CARE Outpatient Treatment of COVID-19





FACULTY AND DISCLOSURES



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Advisory Board AbbVie, Flambeau Diagnostics

Ownership Interest (Excluding Diversified Mutual Funds) nference, Splissen Therapeutics, Zentalis

Other

Data Safety and Monitoring Board— Corvus, Equillium



Chad Worz, PharmD, BCGP, FASCP

Chief Executive, American Society of Consultant Pharmacists Alexandria, Virginia 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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WE ENCOURAGE INTERACTION

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



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, SpO₂ of 95% on RA. Physical exam was unremarkable.

DM2=myotonic dystrophy type. COPD=chronic obstructive pulmonary disease. SpO₂=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







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

NIH U.S. National Library of Medicine Find S ClinicalTrials.gov	NIH U.S. National Library of Medicine ClinicalTrials.gov Find S
Home > Search Results	Home > Search Results
Modify Search Start Over	Modify Search Start Over
45 Studies found for: Zinc Covid19 Also searched for COVID and SARS-CoV-2 . <u>See Search Details</u>	70 Studies found for: Vitamin D Covid19 Also searched for COVID, SARS-CoV-2, and Vit d. See Search Details



HYDROXYCHLOROQUINE (HCQ)



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



ECMO=extracorporeal membrane oxygenation.

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

NEUTRALIZING mAb

Multiple agents under study

EUA

- Convalescent plasma
- Bamlanivimab
- Casirivimab/imdevimab



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, <u>BEST</u> 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



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

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

LESS THAN 10/

but this environment accounts for

BTUD 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



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.

MAb THERAPIES HAVE AN EUA TO TREAT HIGH-RISK PEOPLE WHO TEST POSITIVE FOR SARS-CoV-2. 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



BMI=body mass index.

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-useauthorization#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-useauthorization#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-useauthorization#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.

BAI	MLANIVIMAB ^{1,2}			
STU	DY DESIGN	PRIMARY ENDPOINT	RESULTS	ADVERSE EVENTS
• P • R n s 7 d	Phase 2 (BLAZE-1) Randomized 452 patients with hild-to-moderate COVID-19 ymptoms and positive test to 00 mg, 2800 mg, or 8000 mg lose 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% Cl; -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
CAS	SIRIVIMAB/IMDEVIMAB [®]		1	
STU	DY DESIGN	PRIMARY ENDPOINT	RESULTS	ADVERSE EVENTS
• P • R a C U U U (1	Phase 1/2 Pandomized 799 nonhospitalized dults with mild-to-moderate COVID-19 symptoms to single / infusion of 2400 mg CAS/IMD i200 mg of each); 8000 mg ;AS/IMD (4000 mg each), r 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 reaction No SAEs
VIR	-78314,5		1	
STU • P • V • P tt • E	DY DESIGN Phase 2/3 Phase 2: All patients receive /IR-7831 Phase 3: Patients randomized to study drug or placebo istimated enrollment: 1360 COVID-19-positive outpatients	PRIMARY ENDPOINT Proportion of participants who progress (hospitalization >24 hours or death at day 8, day 15, or day 22) through day 29	 RESULTS Estimated primary completion date: January 2021 Estimated study completion date: July 2021 	ADVERSE EVENTS 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 **GI Symptoms** Nausea, diarrhea, 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)

VIRAL REPLICATION

Oropharynx Symptoms

Anosmia, dysgeusia, sore throat. rhinorrhea

ACE2+TMPRSS2+ cells Epithelial cells (nasal cavity and respiratory tract)

Renal Symptoms Acute renal injury ACE2+TMPRSS2+ cells

Respiratory

Symptoms

pneumonia.

ARDS.

cough

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

Cardiac Symptoms

Arrhythmia, cardiogenic shock, myocarditis, embolic events

Systemic Symptoms

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

SEVERE/CRITICAL DISEASE

Variable depending on degree and exacerbation and comorbid conditions

INFLAMMATION

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

enteritis

mAb NEUTRALIZATION OF SARS-CoV-2



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.

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 effect³
- Recovery coincident with acquisition of mAb
 - Rapid recovery from symptomatic disease associated with robust mAb response⁴

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. ^{II}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)	Incidence			
	Number o Total N	%			
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)

Trial Day

*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



CASIRIVIMAB/IMDEVIMAB: CLINICAL TRIAL (CONT.)

DEMOGRAPHIC AND BASELINE MEDICAL CHARACTERISTICS*						
	REGN-COV2					
Characteristic	2.4 g (n=92)	8.0 g (n=90)	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±6.96	
Obesity—number (%)	39 (42)	42 (47)	81 (45)	34 (37)	115 (42)	

DEMOGRAPHIC AND BASELINE MEDICAL CHARACTERISTICS* (CONT.)						
		REGN-COV2				
Characteristic	2.4 g (n=92)	8.0 g (n=90)	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 nasoph	naryngeal swa	ab (Log ₁₀ sca	le)			
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 pr	rotein 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 sta	tus—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. ^{II}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 log₁₀ 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.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19

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	<u> </u>	
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.)



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

EUA CRITERIA



BMI ≥35



Chronic kidney disease



Diabetes



Immunosuppressive disease



Currently receiving immunosuppressive treatment



≥65 years of age



BAMLANIVIMAB¹

- 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 medicalrelated 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/IMDEVIMAB²

- High risk
- Are ≥55 years of age AND 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, for example, cerebral palsy, OR medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR asthma, reactive airway

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

Why are authorized monoclonal antibodies rarely being used to treat COVID-19 ?



WS.J

"Without it, I don't know how much worse I would have been," one patient said.

By Sasha Pezenik

December 18, 2020 1:05 PM • 7 min read

OPINION | COMMENTARY

Why Are Covid Antibody Drugs Sitting on Shelves?



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.





PRE-/POST-TEST QUESTIONS



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, SpO₂ 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



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

Rationale: The FDA has issued emergency use authorization (EUA) for three monoclonal antibodies to treat high-risk patients with COVID-19 in the outpatient setting. Clinical trials demonstrated that a single infusion of bamlanivimab or a single infusion of casirivimab plus imdevimab could significantly reduce the risk of hospitalization and/or emergency department use.

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. 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. 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 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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- C. Reduces nasopharyngeal viral loads
- D. Is safe and well-tolerated

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, 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.

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

