID-19

At Least 1 COVID-19-Related Medical Visit Within 29 Days		
Treatment	**Events/Total Patients**	**Incidence**
All patients		
Placebo	6/93	6%
Casirivimab and imdevimab 2.4 g	3/92	3%
Casirivimab and imdevimab 8.0 g	3/90	3%
All doses casirivimab and imdevimab	6/182	3%
Seronegative patients		
Placebo	5/33	15%
Casirivimab and imdevimab 2.4 g	2/41	5%
Casirivimab and imdevimab 8.0 g	3/39	8%
All doses casirivimab and imdevimab	5/80	6%

Weinreich DM, et al. *N Engl J Med*. 2020;Dec 17: Epub ahead of print.

26

Casirivimab/Imdevimab: Efficacy by Baseline Viral Load

Casirivimab/imdevimab (REGN-COV2) provided greater reduction in viral load in those patients with higher viral load at baseline

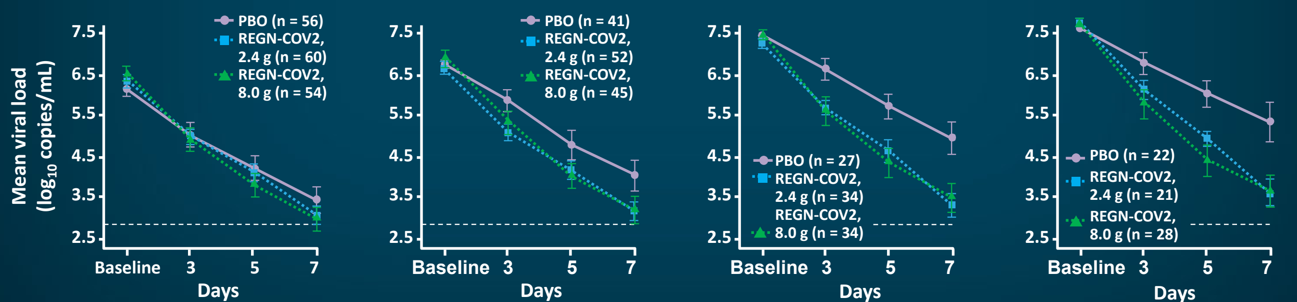
Viral load over time according to baseline viral-load category

	$>10^4$ copies/mL Difference in Change from Baseline, Day 7	
	TWA LS mean	Mean
2.4 g vs PBO	–0.36	–0.64
8.0 g vs PBO	–0.59	–0.90

	$>10^5$ copies/mL Difference in Change from Baseline, Day 7	
	TWA LS mean	Mean
2.4 g vs PBO	–0.59	–0.83
8.0 g vs PBO	–0.75	–1.12

	$>10^6$ copies/mL Difference in Change from Baseline, Day 7	
	TWA LS mean	Mean
2.4 g vs PBO	–0.81	–1.46
8.0 g vs PBO	–1.14	–1.54

	$>10^7$ copies/mL Difference in Change from Baseline, Day 7	
	TWA LS mean	Mean
2.4 g vs PBO	–1.03	–1.84
8.0 g vs PBO	–1.32	–1.75



TWA = time-weighted average; LS = least-squares.

Weinreich DM, et al. *N Engl J Med*. 2020;Dec 17: Epub ahead of print.

27

Casirivimab/Imdevimab Safety

Event	REGN-COV2 2.4 g (n = 88)	REGN-COV2 8.0 g (n = 88)	REGN-COV2 Combined (n = 176)	Placebo (n = 93)
	Number of patients (%)			
Any serious adverse event	1 (1)	0	1 (1)	2 (2)
Any adverse event of special interest* (Grade 2 or higher hypersensitivity or infusion-related reactions)	0	2 (2)	2 (1)	2 (2)
Any serious adverse event of special interest*	0	0	0	0
Grade ≥2 infusion-related reaction within 4 days	0	2 (2)	2 (1)	1 (1)
Grade ≥2 hypersensitivity reaction within 29 days	0	1 (1)	1 (1)	2 (2)
Adverse events that occurred or worsened during the observation period†				
Grade 3 or 4 event	1 (1)	0	1 (1)	1 (1)
Event that led to death	0	0	0	0
Event that led to withdrawal from the trial	0	0	0	0
Event that led to infusion interruption*	0	1 (1)	1 (1)	1 (1)

*Events were grade 2 or higher hypersensitivity reactions or infusion-related reactions.
†Events listed here were not present at baseline or were an exacerbation of a preexisting condition that occurred during the observation period, which is defined as the time from administration of REGN-COV2 or placebo to the last study visit.

Weinreich DM, et al. *N Engl J Med*. 2020;Dec 17: Epub ahead of print.

28

mAb Therapies With Emergency Use Authorization

These therapies must be given as soon as possible and within 10 days of symptom onset

Bamlanivimab 700 mg AND Etesevimab 1400 mg

Administer together as single IV infusion over minimum of 21–60 minutes

Casirivimab 1200 mg AND Imdevimab 1200 mg

Must be administered together as a single IV infusion over minimum of 60 minutes

Monotherapy not recommended due to resistance of viral variants

Bamlanivimab 700 mg

Administer as a single IV infusion over minimum of 16–60 minutes

IV = intravenous.

Bamlanimab EUA. (http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf). Bamlanivimab and etesevimab EUA. (www.fda.gov/media/145802/download). Casirivimab and imdevimab EUA. (www.fda.gov/media/143892/download). US Health and Human Services (HHS). (www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab/Pages/default.aspx)

29

Emergency Use Authorization of COVID-19 mAb Therapy

- EUA for the treatment of mild-to-moderate COVID-19 in patients:
  - Who are at least 12 years of age and weigh at least 40 kg
  - Have positive results of direct SARS-CoV-2 viral testing
  - Who are at high risk of progressing to severe COVID-19 or hospitalization
- No benefit in patients hospitalized due to COVID-19
- These therapies may be associated with worse clinical outcomes in hospitalized COVID-19 patients requiring high-flow oxygen or mechanical ventilation

Casirivimab and imdevimab EUA. (www.fda.gov/media/143892/download). Bamlanimab EUA. (http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf). URLs accessed 12/2/2020.

30

Identifying High-Risk Candidates for mAb Therapy

High risk is defined as a patient who meets ≥1 of the following criteria

Patients of any age with:
- BMI ≥35
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Current immunosuppressive therapy

Patients aged ≥65 years

Patients ≥55 years of age with:
- Cardiovascular disease, OR
- Hypertension, OR
- Chronic obstructive pulmonary disease/ other chronic respiratory condition

Patients aged 12–17 years with:
- BMI >85th percentile for age and gender
- Sickle cell disease
- Congenital or acquired heart disease
- Neurodevelopmental disorders (eg, cerebral palsy)
- Asthma, reactive airway, or other chronic respiratory disease that requires daily medication for control
- A medical-related technological dependence (eg, tracheostomy, gastrostomy, positive-pressure ventilation not related to COVID-19)

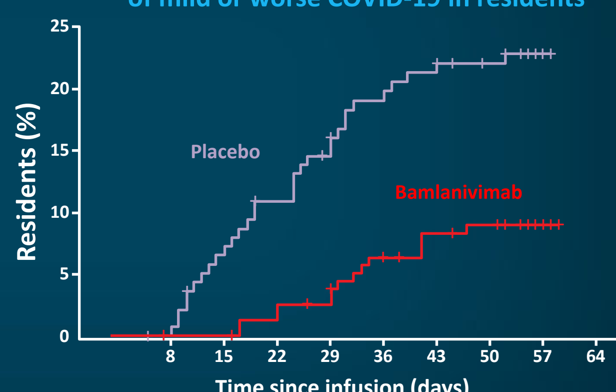
Casirivimab and imdevimab EUA. (www.fda.gov/media/143892/download). Bamlanimab EUA. (http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf). URLs accessed 12/2/2020.

31

Bamlanivimab in Nursing-Home Setting

- 966 participants, including 266 nursing-home residents considered at high-risk for severe COVID-19, were administered a single-dose of bamlanivimab or placebo if a case of SARS-CoV-2 was confirmed in nursing home
- Compared with placebo, bamlanivimab was associated with:
  - Significantly lower proportion of residents with mild or worse COVID-19 by day 57 (OR = 0.20; 95% CI, 0.08–0.49; *P* <.001)
  - Significant reductions in incident SARS-CoV-2 infection by day 29 (OR = 0.23; CI, 0.11–0.48; *P* <.001)
- 5 COVID-19-related deaths (all in placebo group)

Time since treatment to development of mild or worse COVID-19 in residents



OR = odds ratio.

Cohen M, et al. CROI 2021: abstract 121LB. Lilly BLAZE-2 press release. 1/21/2121. (https://investor.lilly.com/node/44291/pdf). Accessed 3/25/2021.

32

Top-line Results on mAb Therapies

- **BLAZE-1: Bamlanivimab plus etesivimab**
  - Phase 3 trial of 769 high-risk, recently diagnosed COVID-19 patients showed that therapy with bamlanivimab and etesevimab reduced hospitalizations and deaths by **87%** (*P*= .0001)
- **Casirivimab and imdevimab for COVID-19 treatment**
  - 70% reduction in risk of hospitalization or death in 4567 high-risk, non-hospitalized COVID-19 patients
- **Casirivimab and imdevimab for COVID-19 prevention**
  - Interim analysis found 100% prevention of symptomatic infection and 50% reduction in rate of COVID-19 infection in a phase 3 trial of 400 individuals with household exposure to COVID-19

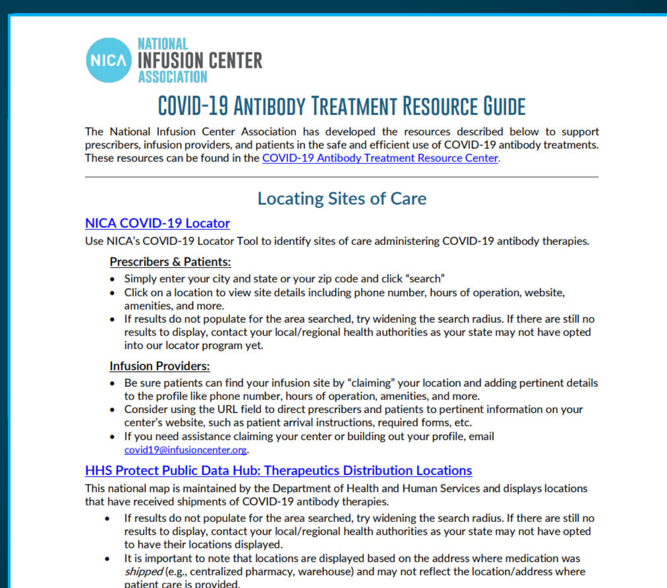
Lilly press release. 3/10/2021. (https://investor.lilly.com/news-releases/news-release-details/lillys-bamlanivimab-and-etesevimab-together-reduced). Regeneron press release. 1/26/21. (https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-reports-positive-interim-data-regen-covtm-antibody). Regeneron press release. 3/23/21. (https://investor.regeneron.com/news-releases/news-release-details/phase-3-trial-shows-regen-covtm-casirivimab-imdevimab-antibody). URLs accessed 3/25/2021.

33

COVID-19 Antibody Treatment Resource Guide

National Infusion Center Association

- Infusion center locator
- Resources for providers
  - Bamlanivimab playbook
  - Casirivimab + imdevimab guidebook
- Patient education resources
- Treatment indication checklist
- Plus, other resources



NATIONAL INFUSION CENTER ASSOCIATION

COVID-19 ANTIBODY TREATMENT RESOURCE GUIDE

The National Infusion Center Association has developed the resources described below to support prescribers, infusion providers, and patients in the safe and efficient use of COVID-19 antibody treatments. These resources can be found in the COVID-19 Antibody Treatment Resource Center.

Locating Sites of Care

NICA COVID-19 Locator

Use NICA's COVID-19 Locator Tool to identify sites of care administering COVID-19 antibody therapies.

Prescribers & Patients:

- Simply enter your city and state or your zip code and click "search"
- Click on a location to view site details including phone number, hours of operation, website, amenities, and more.
- If results do not populate for the area searched, try widening the search radius. If there are still no results to display, contact your local/regional health authorities as your state may not have opted into our locator program yet.

Infusion Providers:

- Be sure patients can find your infusion site by "claiming" your location and adding pertinent details to the profile like phone number, hours of operation, amenities, and more.
- Consider using the URL field to direct prescribers and patients to pertinent information on your center's website, such as patient arrival instructions, required forms, etc.
- If you need assistance claiming your center or building out your profile, email covid19@infusioncenter.org.

HHS Protect Public Data Hub: Therapeutics Distribution Locations

This national map is maintained by the Department of Health and Human Services and displays locations that have received shipments of COVID-19 antibody therapies.

- If results do not populate for the area searched, try widening the search radius. If there are still no results to display, contact your local/regional health authorities as your state may not have opted to have their locations displayed.
- It is important to note that locations are displayed based on the address where medication was *shipped* (e.g., centralized pharmacy, warehouse) and may not reflect the location/address where patient care is provided.

National Infusion Center Association (https://infusioncenter.org/infusion_resources/covid-19-antibody-treatment-resource-center/). Accessed 1/18/2021.

34

Management of Hospitalized Patients with COVID-19

35

IDSA: Recommended Treatment Options for Hospitalized Patients

Treatment	Guidance
Remdesivir	• Recommended for hospitalized patients with severe COVID-19 • Most benefit seen in those with severe COVID-19 on supplemental oxygen rather than patients on mechanical ventilation or ECMO • 5 days of treatment recommended for patients on supplemental oxygen • 10 days of treatment recommended for patients on mechanical ventilation or ECMO
Glucocorticoids	• Recommended for hospitalized patients with severe COVID-19 • Dexamethasone 6 mg IV or PO for 10 days or equivalent • Not recommended for hospitalized patients without hypoxemia (SpO_2 >94%) requiring supplemental oxygen
Baricitinib plus remdesivir	• Baricitinib plus remdesivir recommended over remdesivir alone in hospitalized patients with severe COVID-19 who cannot receive corticosteroids because of a contraindication
Tocilizumab	• Recommended in addition to standard of care in hospitalized patients with progressive severe or critical COVID-19 who have elevated markers of systemic inflammation

IDSA = Infectious Diseases Society of America; ECMO = extracorporeal membrane oxygenation; PO = by mouth.

Bhimraj A, et al. IDSA Guidelines. V3.9.0. (www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/).

36

Adaptive COVID-19 Treatment Trial (NIAID ACTT-1): Trial Design

- Multicenter, adaptive, randomized, double-blind, placebo-controlled phase 3 trial

Inclusion criteria (N = 1062)

- Adult patients ≥18 years of age
- Hospitalized with symptoms of COVID-19/SARS-CoV-2 infection and ≥1 of following:
  - Radiographic infiltrates by imaging
  - SpO_2 ≤94% on room air
  - Requiring supplemental oxygen
  - Requiring mechanical ventilation

Day 10

Remdesivir IV QD
Day 1, 200 mg; days 2–10 100 mg

Placebo IV QD

Daily assessment for time to clinical improvement while hospitalized to day 29; assessments at days 15, 22, and 29 if discharged

- Primary endpoint: time to recovery by day 29 according to 8-point ordinal scale
- Secondary endpoints: treatment-related improvements in ordinal scale at day 15

QD = each day.

Beigel JH, et al. *N Engl J Med*. 2020;383:1813-1826.

37

COVID-19 Clinical Status Ordinal Scale

Clinical Status Ordinal Scale	Clinical Status Description for Assessment
1	Not hospitalized, no limitations on activities
2	Not hospitalized, limitation on activities, and/or requiring home oxygen
3	Hospitalized, not requiring supplemental oxygen, and no longer requires ongoing medical care (if hospitalization extended for infection-control purposes)
4	Hospitalized, not requiring supplemental oxygen; requiring ongoing medical care (COVID-19 related or otherwise)
5	Hospitalized, requiring supplemental oxygen
6	Hospitalized, on noninvasive ventilation or high-flow oxygen devices
7	Hospitalized, on invasive mechanical ventilation or ECMO
8	Death

Beigel JH, et al. *N Engl J Med*. 2020;383:1813-1826.

38

Remdesivir: NIAID ACTT Clinical Trial

- 1062 patients in 68 sites randomized 1:1 to remdesivir or placebo
- Independent data safety monitoring board found that remdesivir shortened time to recovery compared with placebo

	Remdesivir	Placebo	*P*-value
Time to recovery	10 days	15 days	*P* <.001
Mortality	6.7% day 15 11.4% day 29	11.9% day 15 15.2% day 29	*P* = .07 (day 29)

An ICU bed becomes available 5 days earlier
Benefit is in early disease

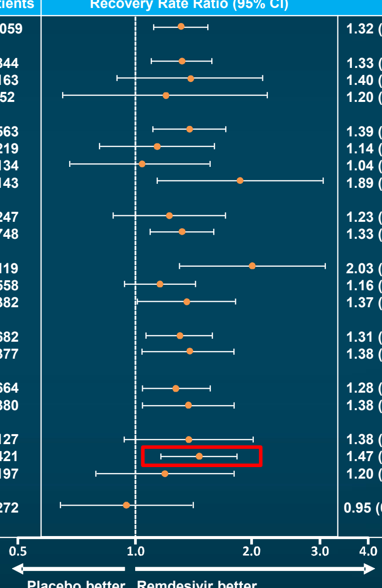
~30% reduction in mortality
Not statistically significant

NIAID = National Institute of Allergy and Infectious Diseases.
Beigel JH et al. *N Engl J Med.* 2020;383:1813-1826 plus supplement.

39

Remdesivir: NIAID ACTT Clinical Trial

Subgroup	No. of Patients	Recovery Rate Ratio (95% CI)
All patients	1059	1.32 (1.12-1.55)
Geographic region		
North America	844	1.33 (1.11-1.59)
Europe	163	1.40 (0.90-2.16)
Asia	52	1.20 (0.65-2.22)
Race		
White	563	1.39 (1.12-1.73)
Black	219	1.14 (0.81-1.61)
Asian	134	1.04 (0.68-1.57)
Other	143	1.89 (1.15-3.10)
Ethnic group		
Hispanic or Latino	247	1.23 (0.88-1.72)
Not Hispanic or Latino	748	1.33 (1.10-1.61)
Age		
18 to <40 years	119	2.03 (1.31-3.15)
40 to <65 years	558	1.16 (0.94-1.44)
≥65 years	382	1.37 (1.02-1.83)
Sex		
Male	682	1.31 (1.07-1.59)
Female	377	1.38 (1.05-1.81)
Duration of symptoms		
≤10 days	664	1.28 (1.05-1.57)
>10 days	380	1.38 (1.05-1.81)
Baseline ordinal score		
4 (not receiving oxygen)	127	1.38 (0.94-2.03)
5 (receiving oxygen)	421	1.47 (1.17-1.84)
6 (receiving high-flow oxygen or noninvasive mechanical ventilation)	197	1.20 (0.79-1.81)
7 (receiving mechanical ventilation or ECMO)	272	0.95 (0.64-1.42))

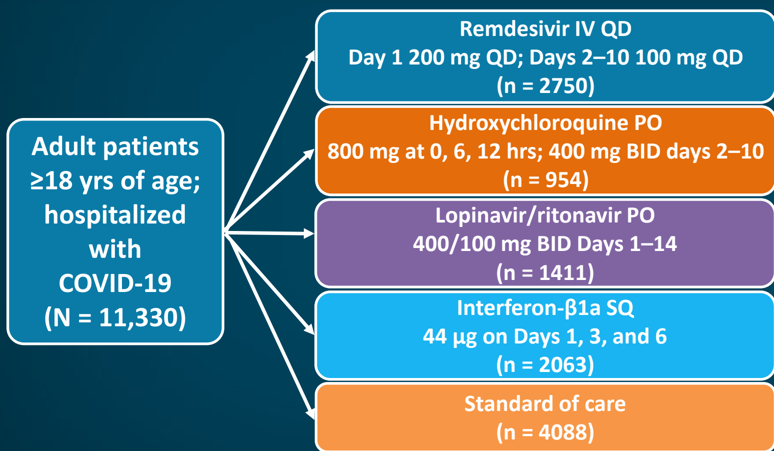


Beigel JH, et al. *N Engl J Med*. 2020;383:1813-1826.

40

WHO SOLIDARITY Trial: Antiviral Drugs in Hospitalized Patients

Open-label, randomized phase 3 trial conducted in 405 hospitals in 30 countries



- **Primary endpoint**
  28-day in-hospital mortality
- **Secondary endpoints**
  - Initiation of ventilation
  - Duration of hospitalization

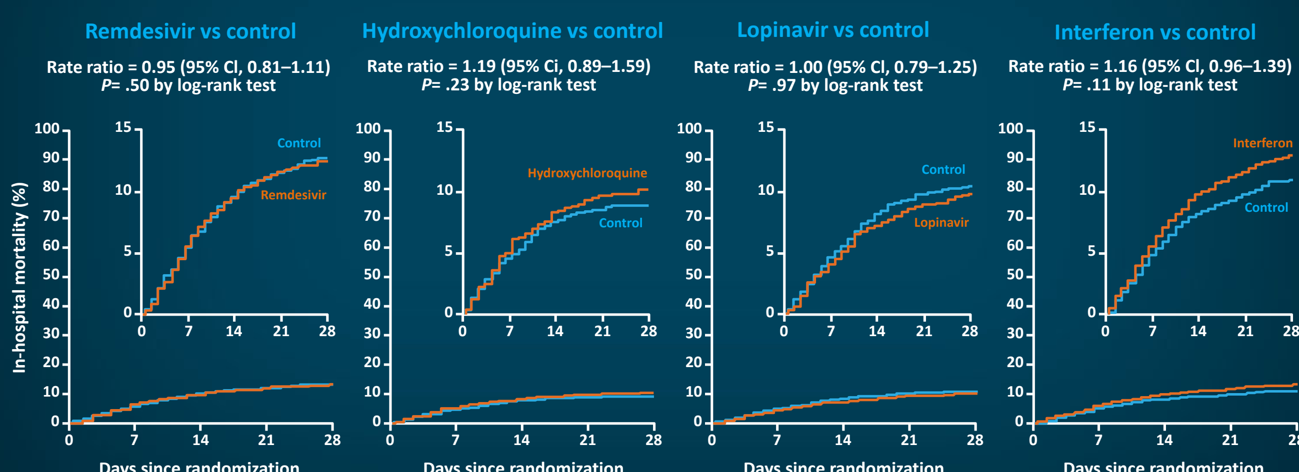
BID = twice daily; SQ = subcutaneous.

Pan H, et al; WHO (World Health Organization) Solidarity Trial Consortium. *N Engl J Med.* 2021;384:497-511.

41

WHO SOLIDARITY Trial: Results

Remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little to no effect on overall mortality, initiation of ventilation, or duration of hospital stay in hospitalized patients with COVID-19



Pan H, et al; WHO Solidarity Trial Consortium. *N Engl J Med.* 2021;384:497-511.

42

RECOVERY Trial Design

- Eligible patients (hospitalized with clinically suspected or laboratory-confirmed SARS-CoV-2 infection) were randomized to:

No additional treatment | **Dexamethasone** | **Hydroxychloroquine** | **Lopinavir/ritonavir** | **Azithromycin**

- Primary endpoint: 28-day mortality
- Patients with progressive disease (hypoxia and an inflammatory state) may undergo second randomization to no additional treatment or **tocilizumab**
- Current RECOVERY trials are investigating **baricitinib, casirivimab/imdevimab, aspirin, dexamethasone** (in children), and **colchicine**

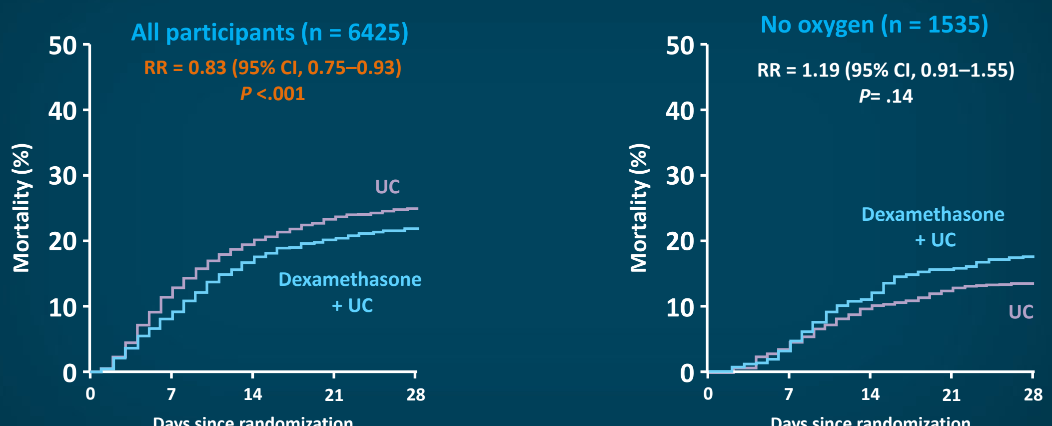
Randomized Evaluation of COVID-19 Therapy—RECOVERY (www.recoverytrial.net/files/recovery-protocol-v7-0-2020-06-18.pdf). Accessed 2/12/2021.

43

RECOVERY Trial

Mortality With Dexamethasone + UC vs UC Alone

2104 patients randomized to dexamethasone 6 mg QD for up to 10 days; 4321 patients received UC alone



No. at risk					
UC	4321	3754	3427	3271	3205
Dexamethasone/UC	2104	1903	1725	1659	1621

No. at risk					
UC	501	463	420	394	383
Dexamethasone/UC	1034	969	890	856	832

UC = usual care.

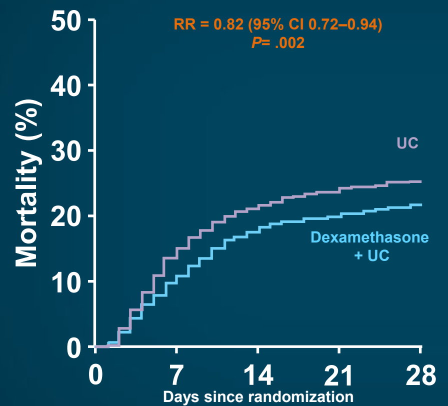
Horby P, et al; RECOVERY Collaborative Group. *N Engl J Med.* 2020;Jul 17:Epub ahead of print.

44

RECOVERY Trial

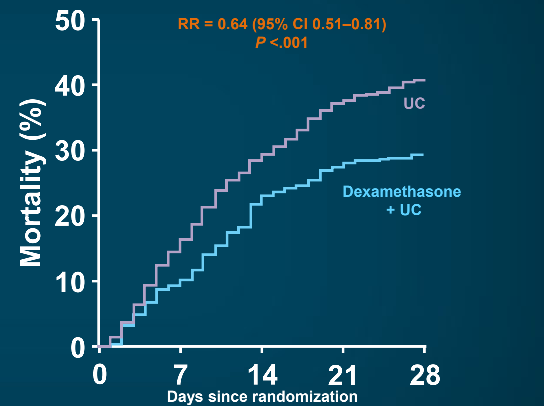
Mortality in Patients On Oxygen or Mechanical Ventilation ± Dexamethasone

Oxygen only (n = 3883)



No. at risk	0	7	14	21	28
Dexamethasone/UC	1279	1135	1036	1006	981
UC	2604	2195	2018	1950	1916

Invasive mechanical ventilation (n = 1007)



No. at Risk	0	7	14	21	28
Dexamethasone/UC	324	290	248	232	228
UC	683	572	481	424	400

Horby P, et al; RECOVERY Collaborative Group. *N Engl J Med.* 2020;Jul 17:Epub ahead of print.

45

EUAs for Hospitalized Patients

46

ACCT-2: Baricitinib Plus Remdesivir in Hospitalized Patients

Inclusion criteria:

- **≥18 years**
- **Hospitalized with COVID-19**
- **≥1 of the following criteria:**
  - **Radiographic infiltrates by imaging**
  - **SpO_2 ≤94% on room air**
  - **Supplemental oxygen, mechanical ventilation, or ECMO**

N = 1033

- Baricitinib (≤14 days) plus remdesivir (≤10 days) (n = 515)
- Placebo plus remdesivir (≤10 days) (n = 518)

- Primary outcome: time to recovery
- Key secondary outcome: clinical status at day 15

Kalil AC, et al. *N Engl J Med.* 2021;384:795-807.

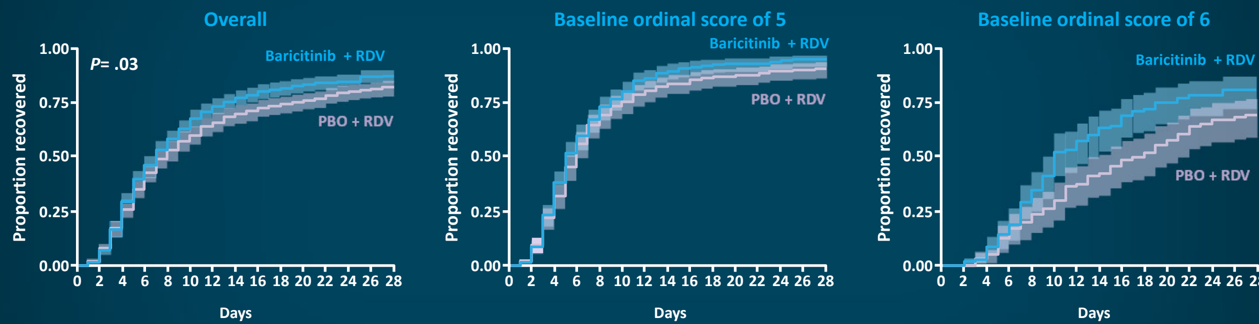
ACTT-2: Ordinal Scale

Ordinal Scale Used for Outcome Measures	
Recovered	
1	Not hospitalized, no limitations on activities
2	Not hospitalized, limitation on activities and/or requiring home oxygen
3	Hospitalized, not requiring supplemental oxygen—no longer requiring ongoing medical care
Population enrolled	
4	Hospitalized, not requiring supplemental oxygen—requiring ongoing medical care
5	Hospitalized, requiring supplemental oxygen
6	Hospitalized, on non-invasive ventilation or high-flow oxygen devices
7	Hospitalized, on mechanical ventilation or ECMO
8	Death

Kalil AC, et al. *N Engl J Med.* 2021;384:795-807.

Baricitinib Plus Remdesivir: Recovery Time

- Recovery time was reduced with baricitinib vs placebo (7 days vs 8 days; rate ratio for recovery = 1.16; 95% CI, 1.01–1.32; *P*= .03)



- Time to recovery was significantly lower with baricitinib in patients receiving high-flow oxygen or noninvasive ventilation at enrollment (10 days vs 18 days; rate ratio for recovery = 1.51)

RDV = remdesivir.

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49

Baricitinib Plus Remdesivir: Results

- Baricitinib was associated with 30% higher odds of improvement in clinical status at day 15 (OR = 1.3)
- 28-day mortality was 5.1% in the combination group and 7.8% in the control group (HR for death = 0.65)

Overall Outcomes

Outcomes	Baricitinib + RDV (n = 515)	Placebo + RDV (n = 518)
Recovery		
No. of recoveries	433	406
Median time to recovery (95% CI), days	7 (6–8)	8 (7–9)
Rate ratio (95% CI)	1.16 (1.01–1.32), *P*= .03	
Mortality over first 14 days		
No. of deaths by day 14	8	15
Kaplan-Meier estimate of mortality by day 14, % (95% CI)	1.6 (0.8–3.2)	3.0 (1.8–5.0)
HR (95% CI) for data through day 14	0.54 (0.23–1.28)	
Mortality over entire trial period		
No. of deaths by day 28	24	37
Kaplan-Meier estimate of mortality by day 28, % (95% CI)	5.1 (3.5–7.6)	7.8 (5.7–10.6)
HR (95% CI)	0.65 (0.39–1.09)	

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50

ACTT-2: Adverse Events

Treatment-Emergent Adverse Events in ACTT-2		
	Baricitinib + RDV (n = 508) No. (%)	Placebo + RDV (n = 509) No. (%)
Grade 3 or 4 AEs	207 (40.7)	238 (46.8)
Hyperglycemia	25 (4.9)	40 (7.9)
Anemia	25 (4.9)	33 (6.5)
Decreased lymphocyte count	24 (4.7)	35 (6.9)
Acute kidney injury	20 (3.9)	36 (7.1)
Venous thromboembolism	21 (4.1)	16 (3.1)

AE = adverse event.

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51

Emergency Use Authorization for Baricitinib

- Baricitinib plus remdesivir was authorized for emergency use in hospitalized adults and pediatric patients ≥2 years of age requiring supplemental oxygen, invasive mechanical ventilation, or ECMO with suspected or confirmed COVID-19
- Recommended dosage:
  - Patients ≥9 years of age: 4 mg baricitinib once daily
  - Patients 2 to 9 years of age: 2 mg baricitinib once daily
- Recommended treatment duration is 14 days or until hospital discharge, whichever comes first
- Evaluate baseline eGFR, liver enzymes, and complete blood count to determine treatment suitability and dose

Baricitinib EUA. (www.fda.gov/media/143823/download). Accessed 1/20/2021.

52

Case Study

Moderate COVID-19 in an Immunocompromised Patient

53

Moderate COVID-19 in an Immunocompromised Patient

- JL is a 28-year old male with AML diagnosed in August 2020 who was treated with 7+3 as induction therapy. He was started on consolidation therapy with HiDAC (high-dose cytarabine) on 10/21/20 and received a 2nd cycle on 11/23/20.
- On 11/28/20, he experiences fevers, chills, shortness of breath, sore throat, and congestion.
  - On 12/1/20, he tested positive for COVID-19.

54

Admitted for COVID-19

- He was admitted on 12/3/20 due to persistent fever, nausea, vomiting and new cough.
- On admission, he was afebrile, not hypoxic, and had tachycardia.
- Labs: WBC 0.2, AST 70, ALT 120

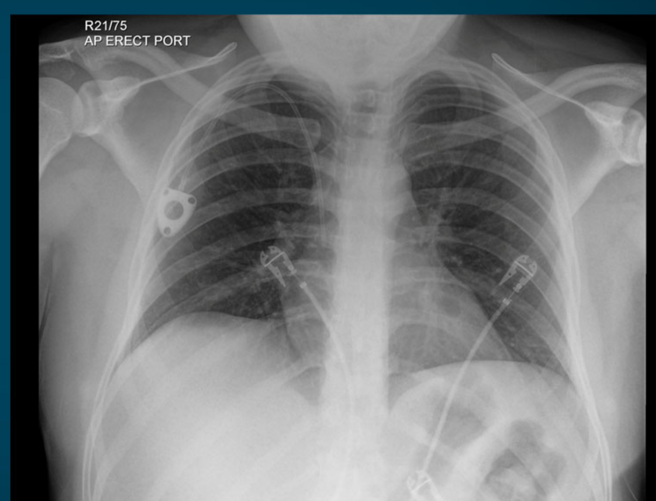
Is JL a candidate for monoclonal antibody therapy?

55

Imaging Results

- Chest CT with contrast showed peripheral ground glass opacities thought to be consistent with COVID-19 and no PE.
- O_2 saturations were continuously monitored and remained >90% while at rest.

How would you manage JL?



56

Further Management

- JL did not experience episodes of hypoxia and was not given remdesivir, steroids, and/or baricitinib.
- On 12/9, his absolute neutrophil count (ANC) was >500.
- On 12/14, he was afebrile. His ambulatory saturation was assessed and >90% so he was discharged 24 hours later.
- Following discharge, JL's COVID-19 symptoms completely resolved and he was readmitted on 1/16 for cycle 3 of HiDAC.

57

Case Study

Sickle Cell Disease

58

History of Present Illness

- WH is a 17-year-old African-American male who presents with 2 day history of fever, headache, and loss of smell. He denies any SOB, DOE, or chest pain
- His past medical history is significant for sickle cell disease
- He tests positive for SARS-CoV-2
- His SpO2 is 95% on room air and his BP is 140/86 mmHg

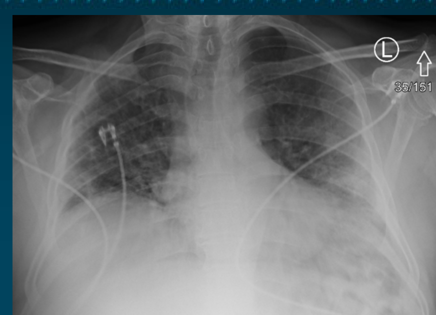
Is WH a candidate for monoclonal antibody therapy?

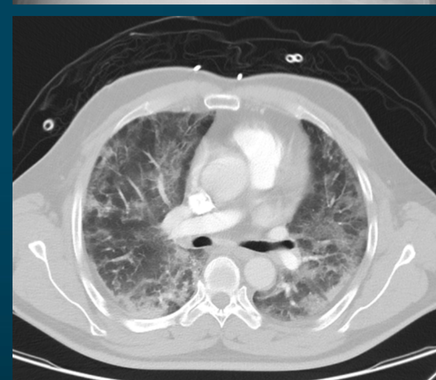
59

Hospital Admission

- Patient and family refused monoclonal antibody therapy in the ED
- Patient developed chest pain and hypotension and was admitted.
- SpO2 fell to 88% on room air
- CXR showed scattered bilateral lung infiltrates; chest CT showed bilateral pulmonary infiltrates (multi-lobar pneumonia)

How would you manage WH?





60

Clinical Course

- Patient was managed for sickle cell crisis with hydration and broad spectrum antibiotics (vancomycin and piperacillin/tazobactam)
- The patient received remdesivir for 5 days and dexamethasone for 10 days
- By hospital day 11, he was no longer hypoxic and was discharged home

61

Summary

- Several neutralizing mAb therapies are authorized for treatment of mild-to-moderate COVID-19 in patients at high risk of progressing to severe COVID-19 or hospitalization
  - mAbs against SARS-CoV-2 reduced the risk of COVID-19-related hospitalization
  - These therapies may be associated with worse clinical outcomes in hospitalized COVID-19 patients requiring high-flow oxygen or mechanical ventilation
  - Therapy should be provided as soon as possible and within 10 days of symptoms onset
  - Due to the emergence of viral resistance, dual monoclonal antibody therapies—bamlanivimab plus etesevimab or casirivimab plus imdevimab—should be used
- Baricitinib plus remdesivir is authorized for emergency use in hospitalized adults and pediatric patients ≥2 years of age requiring supplemental oxygen, invasive mechanical ventilation, or ECMO with suspected or confirmed COVID-19
  - Recommended treatment duration is 14 days or until hospital discharge, whichever comes first
  - Baricitinib plus remdesivir associated with improvements in recovery time

62

Thank you!

63

COVID-19 Frontline website

Project ECHO®

Med Learning Group - COVID-19 Frontline

https://covid-frontline.com

64

A Light in the Darkness: New Virus-neutralizing Monoclonal Antibodies and Other Point-of-Care Therapies Recently Granted Emergency Use Authorizations for Patients with COVID-19

Resource	Address
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