
CONNECTING
CARE
Outpatient Treatment of COVID-19
With Neutralizing Monoclonal Antibodies
forefront
COLLABORATIVE

FACULTY AND DISCLOSURES

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Dr. Worz has indicated that neither he nor his spouse/partner have had, in the past 12 months, financial relationship(s) with commercial interests relative to the content of this CME activity.

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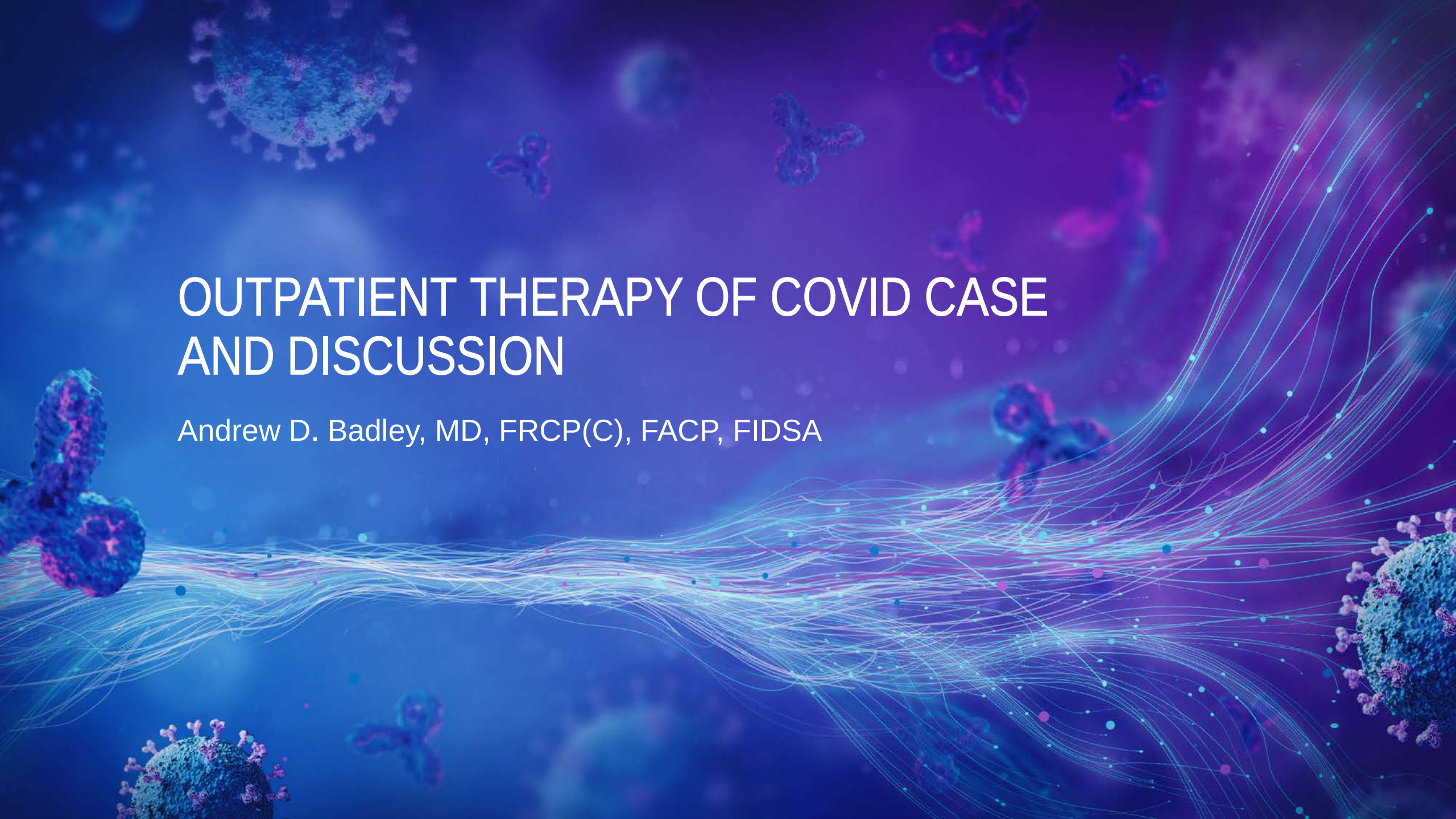
Polling questions

Submit your questions anytime

This continuing medical education activity will include reference(s) to unlabeled or unapproved uses of drugs or devices.



OUTPATIENT THERAPY OF COVID CASE AND DISCUSSION

Andrew D. Badley, MD, FRCP(C), FACP, FIDSA

CASE

69-year-old woman presenting after she tested positive for SARS-CoV-2 on December 27.

Her initial symptoms were cough, pleuritic chest pain, and post-tussive vomiting that worsened on day of diagnosis.

She also reports poor appetite. She denies diarrhea, dysuria, hematuria, sore throat, or rhinorrhea.

PAST MEDICAL AND SURGICAL HISTORY

- DM2
- COPD
- Iron deficiency anemia
- Hypertension

LABS

- WBC of 3.1, with leukopenia 0.86
- D-dimer of 564, normal creatinine
- ALT of 65 an AST of 59, C-reactive of 50.1, ferritin of 564
- CXR normal

Hemodynamically stable, afebrile, SpO_2 of 95% on RA.

Physical exam was unremarkable.

DM2=myotonic dystrophy type. COPD=chronic obstructive pulmonary disease. SpO_2=oxygen saturation. RA=radial artery. WBC=white blood count. ALT=alanine transaminase. AST=aspartate aminotransferase. CXR=chest X-ray.

WHAT IS THE BEST, EVIDENCE-BASED APPROACH TO MANAGEMENT?

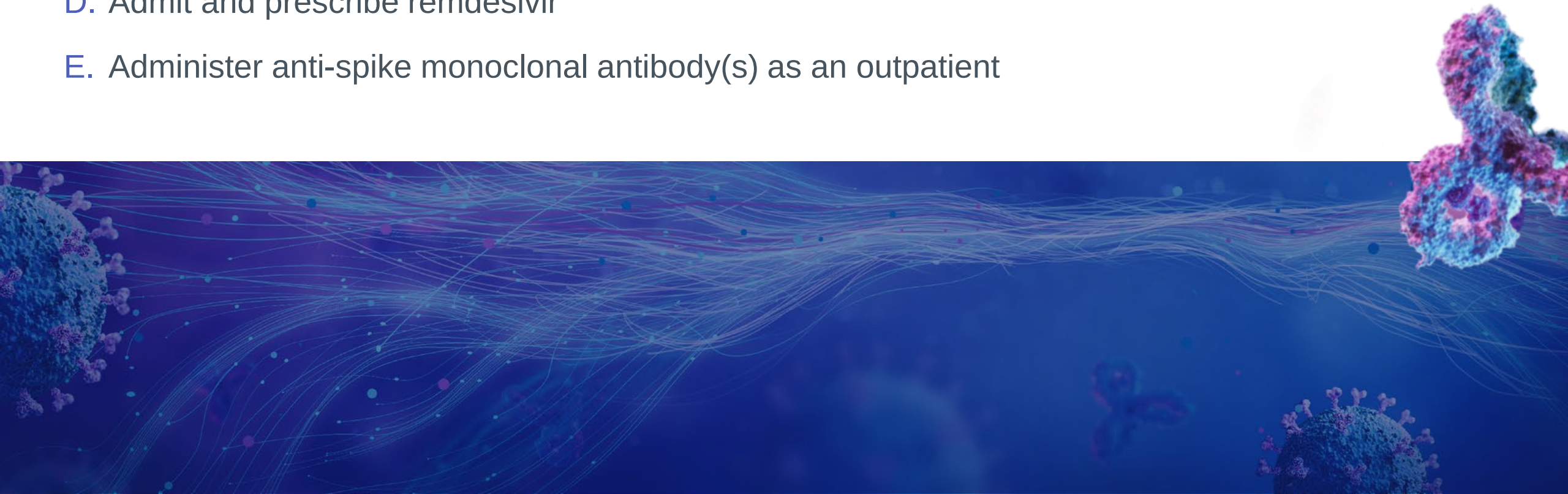
A. Observe and monitor symptoms

B. Give zinc/vitamin D or both

C. Prescribe hydroxychloroquine

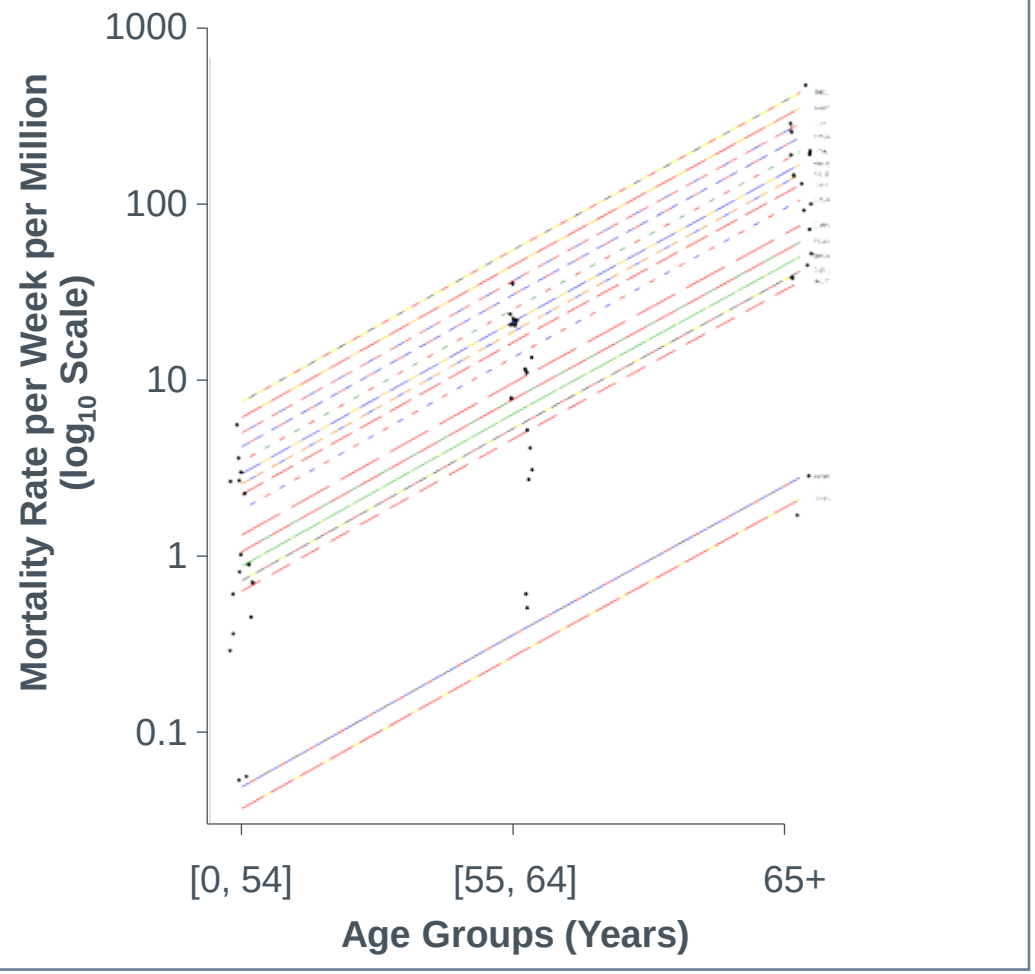
D. Admit and prescribe remdesivir

E. Administer anti-spike monoclonal antibody(s) as an outpatient

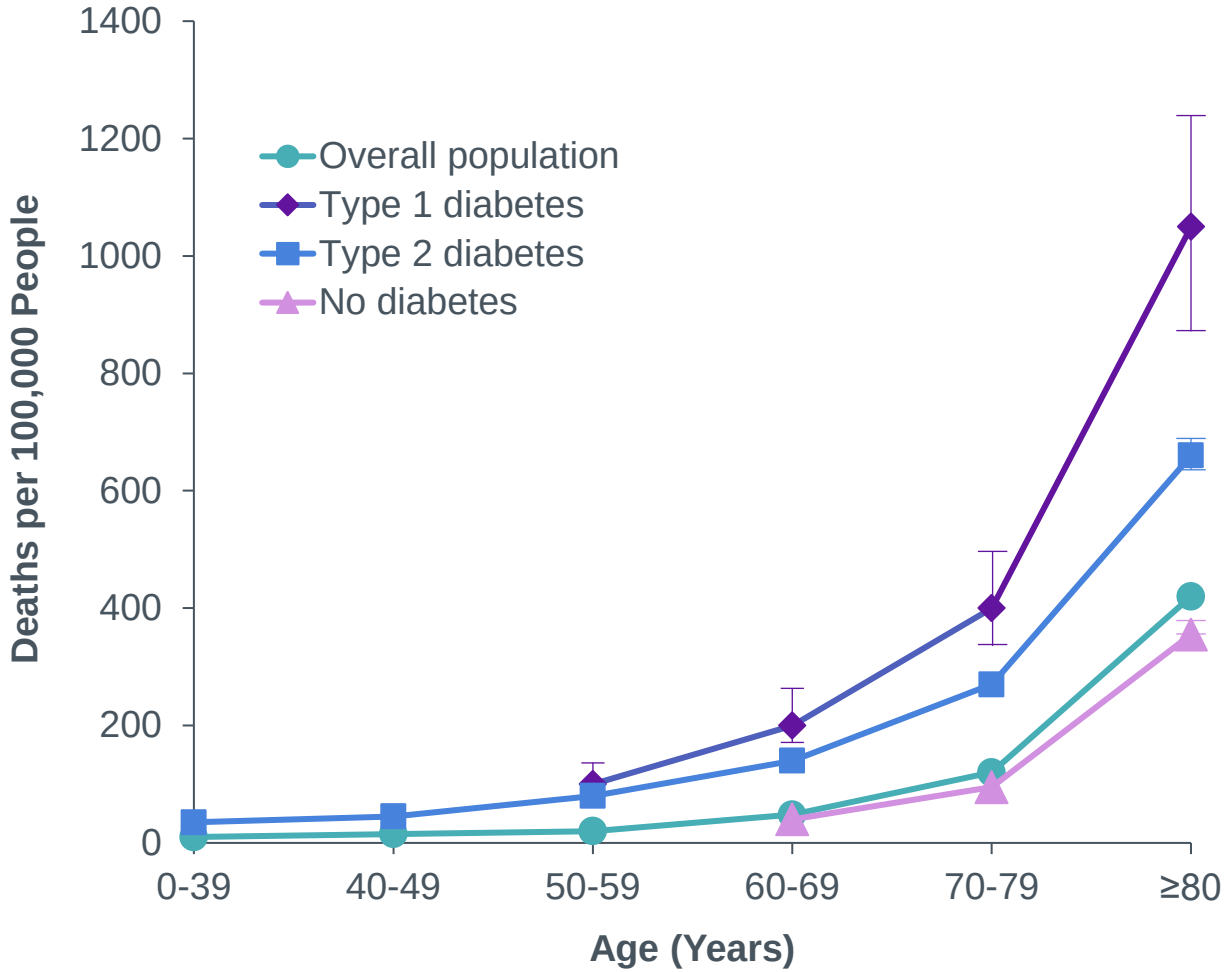


OBSERVATION

Mortality Rate[1]



Deaths[2]



1. Yanez ND, et al. *BMC Public Health*. 2020;20(1):1742. 2. Barron E, et al. *Lancet Diabetes Endocrinol*. 2020;8(10):813-822.

ZINC/VITAMIN D

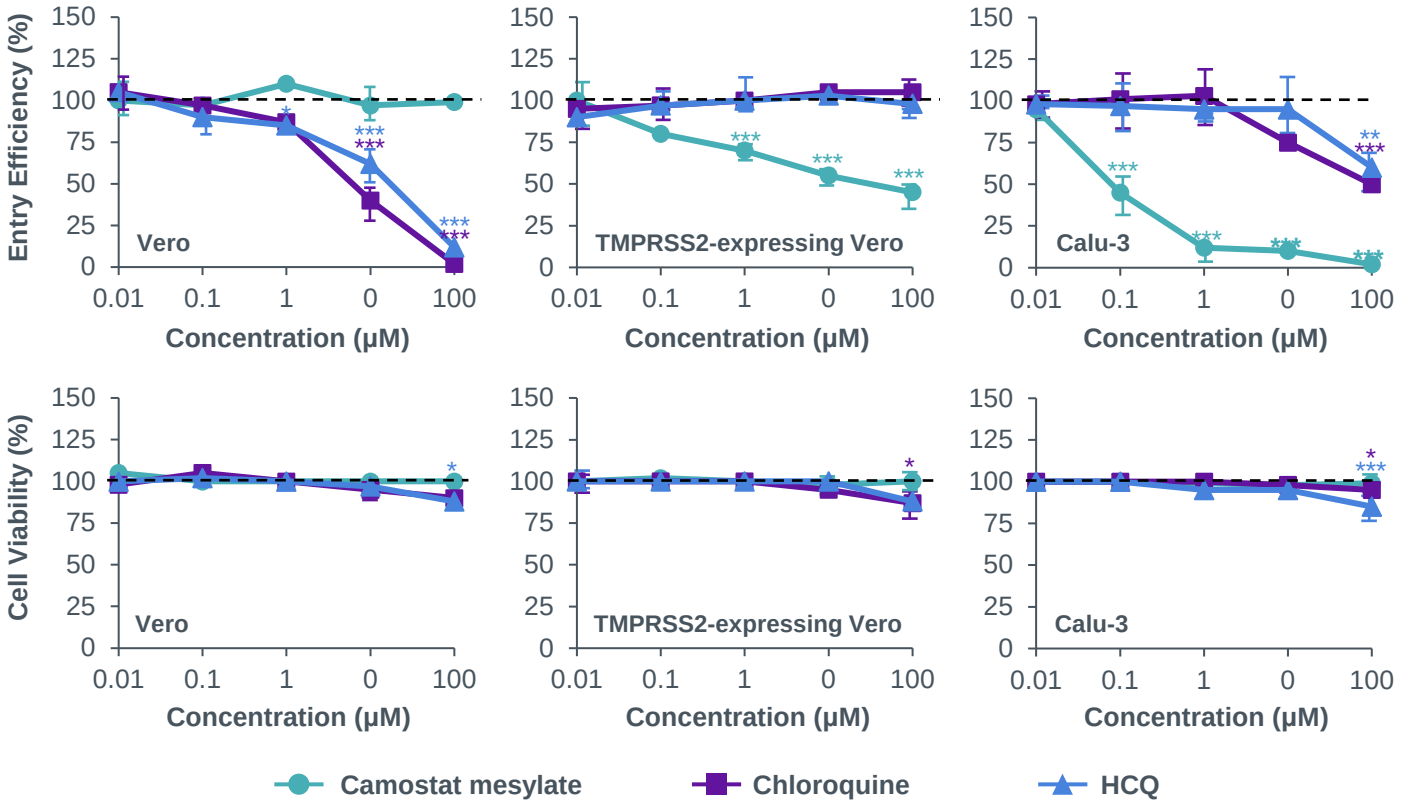
Biologic rationale for each[1,2]

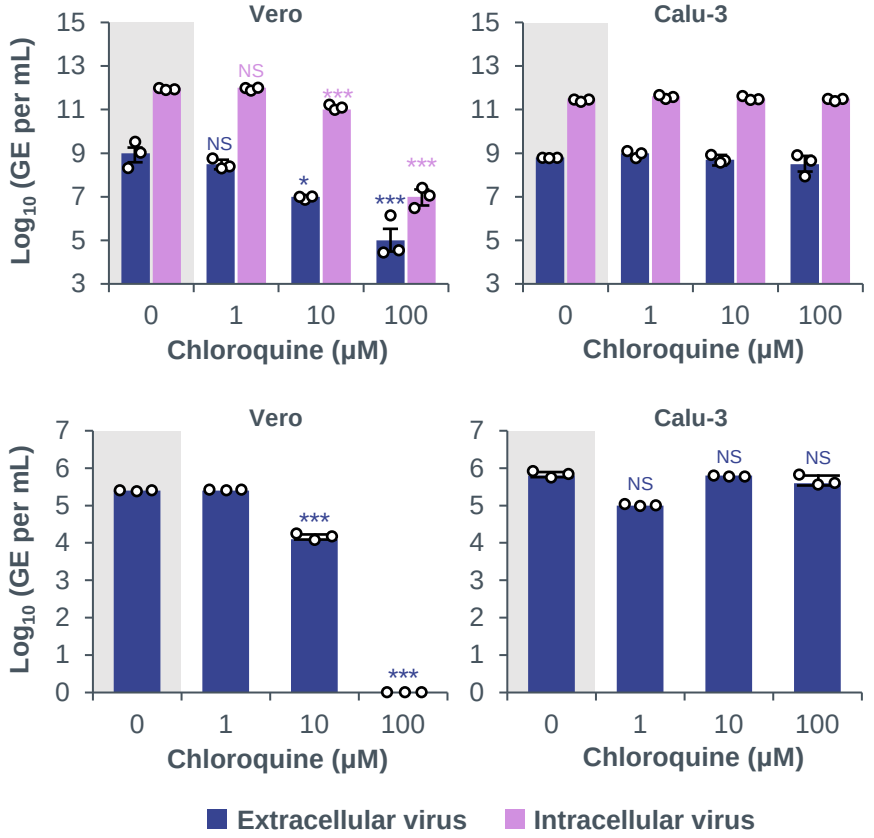
No definitive evidence of safety/effect

1. Joachimiak MP. *PLoS Negl Trop Dis*. 2021;15(1):e0008895. 2. Boulkrane MS, et al. *Front Pharmacol*. 2020;11:604579.

HYDROXYCHLOROQUINE (HCQ)

No Effect in Vivo Models[1]





*P≤0.05. **P≤0.01. ***P≤0.001.

IDSA recommends against HCQ.
Several RCT, multiple, open-label trials.

FDA cautions against use of HCQ for COVID-19 outside of the hospital setting.[2]

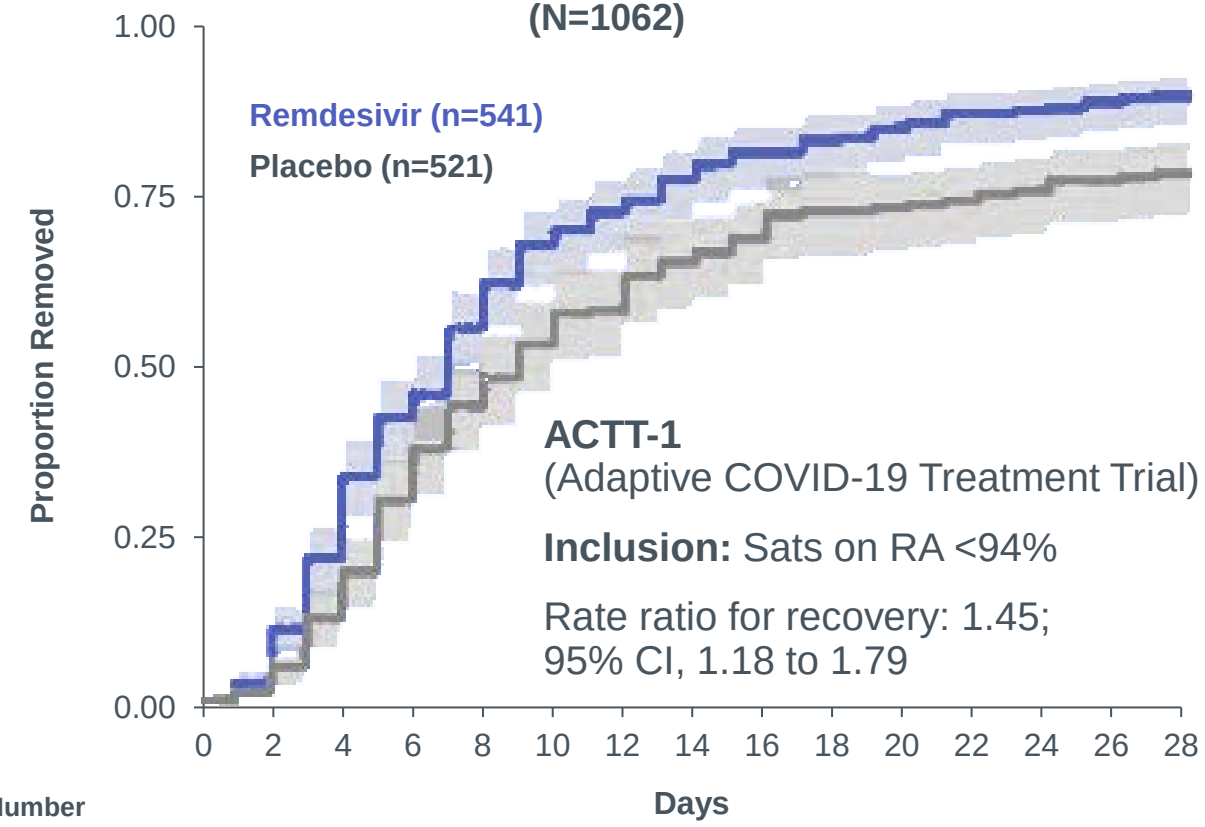
NS=not significant (P>0.05). IDSA=Infectious Diseases Society of America. RCT=randomized controlled trial.

1. Hoffmann M, et al. *Nature*. 2020;585(7826):588-590. 2. https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or. Accessed January 11, 2021.

REMDESIVIR

Patients Receiving Oxygen

(N=1062)



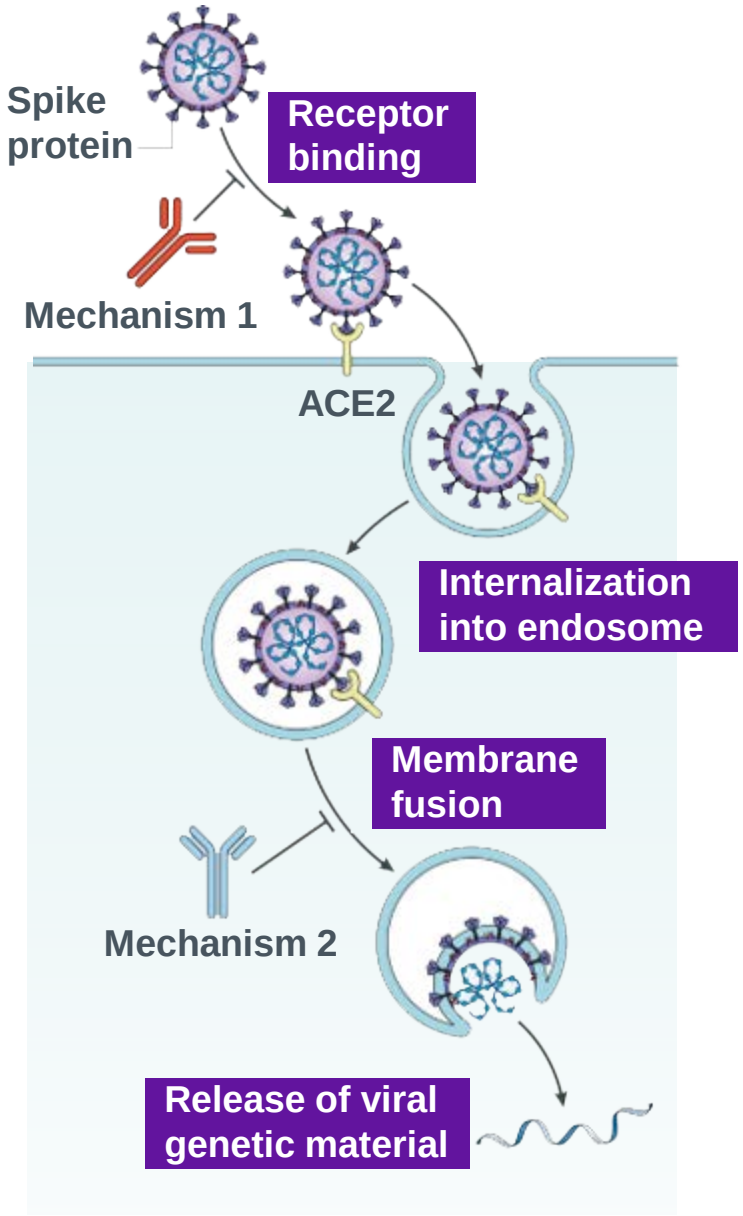
Number at risk															
Remdesivir	232	223	181	132	101	73	62	51	42	38	34	29	28	24	13
Placebo	203	199	175	140	111	93	83	69	62	54	53	51	48	44	28

Severe Disease

(SpO_2) ≤94% on room air requiring supplemental oxygen mechanical ventilation (ECMO)

ECMO=extracorporeal membrane oxygenation.

Beigel JH, et al. *N Engl J Med*. 2020;383(19):1813-1826.



ACE2=angiotensin-converting enzyme. mAb=monoclonal antibody. EUA=emergency use authorization.

1. (Figure) Abraham J. *Nat Rev Immunol*. 2020;20(7):401-403. 2. Abraham J. *Nat Rev Immunol*. 2020;20(7):401-403.

WHAT IS THE BEST, EVIDENCE-BASED APPROACH TO MANAGEMENT?

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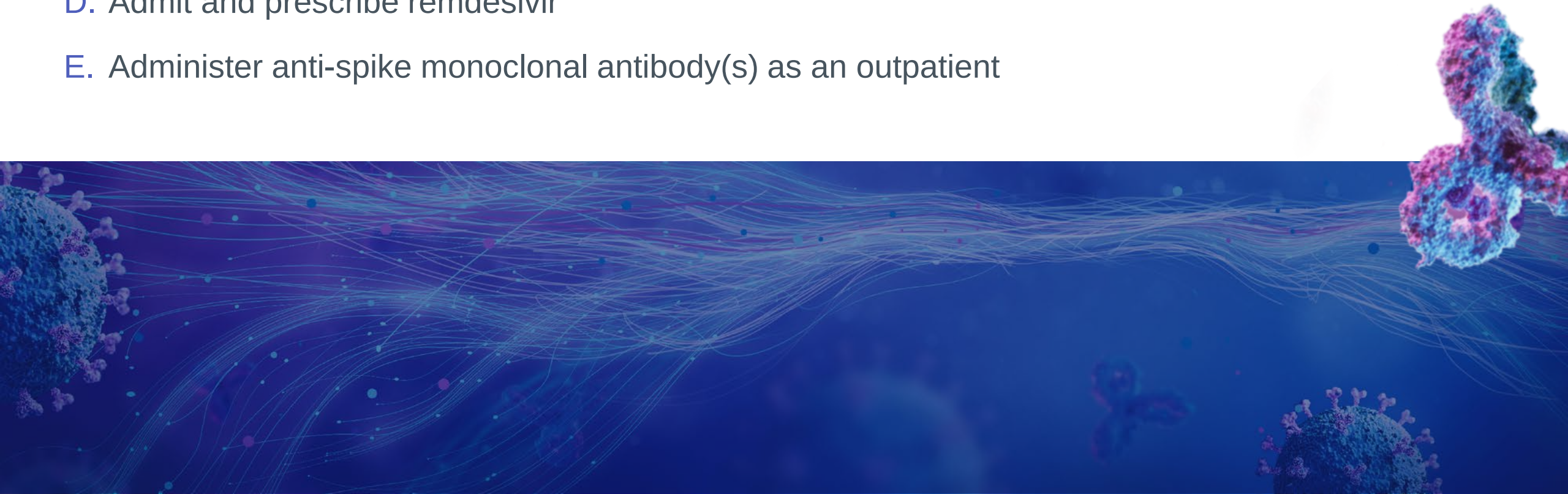


REMINDER

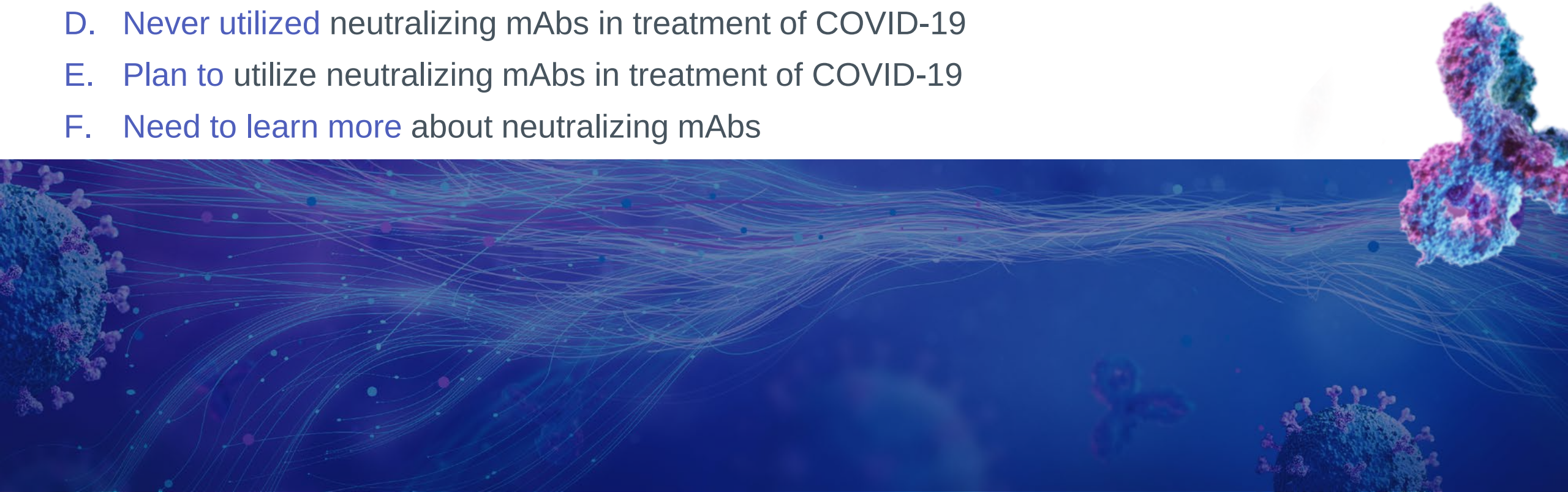
Submit questions for faculty response.

LONG-TERM CARE, COVID CASE, AND DISCUSSION

Chad Worz, PharmD, BCGP, FASCP

WHICH OF THE FOLLOWING STATEMENTS REGARDING NEUTRALIZING mAbs FOR TREATING COVID-19, SUCH AS BAMLANIVIMAB, CASIRIVIMAB/IMDEVIMAB, BEST APPLY TO YOUR PRACTICE?

A. Identify patient with COVID-19 who would benefit from neutralizing mAbs therapy
B. Prescribe neutralizing mAbs
C. Administer neutralizing mAbs
D. Never utilized neutralizing mAbs in treatment of COVID-19
E. Plan to utilize neutralizing mAbs in treatment of COVID-19
F. Need to learn more about neutralizing mAbs



CASE

78-year-old man tested positive for SARS-CoV-2 in a 120-bed skilled nursing facility yesterday.

He was transferred to the facility's COVID unit and placed in isolation.

He is asymptomatic at this time.

PAST MEDICAL AND SURGICAL HISTORY

- Alzheimer's dementia
- Congestive heart failure
- Hypercholesterolemia
- Hypertension

COVID-19 AT LONG-TERM CARE FACILITIES

LESS THAN 1%

of America's population lives in long-term care facilities

but this environment accounts for

37% of all COVID-19 deaths in the United States

Over **1,000,000** cases

Over **130,000** deaths

https://covidtracking.com/data/long-term-care. Accessed January 11, 2021.

MORTALITY IN 65 AND OLDER INDIVIDUALS

An analysis of more than **114,000** COVID-19–associated deaths

from 

to 

found that

78% of the people who died were aged 65 and older

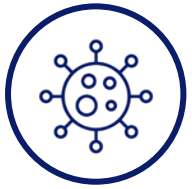
https://www.cdc.gov/mmwr/volumes/69/wr/mm6942e1.htm?s_cid=mm6942e1_e&ACSTrackingID=USCDC_921-DM40574&ACSTrackingLabel=MMWR%20Early%20Release%20-%20Vol.%2069,%20October%2016,%202020&deliveryName=USCDC_921-DM40574. Accessed January 11, 2021.

High risk is defined as patients who meet at least 1 of the following criteria:

BMI ≥35

Chronic kidney disease

Diabetes



Immunosuppressive disease

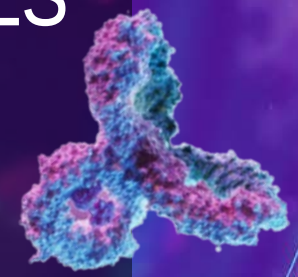
Currently receiving immunosuppressive treatment

≥65 years of age

BMI=body mass index.

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs. Accessed January 11, 2021.

ADMINISTRATION OF mAb THERAPIES FOR COVID TREATMENT



Intravenous administration: a 60-minute infusion with 60 minutes of post-infusion monitoring.

May only be administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs. Accessed January 11, 2021.

RESOURCES FOR ADDITIONAL INFORMATION

Long-Term Care Pharmacy: a pharmacy licensed under applicable state law that is able to provide enhanced pharmacy and clinical services to individuals who require enhanced medication services and reside in a facility.

The American Society of Consultant Pharmacists (www.ASCP.com)

Home Infusion Pharmacy: a pharmacy licensed under applicable state law that is able to provide pharmaceutical infusion therapy services to individuals in an outpatient setting, typically in the person's home or an infusion suite.

The National Home Infusion Association (www.NHIA.com)

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs. Accessed January 11, 2021.

REMINDER

Submit questions for faculty response.

EVIDENCE OF THERAPEUTIC EFFECT OF MONOCLONALS FOR COVID

Andrew D. Badley, MD, FRCP(C), FACP, FIDSA

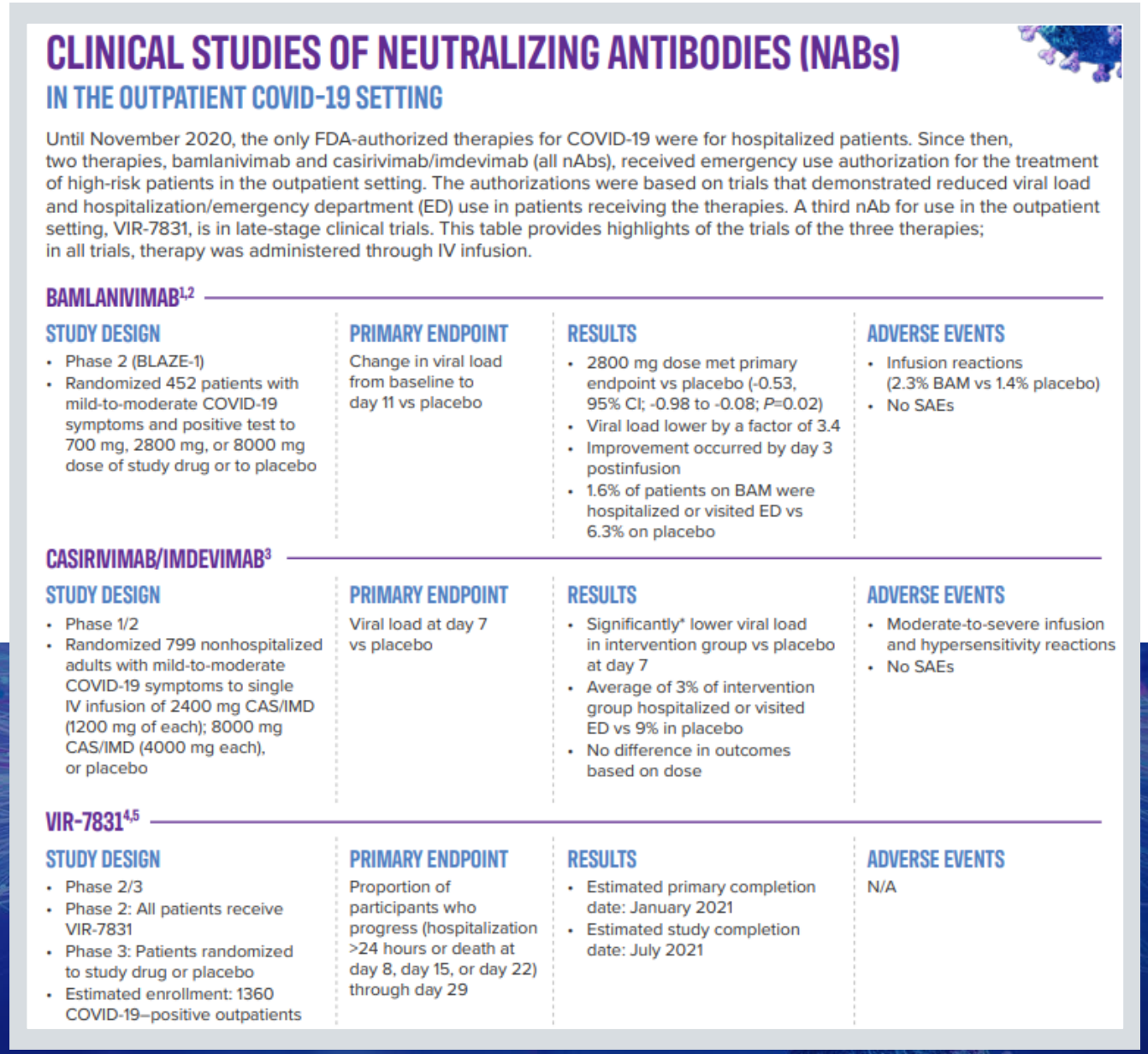
DID YOU REVIEW THE PRE-READ PROVIDED TO REGISTRANTS BEFORE THE BROADCAST?

A. Yes

B. No

C. Not sure

Note: The pre-read will continue to be available in the Additional Resources section.



CLINICAL STUDIES OF NEUTRALIZING ANTIBODIES (NABs)

IN THE OUTPATIENT COVID-19 SETTING

Until November 2020, the only FDA-authorized therapies for COVID-19 were for hospitalized patients. Since then, two therapies, bamlanivimab and casirivimab/imdevimab (all nAbs), received emergency use authorization for the treatment of high-risk patients in the outpatient setting. The authorizations were based on trials that demonstrated reduced viral load and hospitalization/emergency department (ED) use in patients receiving the therapies. A third nAb for use in the outpatient setting, VIR-7831, is in late-stage clinical trials. This table provides highlights of the trials of the three therapies; in all trials, therapy was administered through IV infusion.

BAMLANIVIMAB[1,2]

STUDY DESIGN	PRIMARY ENDPOINT	RESULTS	ADVERSE EVENTS
• Phase 2 (BLAZE-1) • Randomized 452 patients with mild-to-moderate COVID-19 symptoms and positive test to 700 mg, 2800 mg, or 8000 mg dose of study drug or to placebo	Change in viral load from baseline to day 11 vs placebo	• 2800 mg dose met primary endpoint vs placebo (-0.53, 95% CI; -0.98 to -0.08; *P*=0.02) • Viral load lower by a factor of 3.4 • Improvement occurred by day 3 postinfusion • 1.6% of patients on BAM were hospitalized or visited ED vs 6.3% on placebo	• Infusion reactions (2.3% BAM vs 1.4% placebo) • No SAEs

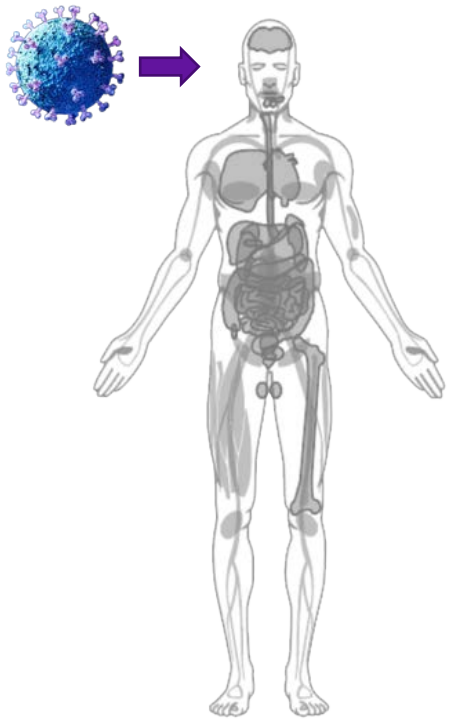
CASIRIVIMAB/IMDEVIMAB[3]

STUDY DESIGN	PRIMARY ENDPOINT	RESULTS	ADVERSE EVENTS
• Phase 1/2 • Randomized 799 nonhospitalized adults with mild-to-moderate COVID-19 symptoms to single IV infusion of 2400 mg CAS/IMD (1200 mg of each); 8000 mg CAS/IMD (4000 mg each), or placebo	Viral load at day 7 vs placebo	• Significantly* lower viral load in intervention group vs placebo at day 7 • Average of 3% of intervention group hospitalized or visited ED vs 9% in placebo • No difference in outcomes based on dose	• Moderate-to-severe infusion and hypersensitivity reactions • No SAEs

VIR-7831[4,5]

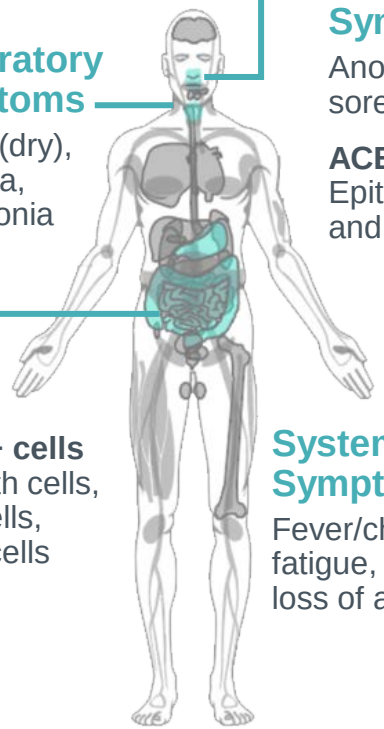
STUDY DESIGN	PRIMARY ENDPOINT	RESULTS	ADVERSE EVENTS
• Phase 2/3 • Phase 2: All patients receive VIR-7831 • Phase 3: Patients randomized to study drug or placebo • Estimated enrollment: 1360 COVID-19–positive outpatients	Proportion of participants who progress (hospitalization >24 hours or death at day 8, day 15, or day 22) through day 29	• Estimated primary completion date: January 2021 • Estimated study completion date: July 2021	N/A

PATHOGENESIS FOLLOWS ACE2 RECEPTOR EXPRESSION PROFILES



ASYMPTOMATIC

Variable incubation period following SARS-CoV-2 infection (days 0-5)



Respiratory Symptoms

Cough (dry), dyspnea, pneumonia

Oropharynx Symptoms

Anosmia, dysgeusia, sore throat, rhinorrhea

ACE2+TMPRSS2+ cells

Epithelial cells (nasal cavity and respiratory tract)

GI Symptoms

Nausea, diarrhea, enteritis

ACE2+TMPRSS2+ cells

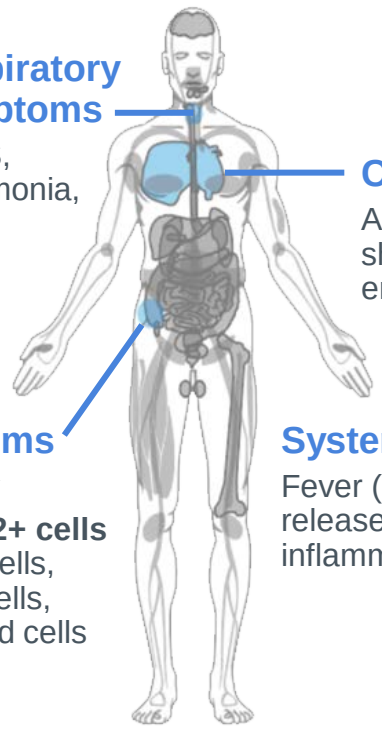
Enterocytes, Paneth cells, enteroendocrine cells, stem cells, goblet cells

Systemic Symptoms

Fever/chills, fatigue, myalgias, loss of appetite

MILD/MODERATE DISEASE

Disease manifestation (days 2-14)



Respiratory Symptoms

ARDS, pneumonia, cough

Cardiac Symptoms

Arrhythmia, cardiogenic shock, myocarditis, embolic events

Renal Symptoms

Acute renal injury

ACE2+TMPRSS2+ cells

Pelvis epithelial cells, proximal tubule cells, type A intercalated cells

Systemic Symptoms

Fever (persistent), cytokine release syndrome-like inflammatory response

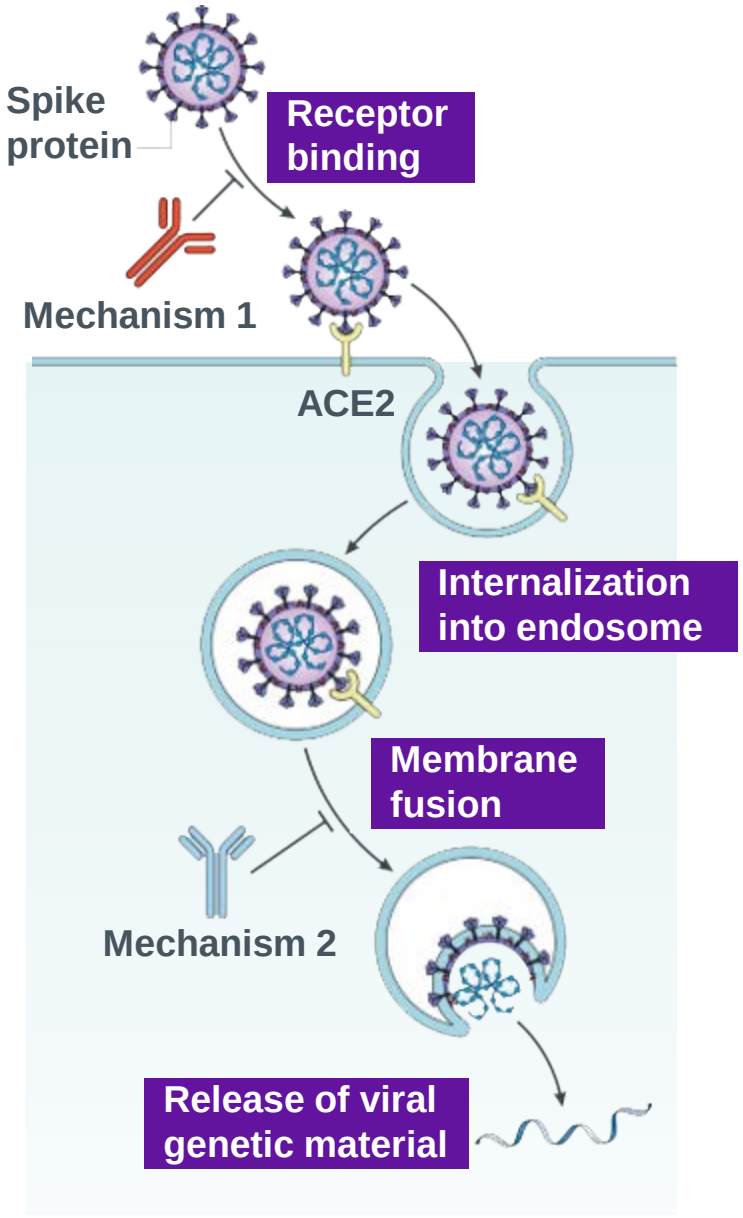
SEVERE/CRITICAL DISEASE

Variable depending on degree and exacerbation and comorbid conditions

VIRAL REPLICATION

INFLAMMATION

TMPRSS2=transmembrane serine protease. ARDS=acute respiratory distress syndrome.



SARS-CoV-2 correlative evidence

- Convalescent plasma
  - High titer plasma, mild illness—CP 16% pneumonia, vs placebo 31% (*P*=0.03)[2]
  - Unscreened plasma, pneumonia—no effect[3]
- Recovery coincident with acquisition of mAb
  - Rapid recovery from symptomatic disease associated with robust mAb response[4]

CP=convalescent plasma.

1. (Figure) Abraham J. *Nat Rev Immunol*. 2020;20(7):401-403. 2. Libster R, et al. *N Engl J Med*. 2021. 3. Simonovich VA, et al. *N Engl J Med*. 2020. 4. Chen Y, et al. *Cell*. 2020;183(6):1496-1507.e1416.

BAMLANIVIMAB: CLINICAL TRIAL

101 patients were enrolled and assigned to 700 mg of LY-CoV555 monotherapy

107 patients were enrolled and assigned to 2800 mg of LY-CoV555 monotherapy

101 patients were enrolled and assigned to 7000 mg of LY-CoV555 monotherapy

143 patients were enrolled and assigned to placebo

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

PATIENT CHARACTERISTICS AT BASELINE*

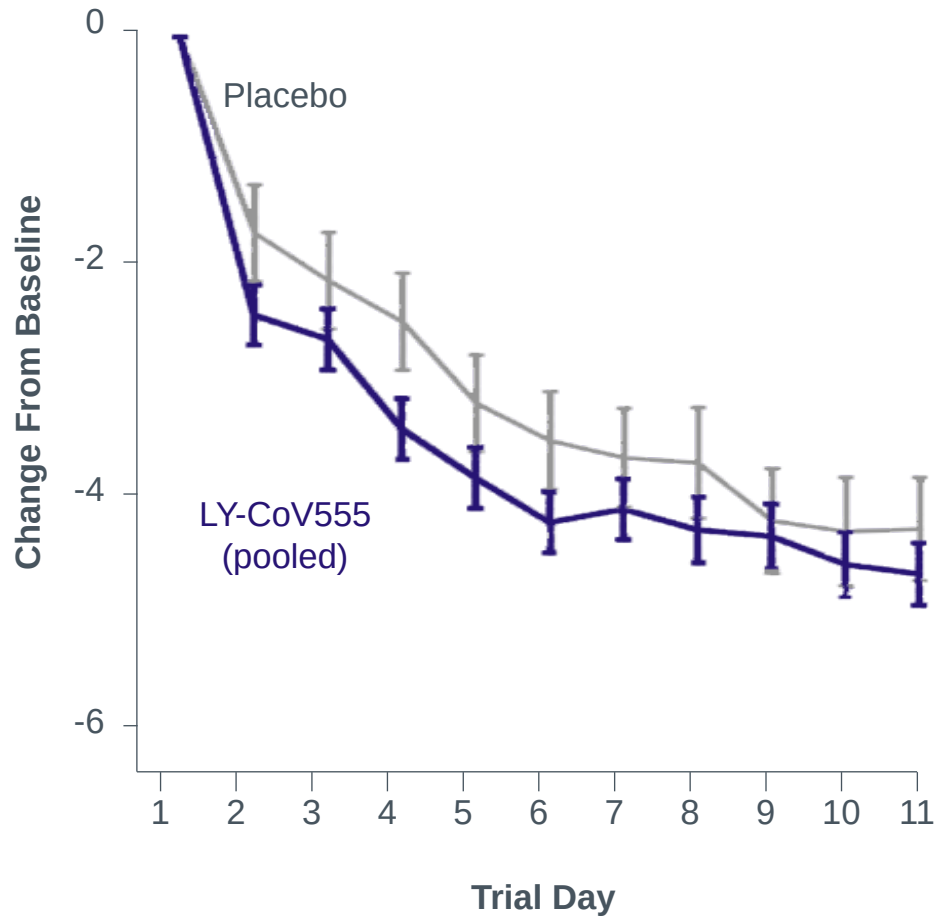
Characteristic	LY-CoV555 (n=309)	Placebo (n=143)
Age		
Median (range)—years	45 (18-86)	46 (18-77)
≥65 years old—number (%)	33 (10.7)	20 (14.0)
Female—number (%)	171 (55.3)	78 (54.5)
Race or ethnic group—number/total number (%)†		
White	269/305 (88.2)	120/118 (87.0)
Hispanic or Latino	135/309 (43.7)	63/143 (44.1)
Black	22/305 (7.2)	7/138 (5.1)
BMI‡		
Median	29.4	29.1
≥30 to <40—number/total number (%)	112/304 (36.8)	56/139 (40.3)
≥40—number/total number (%)	24/304 (7.9)	9/139 (6.5)
Risk factors for severe COVID-19—number (%)§	215 (69.6)	95 (66.4)
Disease status—number (%)		
Mild	232 (75.1)	113 (79.0)
Moderate	77 (24.9)	30 (21.0)
Median number of days since onset of symptoms	4.0	4.0
Mean viral load—Ct value‖	23.9	23.8

*COVID-19 denotes coronavirus disease 2019. †Race or ethnic group was reported by the patients, who could choose more than 1 category. ‡BMI is the weight in kilograms divided by the square of the height in meters. §Risk factors were an age of 65 years or older, a BMI of 35 or more, or at least one coexisting illness in certain prespecified categories. ‖Ct denotes the cycle threshold of the reverse-transcriptase–polymerase-chain-reaction assay.

Chen P, et al. *N Engl J Med*. 2020.

BAMLANIVIMAB: CLINICAL TRIAL (CONT.)

HOSPITALIZATION*			
Key Secondary Outcome	LY-CoV555 (n=309)	Placebo (n=143)	Incidence
	Number of Patients/ Total Number		%
Hospitalization		9/143	6.3
700 mg	1/101		1.0
2800 mg	2/107		1.9
7000 mg	2/101		2.0
Pooled doses	5/309		1.6



	Delta Value (95% CI)
Day 2	-0.79 (-1.35 to -0.24)
Day 3	-0.57 (-1.12 to -0.01)
Day 4	-1.04 (-1.60 to -0.49)
Day 5	-0.73 (-1.28 to -0.17)
Day 6	-0.79 (-1.35 to -0.23)
Day 7	-0.50 (-1.06 to 0.07)
Day 8	-0.65 (-1.28 to -0.02)
Day 9	-0.15 (-0.75 to 0.45)
Day 10	-0.32 (-0.94 to 0.29)
Day 11	-0.44 (-1.02 to 0.15)

*Data for patients who presented to the emergency department are included in this category.

Chen P, et al. *N Engl J Med*. 2020.

CASIRIVIMAB/IMDEVIMAB: CLINICAL TRIAL

306 patients were assessed for eligibility

31 were excluded
- 29 were excluded at screening
- 2 withdrew

275 underwent randomization
- 269 received REGN-CoV2 or placebo
- 6 did not receive REGN-CoV2 or placebo
- 5 withdrew
- 1 discontinued due to randomization error

93 were assigned to receive placebo
- 1 currently in ongoing trial
- 4 discontinued due to being lost to follow-up

88 completed the trial

92 were assigned to receive REGN-CoV2, 2.4 g
- 3 currently in ongoing trial
- **9 discontinued** (1 withdrawn by sponsor, 3 lost to follow-up, 4 withdrew, 1 had unknown reason)

80 completed the trial

90 were assigned to receive REGN-CoV2, 8.0 g
- 2 currently in ongoing trial
- **4 discontinued** (1 lost to follow-up, 3 withdrew)

84 completed the trial

Weinreich DM, et al. *N Engl J Med*. 2020.

CASIRIVIMAB/IMDEVIMAB: CLINICAL TRIAL (CONT.)

DEMOGRAPHIC AND BASELINE MEDICAL CHARACTERISTICS*

Characteristic	REGN-COV2 2.4 g (n=92)	REGN-COV2 8.0 g (n=90)	REGN-COV2 Combined (n=182)	Placebo (n=93)	Total (N=275)
Median age (IQR)—years†	43.0 (33.5-51.0)	44.0 (36.0-53.0)	43.0 (35.0-52.0)	45.0 (34.0-54.0)	44.0 (35.0-52.0)
Male—number (%)	46 (50)	38 (42)	84 (46)	50 (54)	134 (49)
Hispanic or Latino—number (%)‡	52 (57)	55 (61)	107 (59)	46 (49)	153 (56)
Race—number (%)‡					
White	74 (80)	78 (87)	152 (84)	72 (77)	224 (81)
Black or African American	15 (16)	6 (7)	21 (12)	14 (15)	35 (13)
Asian	0	1 (1)	1 (1)	2 (2)	3 (1)
American Indian or Alaska Native	0	0	0	2 (2)	2 (1)
Unknown	0	1 (1)	1 (1)	2 (2)	3 (1)
Not reported	3 (3)	4 (4)	7 (4)	1 (1)	8 (3)
Median weight (IQR)—kg†	85.65 (72.20-97.10)	86.25 (72.60-98.30)	86.10 (72.60-97.30)	83.90 (72.90-97.70)	86.00 (72.60-97.50)
BMI§	30.39±6.578	30.63±7.216	30.51±6.874	29.73±7.149	30.25±6.961
Obesity—number (%)‖	39 (42)	42 (47)	81 (45)	34 (37)	115 (42)

DEMOGRAPHIC AND BASELINE MEDICAL CHARACTERISTICS* (CONT.)

Characteristic	REGN-COV2 2.4 g (n=92)	REGN-COV2 8.0 g (n=90)	REGN-COV2 Combined (n=182)	Placebo (n=93)	Total (N=275)
Baseline viral load in nasopharyngeal swab (raw values)					
Number of patients	84	83	167	91	258
Mean viral load—copies/mL	16,080,000± 28,810,000	19,170,000± 29,120,000	17,620,000± 28,420,000	12,950,000± 25,620,000	15,970,000± 27,510,000
Baseline viral load in nasopharyngeal swab (Log_{10} scale)					
Number of patients	84	83	167	91	258
Mean viral load—copies/mL	5.04±2.495	5.00±2.527	5.02±2.503	4.67±2.366	4.90±2.457
Mean viral load (range)—log_{10} copies/mL	5.41 (0.0-7.9)	5.29 (0.0-7.9)	5.30 (0.0-7.9)	4.70 (0.0-7.9)	5.19 (0.0-7.9)
Positive baseline qualitative RT-PCR—number (%)¶	73 (79)	74 (82)	147 (81)	81 (87)	228 (83)
Baseline serum C-reactive protein level					
Number of patients	87	86	173	92	265
Mean level—mg/L	3.0 (0.2-239.7)	4.8 (0.1-138.7)	3.7 (0.1-239.7)	4.8 (0.1-232.0)	4.1 (0.1-239.7)
Baseline serum antibody status—number (%)					
Negative	41 (45)	39 (43)	80 (44)	33 (35)	113 (41)
Positive	37 (40)	39 (43)	76 (42)	47 (51)	123 (45)
Unknown#	14 (15)	12 (13)	26 (14)	13 (14)	39 (14)
Median time from symptom onset to randomization (range)—days	3.5 (0-7)	3.0 (0-8)	3.0 (0-8)	3.0 (0-8)	3.0 (0-8)
At least one risk factor for hospitalization—number (%)**	57 (62)	61 (68)	118 (65)	58 (62)	176 (64)

Percentages may not total 100 because of rounding.

IQR=interquartile range. RT-PCR=reverse-transcriptase polymerase chain reaction.

*Plus-minus values are means±SD. †The IQR is defined as quartile 1 to quartile 3. ‡Race and ethnic group were reported by the patients. §BMI is the weight in kilograms divided by the square of height in meters. ‖Obesity is defined as a BMI >30. ¶A positive result was defined as a viral load greater than or equal to the lower limit of detection (714 copies/mL [2.85 log_{10} copies/mL]). #An unknown serum antibody status indicates that the status could not be evaluated or that the results were borderline. **Risk factors for hospitalization include an age or >50 years, obesity, cardiovascular disease (including hypertension), chronic lung disease (including asthma), chronic metabolic disease (including diabetes), chronic kidney disease (including receipt of dialysis), chronic liver disease, and immunocompromise (immunosuppression or receipt of immunosuppressants.)

Weinreich DM, et al. *N Engl J Med*. 2020.

CASIRIVIMAB/IMDEVIMAB: CLINICAL TRIAL (CONT.)

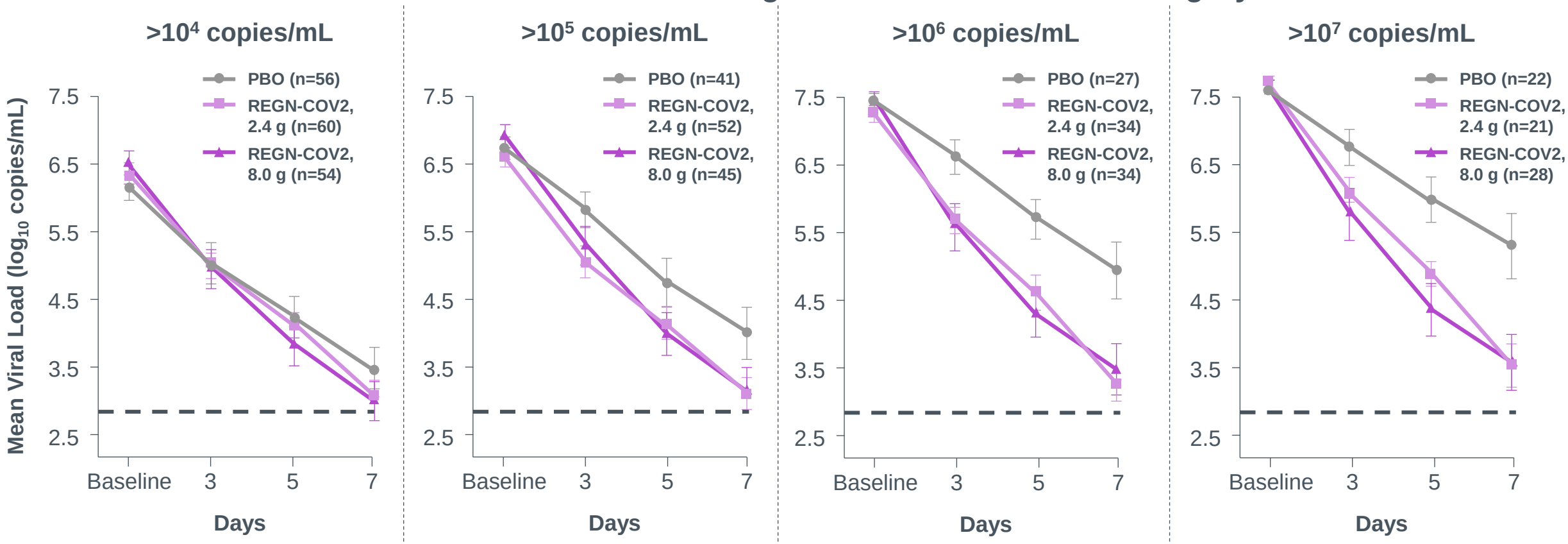
KEY VIROLOGIC AND CLINICAL ENDPOINTS*				
	REGN-COV2			
Endpoint	2.4 g	8.0 g	Combined	Placebo
At least one COVID-19–related, medically attended visit within 29 days¶				
Full analysis set				
Number of patients	92	90	182	93
Patients with ≥1 visit within 29 days—number (%)	3 (3)	3 (3)	6 (3)	6 (6)
Difference vs placebo—percentage points	-3	-3	-3	—
95% CI	-18 to 11	-18 to 11	-16 to 9	—
Baseline serum antibody status: negative				
Number of patients	41	39	80	33
Patients with ≥1 visit within 29 days—number (%)	2 (5)	3 (8)	5 (6)	5 (15)
Difference vs placebo—percentage points	-10	-8	-9	—
95% CI	-32 to 13	-30 to 16	-29 to 11	—
Baseline serum antibody status: positive				
Number of patients	37	39	76	47
Patients with ≥1 visit within 29 days—number (%)	1 (3)	0	1 (1)	1 (2)
Difference vs placebo—percentage points	1	-2	-1	—
95% CI	-21 to 22	-23 to 19	-19 to 17	—
Baseline serum antibody status: unknown§				
Number of patients	14	12	26	13
Patients with ≥1 visit within 29 days—number (%)	0	0	0	0

*Plus-minus values are means±SD. †The time-weighed average change in viral load was based on an analysis-of-covariance model with treatment group, risk factor, and baseline serum antibody status as fixed effects and baseline viral load and treatment group-by-baseline viral load as covariates. Confidence intervals were not adjusted for multiplicity. ‡The modified full analysis set excluded patients who tested negative SARS-CoV-2 by qualitative reverse-transcriptase polymerase chain reaction at baseline. §An unknown serum antibody status indicates that the status could not be evaluated or that the results were borderline. ¶Confidence intervals for the difference (REGN-COV2 minus placebo) were based on the exact method and were not adjusted for multiplicity.

Weinreich DM, et al. *N Engl J Med*. 2020.

CASIRIVIMAB/IMDEVIMAB: CLINICAL TRIAL (CONT.)

Viral Load Over Time According to Baseline Viral Load Category



Difference in Change From Baseline, Day 7

	>10⁴ copies/mL		>10⁵ copies/mL		>10⁶ copies/mL		>10⁷ copies/mL	
	TWA LS Mean	Mean	TWA LS Mean	Mean	TWA LS Mean	Mean	TWA LS Mean	Mean
2.4 g vs PBO	-0.36	-0.64	-0.59	-0.83	-0.81	-1.46	-1.03	-1.84
2.4 g vs PBO	-0.36	-0.64	-0.75	-1.12	-1.14	-1.54	-1.32	-1.75

Weinreich DM, et al. *N Engl J Med*. 2020.

BMI ≥35

Chronic kidney disease

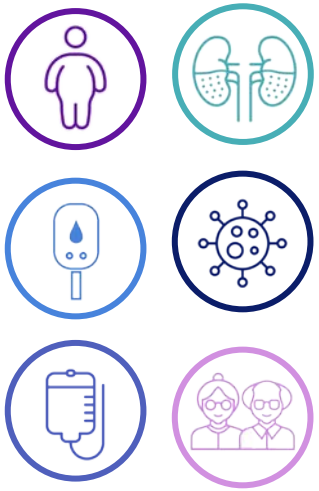
Diabetes

Immunosuppressive disease

Currently receiving immunosuppressive treatment

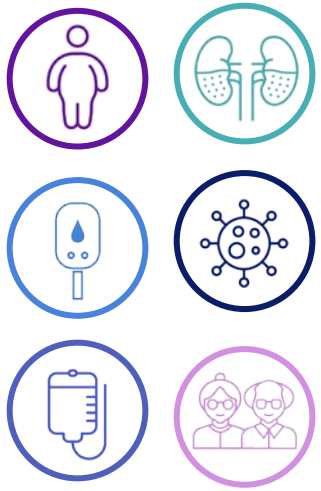
≥65 years of age

BAMLANIVIMAB[1]



- High risk
- Are ≥55 years of age AND have cardiovascular disease, OR hypertension, OR chronic obstructive pulmonary disease/other chronic respiratory disease
- Are 12-17 years of age AND have BMI ≥85th percentile OR sickle cell disease, OR congenital or acquired heart disease, OR neurodevelopmental disorders, a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR asthma, reactive airway or other chronic respiratory disease that requires daily medication for control

CASIRIVIMAB/IMDEVIMAB[2]



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1. https://www.covid19.lilly.com/assets/pdf/bamlanivimab/lilly-antibodies-playbook.pdf. Accessed January 11, 2021.
2. https://www.regeneron.com/casirivimabimdevimab. Accessed January 11, 2021.

UNDERUSE OF THERAPIES

CHALLENGES TO OUTPATIENT ADMINISTRATION OF mAb

Existing infusion centers have sick patients

Challenge to identify those at risk of progression

Difficulty identifying patients within therapeutic window

Hospital staffing shortages

Relatively limited evidence of effect

Patient transportation

POSSIBLE SOLUTIONS

Dedicated, COVID-specific infusion centers in hospital/clinic settings

Mobile units

Commercial infusion centers

THANK YOU!

Slides, including explanations to the pre-/post-test questions, can be found in the PDF resource associated with this activity.

Q&A


PRE-/POST-TEST QUESTIONS

CASE

69-year-old woman presenting after she tested positive for SARS-CoV-2 on December 27.

Her initial symptoms were cough, pleuritic chest pain, and post-tussive vomiting that worsened on the day of diagnosis.

She also reports poor appetite. She denies diarrhea, dysuria, hematuria, sore throat, or rhinorrhea.

PAST MEDICAL AND SURGICAL HISTORY

- DM2
- COPD
- Iron deficiency anemia
- Hypertension

LABS

- WBC of 3.1, with leukopenia 0.86
- D-dimer of 564, normal creatinine
- ALT of 65 an AST of 59, C-reactive of 50.1, ferritin of 564
- CXR normal

Hemodynamically stable, afebrile, SpO_2 of 95% on RA.

Physical exam was unremarkable.

CURRENT EVIDENCE SUPPORTS THE USE OF WHICH OUTPATIENT THERAPY FOR HIGH-RISK PATIENTS WITH COVID-19?

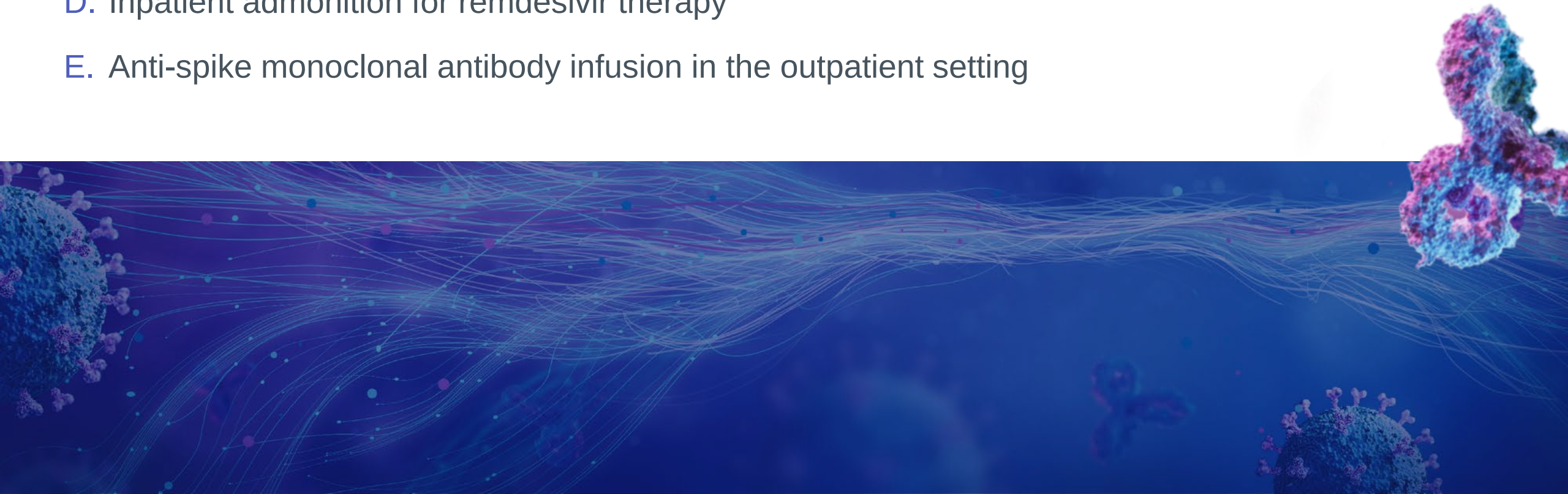
A. Observation

B. Zinc and/or vitamin D

C. Hydroxychloroquine

D. Inpatient admonition for remdesivir therapy

E. Anti-spike monoclonal antibody infusion in the outpatient setting



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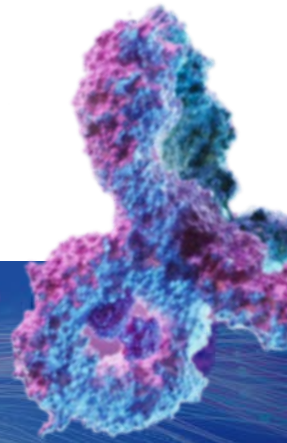


Rationale: The FDA has issued emergency use authorization (EUA) for monoclonal antibodies to treat high-risk patients with COVID-19 in the outpatient setting.

Food and Drug Administration. Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19. Published November 21, 2020. Accessed December 17, 2020.

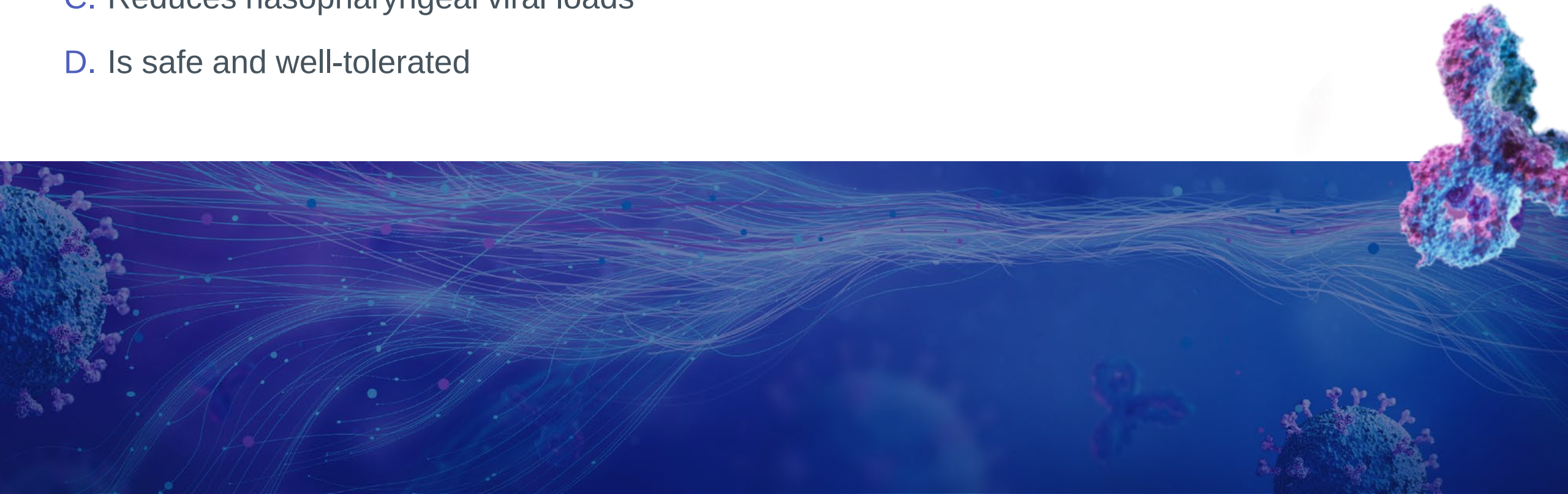
WHICH OF THE FOLLOWING WAS NOT DEMONSTRATED IN THE CLINICAL TRIALS FOR BAMLANIVIMAB BAMLANIVIMAB (NO LONGER BEING DISTRIBUTED) AND CASIRIVIMAB/IMDEVIMAB?

A. Reduces hospitalization and emergency room visits

B. Renders infected patients noninfectious

C. Reduces nasopharyngeal viral loads

D. Is safe and well-tolerated



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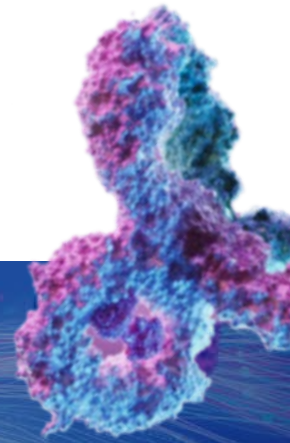


Rationale: Clinical trials for the monoclonal antibodies showed they reduced hospitalizations and emergency room visits as well as nasopharyngeal viral loads. They were also found to be safe and well-tolerated. However, there was no evidence in these trials that they reduced transmission.

Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. *NEJM*. 2020. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. *NEJM*. 2020.

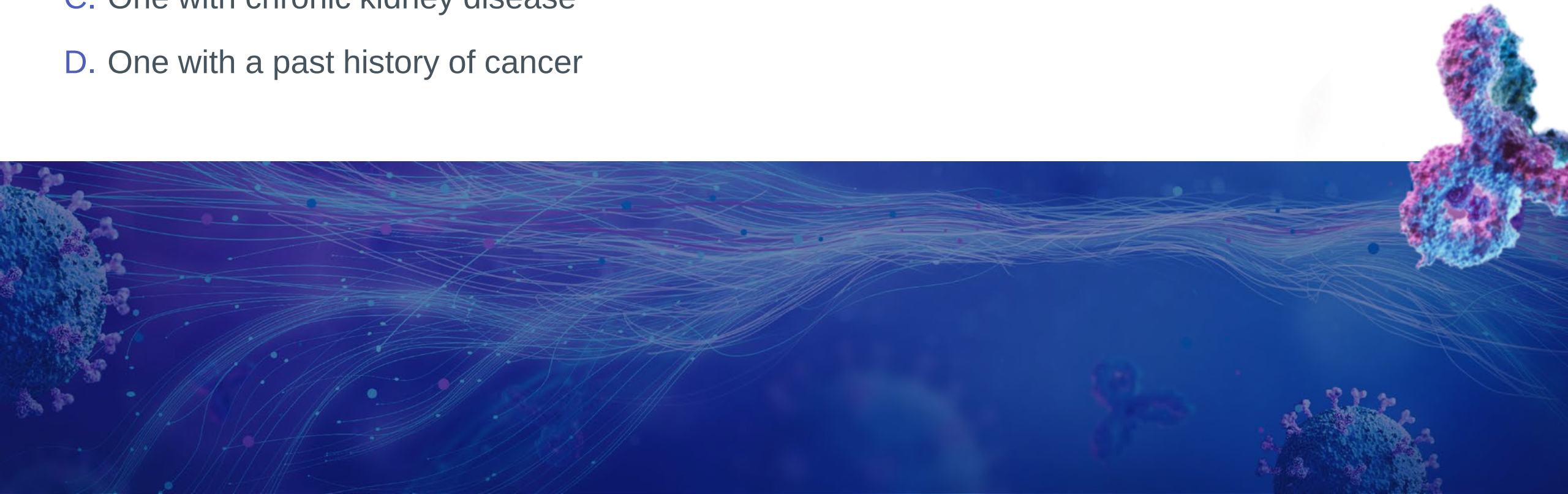
WHICH PATIENT WOULD NOT QUALIFY FOR OUTPATIENT mAb TREATMENT FOR SARS-CoV-2 BASED ON THE CURRENT EUAs?

A. One age >65 years

B. One with diabetes mellitus

C. One with chronic kidney disease

D. One with a past history of cancer



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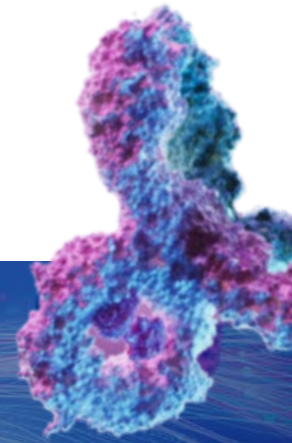

Rationale: The EUA for these monoclonal antibodies define high risk as patients who meet at least one of the following criteria: BMI ≥35 (25 in updated criteria), chronic kidney disease, diabetes, immunosuppressive disease, currently receiving immunosuppressive treatment, ≥65 years of age, ≥55 years of age AND have cardiovascular disease, OR hypertension, OR chronic obstructive pulmonary disease/other chronic respiratory disease, 12-17 years of age AND have BMI ≥85th percentile for their age and gender based on CDC growth charts, OR sickle cell disease, OR congenital or acquired heart disease, OR neurodevelopmental disorders, for example, cerebral palsy, OR a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Food and Drug Administration. Fact Sheet For Health Care Providers Emergency Use Authorization (EUA) Of Bamlanivimab. https://www.fda.gov/media/143603/download. Published December 2020. Accessed January 5, 2021.
Food and Drug Administration. Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab. Available at: https://www.fda.gov/media/143605/download. Accessed January 17, 2021.

PATIENT RECEIVING mAb TREATMENT FOR COVID-19 INFECTION MUST BE MONITORED FOR HOW LONG AFTER INFUSION?

A. 15 minutes

B. 30 minutes

C. 60 minutes

D. 2 hours

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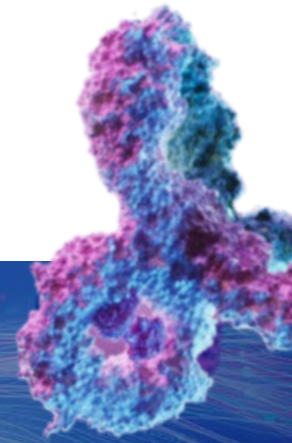

Rationale: The EUA for these medications requires that patients be monitored for 60 minutes after receiving their infusion and that the infusion is administered in settings in which healthcare providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS).

Food and Drug Administration. Fact Sheet For Health Care Providers Emergency Use Authorization (EUA) Of Bamlanivimab. https://www.fda.gov/media/143603/download. Published December 2020. Accessed January 5, 2021.
Food and Drug Administration. Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab. Available at: https://www.fda.gov/media/143605/download. Accessed January 17, 2021.

CASE

78-year-old man tested positive for SARS-CoV-2 in a 120-bed skilled nursing facility yesterday.

He was transferred to the facility's COVID unit and placed in isolation.

He is asymptomatic at this time.

PAST MEDICAL AND SURGICAL HISTORY

- Alzheimer's dementia
- Congestive heart failure
- Hypercholesterolemia
- Hypertension

THE FACILITY COMMONLY ADMINISTERS INTRAVENOUS MEDICATIONS. WHAT SPECIAL TRAINING SHOULD NURSES ACQUIRE FOR ADMINISTERING THE MEDICATION?

A. No special training is needed beyond reading the emergency use authorization

B. A certification in intravenous therapy

C. A continuing education course on the products

D. Direct training from the department of health