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Released: 10/13/2022
Valid until: 10/13/2023
Time needed to complete: 15 minutes

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COVID-19: Differentiating Disease Course and Updates on Treatment

Announcer:
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Dr. Vega:
For patients at high risk of severe COVID-19, therapeutic advances offer an opportunity to treat infection early and reduce the risk of disease progression. How confident are you in identifying high-risk patients and selecting the most appropriate treatment for them?

This is CME on ReachMD, and I'm Dr. Charles Vega.

Dr. Cennimo:
And I'm Dr. David Cennimo. So to start things off for us, Chuck, can you explain how to differentiate mild, moderate, and severe COVID-19?

Dr. Vega:
Right, I think it's important to be able to differentiate the illness you're seeing in front of you. And I've certainly seen all 3 types of COVID-19 in my outpatient practice. And that is my practice and my bias. I come at this from the outpatient-based perspective, where most cases fit into this mild illness category, historically about 80%. And maybe slightly more now with omicron. And that includes things like fever, but also the cough or sore throat that we're seeing more of now with omicron. I think, very importantly, mild illness. Those folks don't have lower respiratory symptoms; they don't have a lot of wheezing; they don't have dyspnea.

Whereas moderate illness, that's the group that has more lower respiratory tract symptomatology. But importantly, they are actually maintaining their oxygen saturation. So they're not in respiratory distress; they don't look like they have any warning signs of decompensation, where they might need to be hospitalized.

And then severe illness are folks, their oxygen saturation in your clinic is going to be below 94%. They may have to tachypnea with breathing rates of 30 or more. And so those are folks who we want to transfer to the emergency department from my center, and then get the appropriate treatment on board.

But as I said, most patients do fit this category, who are in the mild to more moderate category. Although many of them are at high risk for complications. This is where I'd love to have a polling option for our audience. But I have a feeling if you're in primary care, the majority of adults you see actually fit into a high-risk category. I see a primarily older age group, and there's a lot of comorbid conditions in that age group. And so therefore, many of them should be considered.

But just to cover the ground rules of who should be considered for treatment in the outpatient setting, age over 50 is an important risk factor. So age is one of the most important risk factors for complications of COVID-19. And particularly if they haven't been vaccinated or even undervaccinated, I'm going to more strongly consider therapy for them. And then there's a very wide range of high-risk

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conditions. Certainly, immunocompromised stands out as one of the most important in terms of folks who are risk of complications of COVID-19 and getting treatment on board earlier. But if they have chronic lung disease, chronic kidney disease, a history of chronic liver disease or heart failure, diabetes, you can see why these conditions are so prevalent in primary care practice.

And so, if I have a patient in front of me, they have a positive test for SARS-CoV-2, they're symptomatic, and particularly if they're within 5 days of therapy, when we think about certain treatments, you can – extending out to 7 days, I'm a believer that, unfortunately, the efficacy of treatment against SARS-CoV-2 goes down as they progress more into their illness. So I want to get treatment on board as soon as possible. And if they have a risk factor present, I'm going to talk about them with treatment.

David, does that sound like a reasonable approach? Or anything else you have to add to that approach to therapy?

Dr. Cennimo:
No, absolutely. I think that that's the exact way that I look at it as well. I have sort of a joint practice where I see patients inpatient and outpatient, and also many of mine are high risk. Many of my patients are living with HIV as well.

And it strikes me that in the beginning of this pandemic, we were really thinking about the severely ill patient. But as you correctly point out, the majority of patients will have mild illness and never have to be in a hospital. And that number is increasing.

So the fact that we really need to keep an eye out for those patients who have the higher risk, who may decompensate in the days to come, becomes in some ways all the more important because we have now, blessedly, you know, amazingly, we've had the rapid introduction of multiple drugs that can affect this treatment course. We just need to know who to use them on.

Dr. Vega:
So maybe you could walk us through those available treatment options for our outpatients?

Dr. Cennimo:
Certainly. So first thing to point out is that your low-risk patients will likely do fine without any specific intervention. They need supportive care, like many other viral respiratory illnesses. But I'm always very, very cognizant of talking with them about what disease progression may look like. And if they start developing dyspnea, or signs that their lower respiratory tract is becoming involved, they need to come back or call me.

So right now, we have 4 therapies that are available. And really, we look at how do we pick the right patient? So the majority of patients right now are getting nirmatrelvir and ritonavir. And I think that that is very much driven by the fact that it has the strongest recommendation in both the IDSA [Infectious Diseases Society of America] and NIH [National Institutes of Health] treatment guidelines. It is indicated if you're less than 5 days ill, and to recapitulate, I do agree with you. Whenever we're looking at things that will block viral replication, we should start them as soon as possible because we want as little viral replication going on in the host as we can afford.

The drawback for this drug is that it does require some renal dose adjustment. It's not indicated for creatinine clearance less than 30 or in severe liver disease, Child-Pugh score C. We also have the ability to use remdesivir as a 3-day dose, not the longer in-hospital dose. In my practice, I find that that's an option for patients in long-term care. But I do have some difficulty getting the outpatient, community-living person in for 3 days straight while they're already ill with COVID, to get an infusion. But we were able to operationalize that in some long-term care facilities. And I think that that did make a difference in breaking the chain of transmission as well as individual patients getting worse.

There's molnupiravir, which is another oral antiviral that again can be used within 5 days. And 1 remaining, a monoclonal antibody bebtelovimab.

Now I think that it's important for us to continue to watch the monoclonal antibodies. As you know, they're tuned, if you will, to certain variants of the virus. And as omicron gained population prevalence in this country, we did lose the effectiveness of many of our monoclonal antibodies. This one still remains. In the future, I would anticipate having this discussion again, as we get new variants and deciding what are the possible monoclonal antibodies. But in the meantime, the vast majority of patients are being treated with 1 of the 2 oral antivirals. And that makes sense because these are patients who are otherwise home.

Dr. Vega:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Charles Vega, and here with me today is Dr. David Cennimo. We're discussing the COVID-19 disease course and the evolving treatment landscape.

That's a great point with nirmatrelvir and ritonavir. I think the biggest drug interaction that I run into, because so many of my adults are taking them, are statins, which are easily held, as you mentioned. The other big one, which is a thornier issue and take some decision-making together and potentially use of a bridging agent would be anticoagulants. And it's really the ritonavir that I understand is the

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culprit when it comes to those drug interactions. Is that right?

Dr. Cennimo:
That's correct. And actually, many of the side effects that we're hearing about, the taste disturbances, is also likely driven by the ritonavir.

Dr. Vega:
Yeah, and there will be more agents, you know, that are in development that may not have as many drug interactions. And you're right, monoclonal antibodies, they tend to come in and out a little bit. And so it continues to be a space to watch as we move forward.

Now, the Infectious Disease Society of America has created a roadmap to follow when selecting treatment options for outpatients with COVID-19. And let's use a case to kind of put it to the test. So, David, I'm going to present you with a 62-year-old man. He comes to the urgent care with symptoms of COVID-19. He's been experiencing these symptoms for about 3 days now, and he's looking for treatment to hopefully decrease the chance of disease progression, which is great that he's already thinking that way because that's exactly where these drugs can be effective. How would you assess and treat this patient just from that thumbnail sketch I provided?

Dr. Cennimo:
So, this is a great sketch because it opens a lot of questions that we can discuss. So he's 62. So he's older than 50, which we know is an increased risk. He's less than 65; we know that 65 is a higher risk. I'd want to know some more about his history. I want to know, does he have any of those medical conditions that you initially mentioned that would make him particularly high risk for progression to severe COVID? I'd like to know his renal function and his liver function. I'd like to see how he is feeling symptomatically. And something that we haven't really touched on too much is what's his vaccination status, both the initial vaccine and has he received any booster doses?

So he probably will meet some criteria for treatment. And I think that the most salient point of this is that he's coming to you saying, "I want to decrease my risk for progression." So I would, if at all possible, attempt to treat him. So if you think back and you look back at the IDSA roadmap, we're less than 5 days, so everything is open to us. We have the ability to use our 2 oral agents, but maybe they won't be the best. So first thing I want to know about him, besides his age, which does put him in a risk category, is comorbid conditions, anything specific that's making him higher risk and needing treatment. We need to know his renal function and his liver function, because we might need to not use, for instance, nirmatrelvir or ritonavir, based on severe liver or renal disease. There's molnupiravir, which is another oral antiviral that, again, can be used within 5 days. We have 3 different IV options available. There's high-titer convalescent plasma, which in my world is getting harder to find. There's a 3-day course of remdesivir, but I would need to talk to him about bringing him back for 2 more days to get that done. Or there's the monoclonal antibody bebtelovimab, and that is a good option for patients that are unable to use some of the other therapeutics because of those drug-drug interactions.

So I would have a real conversation, and we would figure out what is best for him based on the medications he's on, as I said, his comorbidities, and what he's able to do lifestyle-wise as far as timing of these treatments.

The other part about vaccination status, I think, is something that we will learn more about very soon. There are studies that are in trial right now and almost finished. Because I think we have to remember that the initial studies that brought most of these drugs out into the marketplace for use were in unvaccinated individuals. And we're seeing that, as you might expect, the benefit in a vaccinated person may be less because they've already been protected somewhat by their vaccine. Now, at the individual level, if somebody's high risk, I'm not trusting, if you will, their vaccination status. I'm saying, you know, you're at high risk, and you're clinically ill in front of me, so I do offer treatment. But I recognize that it might not be as beneficial as the person who was unvaccinated.

Dr. Vega:
That's a great point. I think it brings up one of the new points of tension we have when it comes to managing patients with COVID-19. I completely see it, that, you know, folks who have been vaccinated and boosted, you know, much lower likelihood of getting severe illness, of being hospitalized. And that's great. And the virus is obviously changing, too, with new variants. And omicron probably being slightly more benign than previous variants. But we don't know what to expect.

I'll just point out as well, my final point is that we have oral treatments available. They are easy to take; they are well tolerated in general. So therefore, I think we should make sure that we are treating those patients 50 and over with at least 1 high-risk condition. And particularly if they're unvaccinated or undervaccinated, I think it's a time to treat those folks.

David, I don't know if you have any key takeaways or other comments you want to share with us today.

Dr. Cennimo:
We have these treatments available; we should use them in the right patients. And if given the opportunity, I will always make the

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comment that prevention is always better than treatment. So get that booster, get the omicron-specific booster, because you would rather not be infected as opposed to needing one of these treatments. It's a good thing that we have them, but I'd still rather not get sick.

Dr. Vega:
Yeah, absolutely. All right. Unfortunately, that's all the time we have today. So I want to thank our audience for listening in and thank you, Dr. Cennimo, for joining me today and for sharing your all your valuable insights. We know that everybody's very busy, so it means a lot that you took the time to listen to us. And hopefully you found this program helpful to your practice. It was great speaking with you today, David. Take care.

Dr. Cennimo:
You, too. Thanks so much.

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