
COVID19
Keeping Up with a Moving Target

CME Information

Jointly provided by Postgraduate Institute for Medicine, DKBmed, and the Institute for Johns Hopkins Nursing.

Disclosure of Conflicts of Interest

Postgraduate Institute for Medicine (PIM) requires instructors, planners, managers, and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest (COI) they may have as related to the content of this activity. All identified COI are thoroughly vetted and resolved according to PIM policy. PIM is committed to providing its learners with high quality activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of a commercial interest.

The faculty reported the following financial relationships or relationships they or their spouse/life partner have with commercial interests related to the content of this continuing education activity:

Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	JNJ: Ownership equity Scientific Consulting: Verily, EMD Serono DMSB: Humanigen

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials, including monoclonal antibodies, antivirals, and several vaccine platforms.

All activity, content, and materials have been developed solely by the activity directors, planning committee members, and faculty presenters, and are free of influence from a commercial entity.

CME Information

To attest for CME/CE/AAPA credit, please visit

COVID19.dkbmed.com

Learning Objectives

- Describe changes to NIH treatment recommendations for people with mild to moderate COVID-19 at high risk for progression

Thank You

This activity is supported by an educational grant from Gilead Sciences, Inc. and in-kind support by DKBmed LLC

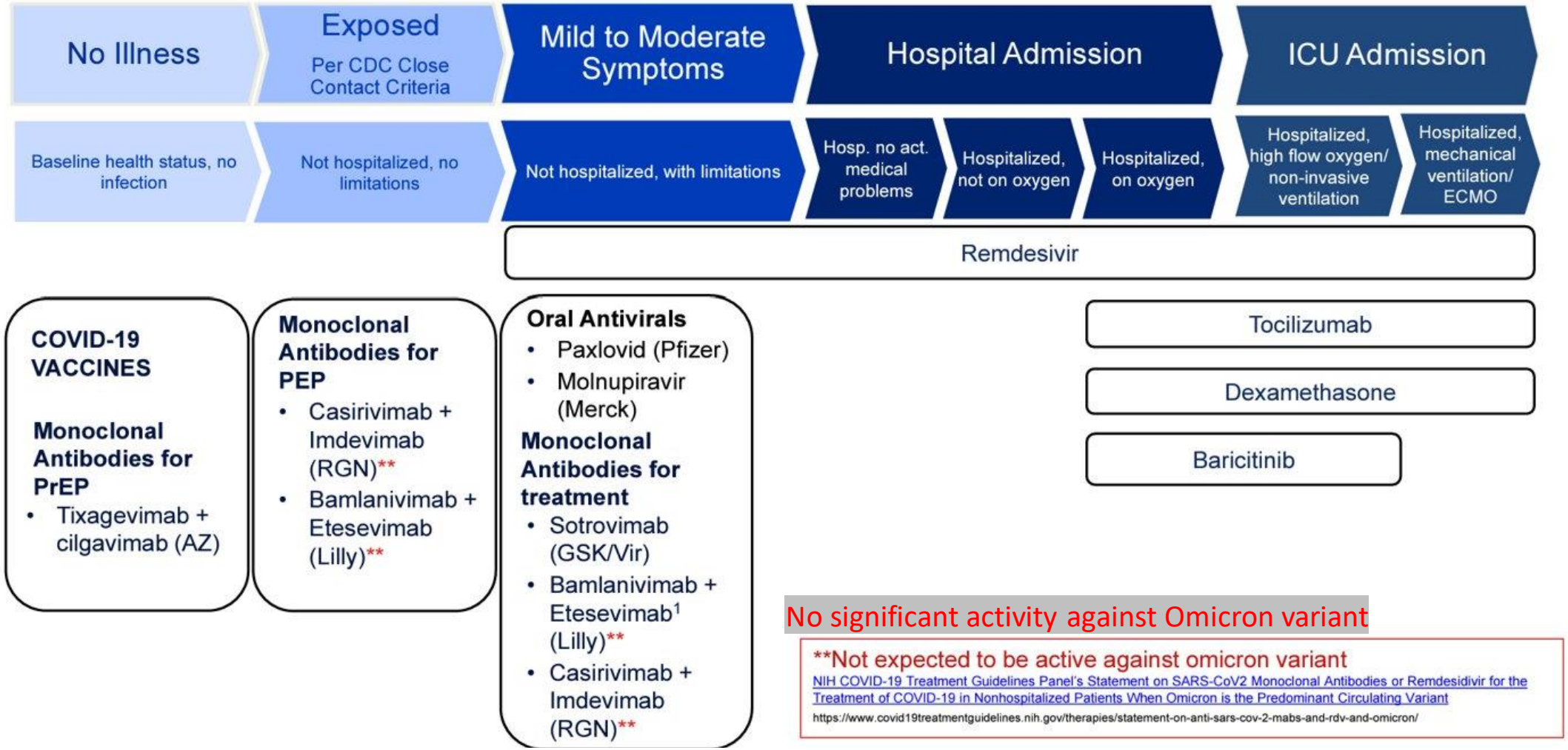
All activity content and materials have been developed solely by the activity directors, planning committee members, and faculty presenters.

Please see **COVID19.DKBmed.com** for additional resources and educational activities

Paul Auwaerter, MD, MBA, FIDSA
Clinical Director, Division of Infectious Diseases
Sherrilyn and Ken Fisher Professor of Medicine
Fisher Center for Environmental Infectious Diseases
Johns Hopkins University School of Medicine

RECENT CHANGES FOR COVID CARE AND PREVENTION

Summary of Preventive Agents and Therapeutics for COVID-19



No significant activity against Omicron variant

**Not expected to be active against omicron variant

NIH COVID-19 Treatment Guidelines Panel's Statement on SARS-CoV2 Monoclonal Antibodies or Remdesidivir for the Treatment of COVID-19 in Nonhospitalized Patients When Omicron is the Predominant Circulating Variant

https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-anti-sars-cov-2-mabs-and-rdv-and-omicron/

USG COVID-19 12/29/21

NIH Recommendations for Mild-Moderate Non-hospitalized COVID-19 w/ Risk Factor(s) for Progression

Nonhospitalized with mild to moderate COVID-19, but at high risk of progression

Recommend using ONE of the following therapeutics (listed in order of preference):

1. Nirmatrelvir 300 mg with ritonavir 100 mg orally twice daily for 5 days, initiated ASAP and within 5 days of symptom onset in those aged ≥12 years and weighing ≥ 40 kg
2. Sotrovimab 500 mg, single IV infusion, ASAP and within 10 days of symptom onset in those aged ≥12 years and weighing ≥ 40 kg
3. Remdesivir 200 mg IV on day 1, followed by remdesivir 100 mg IV daily on days 2 and 3, initiated ASAP and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg
4. Molnupiravir 800 mg orally twice daily for 5 days, initiated ASAP and within 5 days of symptom onset in those aged ≥18 years ONLY when none of the above options can be used

New Monoclonal Antibody: Bebtelovimab

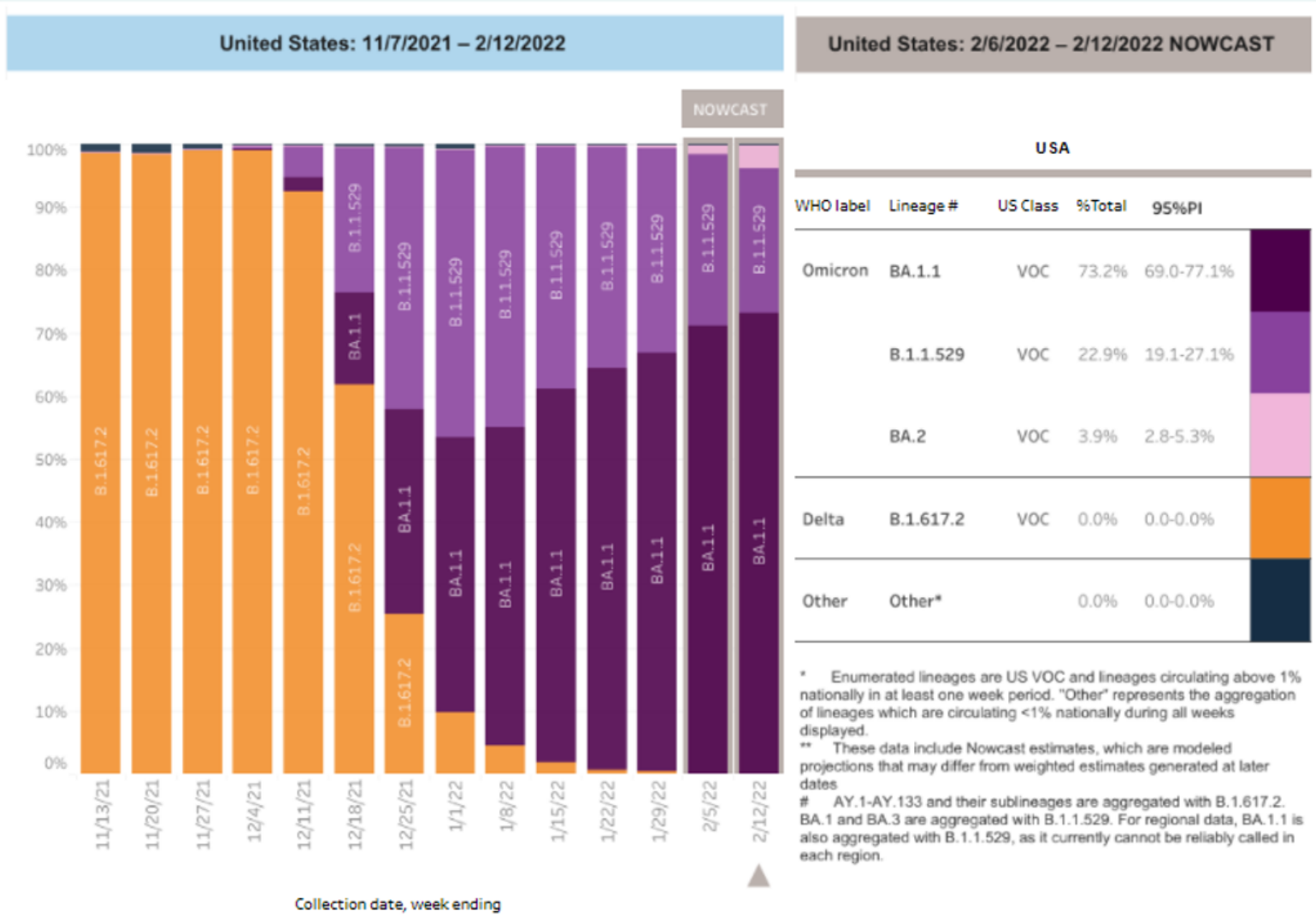
- EUA granted, mild-moderate COVID-19
- ≥ 12 yrs, at least 40 kg + at high risk for severe COVID-19
  - 175 mg IV injection
- Has activity against Omicron variant
- RCT BLAZE-4 Phase 2 (pre-Omicron), limited data, including
- Alone (n=100) or with bamlanivimab/etesevimab (n=50), 91.3% high-risk pts, mean symptom duration 4.7 days, 20.7% at least 1 dose of vaccine
  - Primary outcome: safety
  - Secondary: hospitalization or death by day 29: bebtelovimab alone 3 (3%) v. combo 2 (4%); 1 death (beb, alone)
  - Other data from Phase 2 open label (combo), Phase 2 low risk (combo or beb alone)
- Safety: similar to other mabs

http://pi.lilly.com/eua/bebtelovimab-eua-factsheet-hcp.pdf (accessed 2/15/21)

Potential Issues with Omicron subvariant BA.2

- Derived from BA.1, not labeled a VOC by the WHO
- BA.2 has ~28 mutations in spike protein
- 20 are different from BA.1
- Other than by sequencing, cannot readily differentiate
- Has quickly spread worldwide
- 69 countries, including US

Current Variants: US



United States: 2/6/2022 – 2/12/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.1.1	VOC	73.2%	69.0-77.1%
	B.1.1.529	VOC	22.9%	19.1-27.1%
	BA.2	VOC	3.9%	2.8-5.3%
Delta	B.1.617.2	VOC	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

\# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1 and BA.3 are aggregated with B.1.1.529. For regional data, BA.1.1 is also aggregated with B.1.1.529, as it currently cannot be reliably called in each region.

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Antibody Evasion: Omicron Sublineages

Sotrovimab

Bebtelovimab

b

Fold change in IC_{50} relative to D614G	RBD mAbs																	NTD mAbs	
	Class 1			Class 2				Class 3						Class 4					
	CB6	Bril-196	1-20	REGN 10933	COV2-2196	LY-CoV 555	2-15	REGN 10987	COV2-2130	S309	2-7	Bril-198	LY-CoV 1404	ADG-2	DH1047	10-40	S2X259	4-18	5-7
BA.1	<-428	-298	<-429	<-2201	-306	<-1496	<-2716	<-1716	-83.5	-6.9	-195	2.3	1.4	-11.0	-14.2	-21.1	-13.7	<-26.7	-4.1
BA.1 + R346K	<-428	-135	<-429	-415	-187	<-1496	<-2716	<-1716	<-687	-4.5	-82.1	<-22	1.5	-15.7	-7.9	-20.5	-7.5	<-26.7	-5.5
BA.2	<-428	-322	<-429	<-2201	-680	<-1496	<-2716	-253	-1.9	-27.0	-7.3	-10.5	1.1	<-555	<-58.0	<-114	<-96	<-26.7	<-171
T19I	-3.1	-4.9	-5.3	-3.7	-1.9	-2.2	-2.0	-2.1	-1.5	-1.8	-5.1	-1.6	-1.7	-1.7	-1.5	-2.7	-2.9	-6.1	-3.3
L24S	-2.9	-4.0	-4.6	-3.2	-2.4	-2.4	-2.8	-4.2	-2.1	-1.5	-2.6	-2.2	-1.6	-1.3	-1.1	-2.4	-2.0	-3.1	-1.1
Del25-27	-1.2	-2.6	-2.0	-1.3	-1.0	-1.4	-1.2	-1.3	1.0	-1.3	-2.8	2.0	-1.2	1.1	1.6	-1.8	1.1	-23.1	-16.8
V213G	-2.5	-3.1	-3.0	-3.1	-1.5	-1.1	-1.6	-2.2	-2.0	-1.2	-3.2	-1.1	-1.5	1.1	1.0	-2.0	-1.7	1.9	-2.8
S371F	-143	-126	-95.1	-27.9	-26.1	-5.1	-6.3	-86.6	-1.3	-20.5	-30.6	<-22	-2.4	-43.0	-60.9	<-114	-77.5	7.8	2.3
T376A	-1.9	-3.1	-2.5	-2.1	-1.3	-1.7	-1.3	-1.9	-1.8	1.0	-2.7	2.0	-1.7	1.1	1.1	-1.5	-2.3	1.3	-1.3
D405N	-25.6	-2.3	-2.9	-2.8	-2.1	-1.9	-1.7	-1.6	1.0	1.5	-3.1	-1.6	1.3	3.3	-1.2	-3.9	-2.2	5.6	1.5
R408S	1.4	-1.1	-1.3	-1.1	1.5	-1.6	-1.3	1.2	1.0	1.0	1.2	1.4	-1.4	-1.6	-2.1	-1.2	-3.6	1.1	-1.3

>3	<-3	<-10	<-100

https://www.biorxiv.org/content/10.1101/2022.02.07.479306v1

IMMUNIZATION CHANGES

Booster Change: Severely Immunocompromised

Revised Guidance for a 3-Month Booster Interval After an mRNA COVID-19 Vaccine Primary Series

Current guidance	**Revised** guidance
People who are moderately or severely immunocompromised should receive a booster dose **at least 5 months** after the last (third) dose of an mRNA COVID-19 vaccine.	People who are moderately or severely immunocompromised should receive a booster dose **at least 3 months** after the last (third) dose of an mRNA COVID-19 vaccine.

1. Kamar, N., Abravanel, F., Martion, O. (2021). Assessment of 4 Doses of SARS-CoV-2 Messenger RNA–Based Vaccine in Recipients of a Solid Organ Transplant. *Infectious Diseases, 4*(11), e2136030.
2. Benotmane, I., Bruel, T., Planas, D., et al. (2021). A fourth dose of the mRNA-1273 SARS-CoV-2 vaccine improves serum neutralization against the delta variant in kidney transplant recipients. *medRxiv*. Preprint. doi.org/10.1101/2021.11.25.21266704
3. Alejo, J.L., Mitchell, J., Chiang, T., et al. (2021). Antibody Response to a Fourth Dose of a SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. *Transplantation, 105*(12), e280-281.
4. Munro, A., Janani, L., Cornelius, V. (2021). Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial. *Lancet, 398*, 2258-76.
5. Atmar, R.L., Lyke, K.E., Deming, M.E. (2021). Heterologous SARS-CoV-2 booster vaccinations-preliminary report. *medRxiv*. Preprint. doi: 10.1101/2021.10.10.21264827

CDC

Vaccination Schedule for Immunocompromised

REVISED COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	Vaccination Schedule				
Pfizer-BioNTech (ages 5 years and older)	1st dose	2nd dose (21 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)		Booster dose* (at least 3 months after 3rd dose)
Moderna (ages 18 years and older)	1st dose	2nd dose (28 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)		Booster dose* (at least 3 months after 3rd dose)
Janssen (ages 18 years and older)	1st dose	Additional dose† (at least 28 days after 1st dose)		Booster dose* (at least 2 months after additional dose)	

*Any COVID-19 vaccine can be used for the booster dose in people ages 18 years and older, though mRNA vaccines are preferred. For people ages 12–17 years, only Pfizer-BioNTech can be used. People ages 5–11 years should not receive a booster dose.
†Only Pfizer-BioNTech or Moderna COVID-19 Vaccine should be used

CDC

CDC Antibody Product Guidance

Passive Antibody Products

Current guidance

Defer COVID-19 vaccination for:

- 30 days if product used for post exposure prophylaxis
- 90 days if product used for treatment
- No guidance for pre-exposure prophylaxis

Revised guidance

- No recommended deferral period
- However, tixagevimab/cilgavimab (EVUSHELD™) should be deferred for at least two weeks after vaccination

Benschop, et al. (2021). The effect of anti-SARS-CoV-2 monoclonal antibody, bamlanivimab, on endogenous immune response to COVID-19 vaccination. *medRxiv*. Preprint. **doi:** https://doi.org/10.1101/2021.12.15.21267605

CDC

Do you suspect that changes will be made to the interval between mRNA vaccine doses for younger people?

Why is B2 considered a subvariant and not a new variant?

Thank You!

To receive CME/CE/AAPA credit:

Complete the evaluation on at COVID19.DKBmed.com

Upon registering and successfully completing the activity evaluation, you will have immediate access to your certificate.

To access more resources related to COVID-19:

- Access our resource hub at COVID19.DKBmed.com

To ask your own question, email:

- QA@dkbmed.com