Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Connecting Care: A Multidisciplinary Panel Discussion on the Use of Neutralizing Monoclonal Antibodies in Ambulatory Patients With COVID-19

Announcer:
Welcome to CME on ReachMD. This activity titled "Connecting Care - A Multidisciplinary Panel Discussion On The Use Of Neutralizing Monoclonal Antibodies In Ambulatory Patients With COVID-19" is provided by Forefront Collaborative and AKH, and supported by an educational grant from Lilly. This replay of a live broadcast focuses on how we can overcome challenges in the treatment of COVID-19.

Since the presentation-recording, the Assistant Secretary for Preparedness and Response (ASPR) paused all distribution of bamlanivimab+etesevimab and etesevimab alone (to pair with existing bamlanivimab supply). Two additional changes of note: dosing of casirivimab+imdevimab decreased to 600 mg of each compound; EUA criterion pertaining to BMI was reduced to 25.

Now, here's your moderator, Dr. Mimi Secor.

Dr. Secor:
Hi, I'm Dr. Mimi Secor and I'd like to welcome Dr. Karen Bloch and Mr. Jared Kile to the program. They are joining me to discuss the use of neutralizing monoclonal antibodies in the outpatient treatment of patients with COVID-19. Welcome to the program, Dr. Bloch and Mr. Kile.

Dr. Bloch:
Happy to be here.

Mr. Kile:
Thank you.

Dr. Secor:
Please note, our disclosures are available to you on the event page and are also listed on this slide. During this activity, you will have the opportunity to hear from our multidisciplinary panel as they share clinical information on the new neutralizing monoclonal antibodies, as well as real-world experiences from their own institutions. You will also have an opportunity to have your questions answered live during a Q&A session at the end of the lecture. You'll have a chance to claim credit for completing an evalu- after completing an evaluation after participating in the course. So submit questions during the presentation, type them into the chat control panel on the left side throughout the program, or in your comment box through Facebook live. We will answer as many as we can in the time allotted. We also have three polling questions placed throughout the presentation, so please take out your phone and text ReachMD to the phone number 22333. Alternatively, you can respond via your computer at pollev.com enter ReachMD.

So, Dr. Bloch all the attention in the past few months has been on the COVID-19 vaccines. Lost in the excitement it seems, are the outpatient treatments, ah, that have received emergency use authorization the neutralizing monoclonal antibodies. I'd like to start with a really basic question. What is a neutralizing monoclonal antibody?

Dr. Bloch:

That is an important question can we get the next slide, please? So, a neutralizing monoclonal antibody is a protein that's synthesized in the lab, and this is show pictorially on this slide. The virus is shown in the center with the red components emanating from the circular aspect of it representing spike proteins. Monoclonal antibodies are n- derived from human antibodies. They're naturally made against infection and these work specifically by binding to different epitopes on these spike protein areas. Next slide. In natural infection, The virus is able to get into the human cell by using these spike proteins to bind to a cell-surface receptor, specifically the angiotensin-converting enzyme 2 receptor. Once inside the cell, the virus replicates and ultimately destroys or kills the cell.

If you look at slide B here though, once the antibodies are in place physically the virus is no longer able to attach to this ACE-2 receptor. And so, it is not cytotoxic to the host cell. Currently there are three neutralizing monoclonal antibodies available, all of which have emergency use authorization through the FDA. The first of these, bamlanivimab was authorized for use in November 9th. And shortly thereafter, a combination product or cocktail of two different monoclonal antibodies, both of which are active against different portions of the spike protein was approved. This is Casirivimir- Casirivimab and Imdevimab. Finally, a second combination was just authorized in the last two weeks. This takes the initial protein that we talked about, bamlanivimab, and adds a second antibody that's also active against a different area on the spike protein.

Dr. Secor:
Dr. Bloch, since the FDA has granted emergency authorization to the three neutralizing monoclonal antibody therapies as shown in the slide here, and as you've discussed, how do you explain that to patients?

Dr. Bloch:
That's a- that's a great question. So, it does cause a lot confusion because there are so many options out there. What I tell patients is that they have not been studied head-to-head, so there's not really one that's better than the others, or at least we don't know that there's one that's better than the others. And then the studies all talk about you can see all of them very similarly in terms of beneficial effects. The other thing to keep in mind is we don't really have much of a choice in terms of which product we give our patients. At our institution we are allocated an allotment of antibodies from the State Health Department and it may vary week-to-week which product we are given. And so, our pharmacy decides independent of the clinicians which product we have the most supply of and that's the one that's used for that week.

So shortly after the first monoclonal antibody was given emergency-use authorization a number of expert panels came out with guidelines for their use. The National Institute of Health guidelines suggest that there is insufficient data to recommend either for or against the use of these products. The Infectious Disease Society of America recommends against the routine use in ambulatory patients, however, they do acknowledge that in patients who are at high risk it's reasonable to consider this as a treatment option understanding that we don't know as much about this as we would about a drug that's gone through years and years of development and testing. In late January, the Pediatric ID Group came out with a consensus statement recommending against the routine use of this product in children and adolescents, and that's based on a couple of different, ah, rationales. The first is the studies that led to approval of these different agents were not done in children so we really do not have a lot of data in terms of their efficacy or their safety in this population. And that's balanced against the fact that in children - for most of the cases COVID-19 is a mild disease.

Mr. Kile:
So for the polling questions, please text ReachMD to the phone number 22333. Alternatively, you can respond via your computer at pollev.com and enter ReachMD. Which of the following statements regarding neutralizing monoclonal antibodies for treating COVID-19 best apply to your practice? Is it A) Have prescribed a neutralizing monoclonal antibodies, B) Have administered neutralizing monoclonal antibodies, C) Never utilized the neutralizing monoclonal antibodies, or D) Plan to utilize neutralizing monoclonal antibodies in the treatment of COVID-19?

Dr. Secor:
So we'll give everybody a few seconds and encourage you to submit your responses to the polling question, and then we'll have Mr. Kile discuss your responses.

Mr. Kile:
So definitely it seems like a high number of the people on tonight are looking into it or haven't used it and are little more interested. Nothing seems to be changing. Excellent.

Dr. Bloch:
So hopefully at the end of this this discussion we'll see a clear increase in the number of planning to use these products. Let me go to the next slide. This outlines which clinical studies were done that led to the FDA granting emergency use authorization. Two of these were in New England Journal and the most recent one came out in JAMA and these were all randomized controlled trials and with the

primary end point being viral load in the nasopharynx at 11 days after therapy. Before I get to the question about viral load, I did want to mention one thing because this is something that patients routinely ask me about when we bring up th- the potential for monoclonal antibody treatment, and that is 'Will I feel better with this therapy?' and the answer is 'Maybe,' and this is based on the data from the bamlanivimab study. This was a phase 2 trial. Patients who received placebo are shown in the gray line and those who received therapy in the blue line. These investigators used a composite score for symptoms. And so, this is eight different variables sort of accumulated into a single score. And you can see by day three or four there really is a bit of a difference with a decrease in number of symptoms in patients who'd received therapy. But by day six, these curves start to merge again, so it is likely that there is some symptomatic benefit certainly anecdotally I have had patients tell me that they feel remarkably better very quickly after the infusion but it is somewhat limited. This is data from the fact sheet that accompanied the EUA for bamlanivimab.

Again, I mention that the primary outcome for the studies that led to approval was viral load, and if you look at that first graph you can see there are a number of different dosages that were used, and for some of these there was a significant decrease from the viral load with placebo which is shown again in the gray line. However, I think the take-home message is regardless of whether patients got treatment with a monoclonal antibody or with placebo over that 11-day period the number of viral protocols drops off quite considerably. I think the most clinically-relevant finding from the- this study and one that, ah, again I think led to the emergency-use authorization is shown on the next two bar slides, or bar graphs. When they looked at the total population study the patients who received placebos, 6% required either hospitalization or emergency-room visit in the 28 days after infusion. For those who received the study project, that number decreased to 2%. In a post hoc analysis these investigators looked just at high risk patients and the findings were even more dramatic. Ten percent of those who had received placebo required hospitalization or emergency room evaluation compared to only 3% who received the monoclonal product.

Dr. Secor:
Dr. Bloch, seeing this data is so important to understanding monoclonal antibody therapy, however, can you translate for us what do the- these data mean for you when you're actually seeing a patient?

Dr. Bloch:
So you know, I think that's- that's really a key question. As I said, most patients initially ask "Am I'm going to feel better?" but when they hear that the- real benefit of this treatment is that they will have less severe disease and will be less likely to go into the hospital. I think that's a really compelling reason for many patients to want to proceed with this therapy. So I think the most important finding from the study is that there is a decreased rate of hospitalization. This shows very similar data compared to the previous slide. This is for the combination product Casirivimab and Imdevimab again primary outcome was viral load and while there was a statistically significant decrease with any of the doses of this combination treatment, the placebo also had a sharp drop-off in terms of viral load as well. So getting to our more clinically meaningful variables the middle slide shows all comers in this study and we saw similar to the other study with bamlanivimab, 4% of placebo recipients had to be hospitalized or go to the ER versus 2%, so a 50% drop and even more impressive when it was restricted to these high-risk individuals where placebo the placebo group 9% were hospitalized versus 3% for those that received cocktail treatment.

Dr. Secor:
Dr. Bloch, do we know if these monoclonal antibodies work well with the UK, Brazil, or South-African variants?

Dr. Bloch:
That's a question I'm getting a lot, so it seems to be on everbody's mind. We don't know directly but there is some indirect data that suggests that when the virus mutates it changes specific components of these spike proteins, and so a mutation in one area might prohibit or not allow binding of the antibody to that mutated site but if there are two different antibodies in the cocktail, chances are really good that the second one would still be very active, so I- I think as we see more and more of these mutations I think that there may be a interest in developing products that have multiple antibodies in the infusion.

Dr. Secor:
So far I've talked a lot about what the rationale for the emergency-use authorization is and now I want to talk specifically about what the criteria for emergency use of these agents is?

Dr. Bloch:
There are a number of clinical factors and they're really well laid out in the supporting documentation from these EUAs. Patients need to have a positive test either a PCR or an antigen test, they need to not be hospitalized with mild-to-moderate COVID-19, patients need to receive the infusion within 10 days of symptom onset. And I will say that that's the trickiest part in terms of logistics of giving these infusions, because patients often won't present for testing until several days into their illness, and it may be another day or two for that positive test to return, and so that leaves a really short window for the infusion center to contact- to identify the patient first of all, then

contact the patient, schedule them, and actually give the infusion. So that 10 days really is a clicking tock, clicking ticking clock.

Mr. Kile:
Time bomb.

Dr. Bloch:
Yeah, clicking time bomb, you're exactly right. So we need to be be very cognizant of that although the studies were not done in pediatric population there is approval for use in children 12 years and older as long as they weigh 40 kg or more. And finally a criteria for giving these agents is that patients need to be at high risk for regressing to severe COVID-19 and/or hospitalization. So what constitutes high risk? Patients with a body mass index of 35 or greater would be in that category. Patients with chronic kidney disease and that's not defined in the EUA. Our institution decided that stage 4 or 5 met that threshold so anybody with a GFR of 30 or under would be included as eligible, patients with diabetes mellitus who are on medication, patients who are immunocompromised either because of an underlying health condition or a treatment, and then there's some age criteria. Anybody 65 years of age or older independent of these other risk factors would be a candidate for infusion, and those 55 to 64 who have one of the following would also be eligible. That would be cardiovascular disease, hypertension, or crom- chronic pulmonary disease. The criteria for pediatrics is slightly different, there is a weight criteria as well but rather than an absolute cutoff, it's a percentile based on age and gender. Other unique immunocompromising conditions in children would include sickle-cell disease which might lead to functional asplenia, children with congenital or acquired cardiac disease are considered high risk, as are those with neurodevelopmental disorders. And that could be things like cerebral palsy or muscular dystrophy. Children who have medically-related technological devices - maybe a feeding tube, or a tracheostomy would fall into a high risk category. And finally, children with chronic respiratory disease including asthma requiring daily medication would be eligible.

Dr. Secor:
Dr. Bloch, are there data to support using monoclonal antibody therapy in hospitalized patients that do not yet meet the criteria for treatment with Remdesivir or other treatments?

Dr. Bloch:
So, the emergency-use authorization did not specify that and it wasn't included in any of the studies that led to authorization but just sort of rationalizing it, the same risk factors would be present in a patient who might be hospitalized for reasons unrelated to COVID, so for instance, our hospital does screening at admission and a number of patients who come in for completely unrelated reasons are found incidentally to have COVID. This is a population that we felt would benefit from these treatments and so we actually have extended our eligibility to patients hospitalized so long as the reason for hospitalization is not COVID itself.

There are some contraindications, so let me tell you what those are. These are very clearly laid out in the EUA documentation. That would be hospitalization due to COVID, so sort of a subtle difference from what I talked about before, but if- if patients are hospitalized because of severe disease that would be a reason not to give these therapies, and then regardless of inpatient or outpatient status patients who have either a new need for oxygen or increase in oxygen flow rate from their chronic baseline oxygen requirements.

Now a question that comes up a lot is 'Are women who are pregnant or breastfeeding eligible?' and these are not contraindications but these may be scenarios where talking to the patient about risks and benefits and individualizing therapy would probably be indicated. This shows data from the ACTIV-3 study. This was a treatment that looked at, a monoclonal antibody, specifically bamlanivimab combined with Remdesivir, or placebo with Remdesivir in hospitalized patients. If you look at the bar chart, the,red areas show better pulmonary outcomes and you can look at each of these different data points and the monoclonal antibody performs either equally or less well than those who received placebo, and based on an interim analysis of this data the study was sho- stopped prematurely for medical futility. And so, this sort of supports the reason why this is not indicated in hospitalized patients.

Dr. Secor:
For those just joining us this is ReachMD. I'm Dr. Mimi Secor and joining me to talk about neutralizing monoclonal antibody therapy-treatment for outpatient COVID-19 are Dr. Bloch and Mr. Kile. I want to encourage our viewers to submit questions for them. Also there are two more polling questions, so please take out your phone and texture ReachMD to the number 22333 to set your phone up for polling. Mr. Kile will now speak to us from a pharmacist's perspective. Mr. Kile what should our listener- listening clinicians expect when administering a neutralizing monoclonal antibody therapy?

Mr. Kile:
Thanks Dr. Secor. Next slide, please. So we will discuss a little more about the demographics of the- with the experience for hava-Lehigh Valley network in a future slide but I want to give a quick overview of the, say thousand-foot view on this particular slide, and this entails about 250 patients. We pulled together some data from around late January. From the infusions we have seen mostly mild side effects which really follows with the EUA's- of all the different products that are out there. And I would say that also that when we did

follow-ups, which I think is a- an extremely important part of it, and again that's part of the EUA but I think it really extremely important that when you have to consider doing in a timely manner we did find that there were patients had mild-to-moderate DRs post-infusion where there was nausea and vomiting for a few days, headaches and there's some other- other varying different side effects. We were finding i- it would last sometimes up to a few days.

Now one thing to also note that too is we have not seen any patient so far and we're well beyond that 250 mark but we we've not seen anybody that's had anaphylaxis yet. A- take the group and again look for that 1,000-foot view, we have had 6 patients that have gone back to the ED following infusions and not necessarily due to the the monoclonal antibody. Ee had 13 COVID-related hospital admissions and again this is always difficult to say. Is this, you know - 'Did we get the antibody in in the right amount of time, is this the progression of COVID?' It's always a good question. And when something else is a little bit more passive when it come to data collection and something I never really knew before is you know, how does an EMR actually get updated unfortunately when someone passes? But we had five patients that had gotten the infusions and ended up passing away, and really looking at those patients, you notice there was not, you know, in- instantaneously, it was not within like even 24 hours, really within a week or two. So it was probably more related, again, you can't say totally 100% but probably more related to the COVID disease state more than anything else.

Now one of the things that's really important though, is, and you know this is I think something that pharmacists are u- are uniquely it's one of our, I'd say it is our passions, it is one the things we weren't really taught in college, and just from experience, is looking at patients that might have an EDR and knowing how to d-, you know, follow up with those patients, and that. And then there's two ways really to look at this, and one is doing a- a passive approach and there's doing what's more of an active approach. Again, passive approach is, y- you see is a little bit more easier where you've give out phone number, an e-mail address, We've done somewhat of a hybrid, you know, we started off because we had some availability of providers and from nursing staff. So I really wanted to be getting understanding a little bit more about these drugs compared to just the EUAs, so we actually were doing some televisits and some phone visits. But as it's gotten more busy and then learning a little bit more about what the side-effects protocol might be, and finding that they are relatively safe products we've actually started testing out doing patient portal reminders. So we use our MyLVHN and we actually sent out a little bit of a questionnaire and then our team, will actually will be able to review them.

We're finding that, you know, that's given us a pretty good understanding of the side effects as well in that five-to-seven-day range. And again, you can always do you know, a mix of the two and it really depends, you know, on what is available at your institution. It's anything related to this, as I'm sure Dr. Bloch can attest to it's very labor-intensive and very resource-intensive. Again, this is not something that is intuitive I'd say to a network because now we're doing something where it's really flipping, and it's on it's head, we're worrying about something outpatient but it's sort of decreasing progression inpatient. Again I really feel that you pharmacists are- something that you can use o- inst- in this area.

Dr. Secor:
So now we get to the second polling question, and as a reminder you can either text ReachMD to 22333 or you can respond on your computer by entering pollev.com and then entering ReachMD. So this question: Which of the following COVID-positive patients would not be appropriate for administration of a neutralizing monoclonal antibody: Patient A, who is in the emergency department with chronic kidney disease on room air, patient B who is in an infusion center receiving chemotherapy who is on chronic oxygen but with no change in their requirement, patient C who is in a nursing home and has stable COPD on room air, or patient D who is in the intensive care unit on a ventilator receiving ECMO?

Mr. Kile:
Looks like have a pretty smart group here.

Dr. Secor:
Yeah, fast. They're fast.

Dr. Bloch:
And smart.

Dr. Secor:
So we'll give you a few more seconds to answer but it looks like you're- you're doing a great job and then Dr. Bloch will talk with you about what is the most appropriate answer.

Dr. Bloch:
So 86% chose option D and that is correct. It's a little tricky yeah, yay guys is a little tricky because we don't give ages and- and I did mention that age was a cutoff, but the one contraindication to giving these treatments is in critically-ill patient's hospitalized because, again, there's some preliminary data that suggests perhaps the outcome is worse in this population.

Mr. Kile:
Yeah, and that's really realizing y- when we delve into it too is, we always think of certain walls for infusions, and that doesn't really have to be the case. You know, it could be done in a nursing home, it can be done in a prison, it can be done in- in various places, and going out to certain centers if necessary as long as you meet the EUA and you feel comfortable and have the right ability to handle something like anaphylaxis, if undealt, unfortunately would happen.

Dr. Secor:
Well Mr. Kile, we're learning about neutralizing monoclonal antibodies and what to expect when administering them. How do you choose which patients to give- give it to?

Mr. Kile:
Yeah, great question. Next slide. So this is a quick example from earlier on. Now we- we've taken two modalities and Dr. Bloch will be a little bit more specific in relation to like an EMR-type of setup but I wanted to explain a little bit eh- w- with state difference and even an allocation difference. So, you know, in Pennsylvania when they were first rolling this out the allocations were not for sure. We didn't know exactly what we were going to get, so we really took the EUA and broke it down, the multidisciplinary group, and made tier levels and we- at first we didn't- because we didn't know how much we were getting. You know, it's really based off of, you know, how many patients were admitted, how many patients were in the ICU intubated how many positive tests we're having. We made these tier levels and that's really how we decided what- we- how we're going to move forward and then this example on paper, which we'll explain a little bit more further on, is we also want to get a bigger catchment area.

It's really important to be equitable as much as we could and that was really something important to us. The one on the- on the right side is sort of the version 2.0 and then we found out, you know, what ended up happening for us in Pennsylvania as the state had us start taking over the COVID vaccination they realized that, you know, networks are getting pretty good at handling the- the monoclonal antibodies so they gave that back to the distributor and we can pretty much order, you know, what we felt necessary. Now for us we are always were getting larger shipments of bamlanivimab so we stuck with that because we did not want to have a- more adverse events jump in between different, you know, products. So the- the next version as you can see there is a little bit more cleaned up and that's also because we were beginning to have, a lot of input from outside facilities - nursing facilities, and even some prisons, saying "Well, we need something simple we can work with to help have you help us in giving this product to patients." Dr. Bloch how did your institution look at this?

Dr. Bloch:
So yeah, we go to the next slide please. We struggled a little bit at the beginning with knowing how to best identify patients who are eligible for this treatment and what we started out with was using our electronic medical record which is in our case is Epic and having our IT group build us a report and I have a prototype shown here. What this does is it teases or- or data-mines all the patients who were outpatient or symptomatic and who had a positive SARS-CoV-2 PCR test. And we asked them to also include specific variables from the medical record, so of course, identifying these patients is only as good as the medical record documentation but this really helped in that we didn't have to go through every single chart of every patient. So I think this was a huge timesaver, but we recognized fairly early into the course of setting up our infusion center that just using the EMR and actively reaching out to patients was gonna miss some populations.

As a tertiary care center we have a lot of patients who come receive their very specialized care at Vanderbilt that may live in a community several hundred miles away, and so they would get their testing locally and if we were using our- our EMR mechanism to identify them would miss this group. So we also encourage providers to refer patients that they know of who have a positive test outside of the Vanderbilt system and that is a second way that we, identify patients.

The third way which we have tried to discourage although we certainly have enrolled some patients through this route, is self-referral and I think that's challenging on a couple of different levels because often these patients don't have a very robust medical record so it's hard to determine if they meet those high risk characteristics. But the other thing that's challenging in this group is if they don't meet some of the variables that make them high risk, there's sometimes a little tension in terms of them wanting a treatment that may not be available and we came up with having a appeals process where we have a separate group that looks at these case by case and decides if it's a reasonable therapy and if they meet the EUA criteria. Mr. Kile, what did you do at your institution, has that been initiated there?

Mr. Kile:
Yeah, it's kind of interesting geographically and probably demographically a little bit different but we sort of came to some of the same conclusions on how we handle it, and, you know, we had a core group that started this and as things grew, it expanded as I'll get to a little bit further on but the same thing is i- if there is a major issue the group, the core group that had the most experience goes back to that group and you know for better or for worse, we had something called, you know, for HIPAA Tiger Texting, and it's, you know, the-

text messaging that we use in our network and you're available 24/7 whether you want to like it or not, but, you know, we learned a lot because of that and everyone was in on the group and you get a lot of different mindsets and a lot of different people with a lot of different backgrounds so it's been very beneficial and really rewarding at the same time.

Dr. Secor:
Mr. Kile, I'd like to get your perspective on the use of neutralizing monoclonal antibodies. How can individual clinicians, many of whom are in primary care settings, find where orders of monoclonal antibodies can be written and are available?

Mr. Kile:
Yeah, it can be daunting. I- I think Dr. Bloch probably can, you know, attest to the same thing as she sort of said before that, you know, in our network we have one major, you know, hub of an 800-bed level 1 trauma center and we have two other different hospitals within the network that are the more community and get into more of the- you'd say the rural areas even over an hour, you know, a little over an hour away. So, you know, what do you do? You know, so one of the things is, you know, we've really reached out as much as we can with different meetings of course e-mail which some people read, some people don't.

What the other thing we've ending up doing and I've really been pushing is, you know, again my main job is stewardship, which this is a Brigham stewardship now but we get the Sanford guide, the stewardship assistant, and one of the reasons I wanted that is it's editable, so we actually have our- our COVID guidelines on that as an app version, so, instantaneously if I update it, it updates that. So this gave providers an instant knowledge of any changes that we're doing as part of our COVID steering committee and that's really, you know- you know- you know that's really done well, you know, people- especially this newer generation, they love things they can put in their pocket. The other way you can get it too, you see for us a little bit more senior and older crowd is the HHS website which a lot of people don't realize, they have a list of all the different places that receive these monoclonal antibodies. And I bet you the easiest way to find that is actually to Google 'combat COVID antibody.' Comes right up, you type in your zip code and it'll tell you what's local. Now it will not unfortunately say like where might be all the different little spots within a network but it at least gives you a really good starting point. But like anything else, it's just a lot of, person-to-person communication, you know, meetings just getting the word out as much you can.

Dr. Secor:
For those just joining us, this is ReachMD. I'm Dr. Mimi Secor and joining me to talk about neutralizing monoclonal antibody treatment for outpatient COVID-19 are Dr. Bloch and Mr. Kile. I want to encourage our viewers to submit questions for them by either typing them into the chat control panel on the left side throughout this program or in the comment box on- in Facebook live. We also have three polling questions placed throughout the presentation, so please take out your phone and text ReachMD to the telephone number 22333. Mr. Kile, what does the neutralizing monoclonal antibody program look like at your facility? What surprised you the most? What barriers have you faced, and how have you overcome them? And I know you've mentioned a bit about this already.

Mr. Kile:
Yeah, I'm actually going to answer the second one real quick though, what surprised me the most, and it's just how engaged the public was. You know, I thought a key message here to get to engage the public, you know, they are very tech-savvy, even our 70 to 80-year-olds, you know, with text messaging and such, and we're hearing everything in the news, you know, as soon as something's out there especially with COVID, people are really on it, they're really trying to understand what's going on. Even- and can say what their normal disease state's in, and such. Engaging the providers again is a little bit more work, because you know we're very busy trying to get the "How do you streamline the information they really need and connect them up?"

But really understanding that you're gonna need resources for this so this has kind of partially come from the top down. They didn't understand that you can't just throw this out there and get it done. This is not to say I'd say intuitive, in a grand sense because now we're now we're taking something that- we're trying to decrease someone being admitted. It's an infusion, you have to follow to the letter of the law and which we'll explain a little bit more in one of my next slides, so it takes a little bit of work. And it's very labor intensive in getting up and running.

And another thing that's really important too, is you don't want to forget to review the data once you do get things started up, you know, how can you make it better, you know, when we talk about equitability Dr. Bloch and I think it's important, you know, once your group's served and, you know, how does that come into play with who's been infected and who's getting infected? Yeah the time to positivity 'til the infusion and we talked about that too. You know, the closer you can get to it, is usually when you get the better feedback saying "You know I felt great the next day." And then just making sure per the EUA, and again, you know, putting it in there for us pharmacists. You know, we're great for that thing of you doing the follow-up between five to seven days, and again, if it gets really busy maybe pushing it out a little bit, and looking at how you're going to do that. And looking at admissions, looking at deaths, looking at EDRs, and just taking a, you know, a- a pause, look at what's been done and say "Hey, how can I do this better?" So, when you talk about therapy, you know, specific, um, and again you could say this is geared towards pharmacists, but I don't think so, not necessarily.

You know, we've used bamlanivimab again because it's been the general practice of what we had availability of and partially to what Dr. Bloch was discussing you know, sometimes you have to move between products a little bit. We've been fortunate we don't have to do that and I'm sort of happy about that because that's always when you have the chances of having errors made. One thing to know with bamlanivimab again is, usually- it's usually it's been an hour infusion of 250 mL, they more recently updated that. And now it's, you know, 50 mL/16 minutes, now, or up to I should say, I me- up to 50 mL/16 minutes. And that was done on, in 30 people. We made the decision not to do that we just felt there was more chances for side effects. We just wanted to take a step back and just, you know, keep up with what we were doing.

And another thing to know, is like, what kind of infusion sets are there? You know, and there's a filter that has to specifically go with it, making sure you have the product you need. With that now are going to be using a pump or are you gonna be using, actually there's something called a dial-a-flow tubing, so you don't even need to use a pump. Again, depending on where you're doing it which is always important, you have to consider that. And we're fortunate with the bamlanivimab, at least right now the single product. Now with the combination product, as Dr. Bloch had discussed, that's gonna put a little of monkey wrench in it, so we're gonna have to go back to the drawing board a little bit. But we can actually get something like a Vial-Mate adapter, which basically means you connect the bag up and you could have it stocked somewhere, so it decreases the amount of time from pharmacy to getting to the nurse on the unit. And just taking in that timing, and that prep time. So you know prep time in a bigger institution, you know, the level 1 trauma center.

And we were fortunate, again we have a newer ED but it- it's a little bit of a distance from the pharmacy and these are not products I can throw on my tube station and zip around. So it takes sometimes an hour, you know, realistically thinking of things that are going on, to an hour-and-a-half. It's an hour infusion. We've decided to keep it at that and then you have to have that hour monitoring time, so for us we always do block scheduling of four hours per patient, just to be cautious. So, an- and Dr. Bloch wh- what have you guys seen at your institution? How's has it been sort of the same and different?

Dr. Bloch:
So, it's very similar. One thing from the clinical end that perhaps I didn't realize that has added some time onto our infusions, is based on the population that is eligible. These folks often have, um, mu- multiple phlebotomies and their veins are challenging. And, so, we have really employed our IV therapy team and they have been phenomenal at finding access, but that's another thing we didn't anticipate that slowed down these infusion times.

Mr. Kile:
Mm, yeah. Really important. Next slide please. And this is an example again, you know, we want to make things as equitable as possible. We also want don't want to set ourselves up for failure. So we know we're fortunate, in we're a bigger institution we do have, you can say, quite a few resources. But even for th- us, this was difficult. You know, and I have to give a shout out to all of us everybody that works in health care now, because it's- it's- it's tough, you know, especially on our nursing staff and our, you know, everyone that's on the bedside. So now we have to find something else, to find, to be able to man.

So we decided what we're gonna do is we're gonna start in our ED in our bigger institution, to get, you know, to get the kinks out. We're also fortunate that we did open up the same week our new ED which actually is a hu- the biggest in the state. It's a 120-bed ED, and what we ended up doing is we actually carved out a part of that ED and called it an infusion center, and we actually made it such that, you know, the patients have much easier accessibility getting in and out, and taking into, you know, into consideration infection-control issues, as an example. And then from there, you know, we worked it out, so as you can see is you're moving to the right, we opened up other infusion centers, and starting off in some of the smaller hospitals' EDs.

But we haven't moved into having other parts of our network, other buildings that we've redesigned and, you know, staff to get to the point where we're at now, which we can, with slotted times, we can do about 130 infusions a week. And again if there would be a surge and, again, knock on wood, you know, the numbers have been going down for quite a while, but if we have to surge again we could actually surge into our EDs again and beyond if necessary.

Dr. Secor:
Okay that brings us to our third and last polling question, so I would encourage folks if you haven't already to text ReachMD to 22333. This question gets at what is the greatest challenge in your institution or for you personally in the use of neutralizing monoclonal antibodies? A) I'm concerned about the safety of these therapies, B) It's unclear which patients would benefit from these treatments, C) I'm not in a large medical center, so it's not clear how to connect patients with an infusion center, D) It's too late by the time they see patients recalling that 10-day window E) I don't know how to get infusions covered, or none of the above, F). So, I'll give folks a second to put in their- Please submit your question, your responses and then Dr. Bloch will discuss those with us.

Mr. Kile:
Interesting.

Dr. Bloch:
Okay there may be some late responses coming in, but what I'm seeing is three primary reasons or hesitation or challenge in- in getting these treatments to patients. The largest proportion of patient- of responders said that they are not in large medical centers, so it's now clear how to connect the patient with the infusion center, and then other significant barriers included: It's too late by the time I see patients, or I don't know how to get the infusions covered monetarily.

Dr. Secor:
So, Dr. Kile, it seems that connec- the connection piece is a challenge. How do you find ways to help make these connections between your work in the infusion clinic and with clinicians who are identifying appropriate patients?

Mr. Kile:
Yeah. Excellent question. And you know, it partially gets back to a whole bunch things we've talked about, but, you know, multidisciplinary is really important. And as I said before sort of having something that, you know, for me was killing two birds with one stone, but having something that is portable that our providers that are on the y- see more on the fringes of our network. But again, a lot of it goes into, you know, how you can bring them in in multi-prong approach, and Dr. Bloch's sort of talked about this too, and, we deserve sort of the same thing. You know, we have the Epic, we have the report that's very similar to hers. It's kind of interesting how we all sort of get to the same place eventually. To me it's subtle differences.

And now we use that but I'll be honest with you that- that- that approach actually took some time to get up and running, and, so, what we started with is, you know, providers and Epic acti- actively you know, our network providers putting in referrals. And you know, and now, we had a team that would look at them and make sure they're accepted, and then, you know, set them up. But then we also went again, 'What about those patients that are not actually our patients in our network but are, you know, they're our community members.' So, when it's the nursing homes or- or, you know, for example a prison that, you know, we wanna treat them just as well. It's equitability. And that's where those paper examples came into play. So we used a three-prong approach in, you know, in finding our patients as much as possible.

So, you know, as I sort of described a little bit, you know, there is that equitability, you know, how do you look- you can look at patients either progressively or prospectively, I'm sorry, or passively. And you know, the equitability definitely takes time and is a little bit slower. And passively, of course, you can get things up and running and I think in most institutions it's gonna be a little bit of both depending on where in the situation that you're in, and,you know, how far along you are on your project.

And this one is just a snapshot of data. I wanted to just give, you know, a little example of what we did and, you know, I said before we started, I took a stop, you know, to look at the data and see what has happened. And you know, we did this is the end of, January and we had 612 referrals in multiple avenues, you know, electronically, actively looking, or paper. And then adding that up to 247 infusions, and then I'm thinking just like anything else, you know, we're talking about this 10-day window. Some did fold out because of that, we didn't get to them in time, you know, you'd be amazed how many times the phone number that's on records is not the one that actually on, or the phone's disconnected. It took some time to find them, or, you know, as Dr. Bloch has just said, you know, patients might get worse, so there has been examples where when we did, we called them, they really didn't recommended they come to the hospital and get evaluated and some got admitted in that case.

But of that experience we took the stop, we took the pause and looked. And what was happening, and you notice here that the risk factors of CKD, chronic obstructive pulmonary disorders, diabetes, age greater than 65, immunosuppression, and that's the percent of the cohort at the time. And characteristically, we looked at the ages as well, you know, 60 to greater than 90, you know, amazing we actually worked with someone who was at 102. You know, that's 70% of our group, now, it's about 50/50 men and women and I've listed here Caucasian, more as a discussion point, in that, you know, the greater Lehigh Valley is about, you know, two-thirds Caucasian okay, and when you take the bigger group of looking at it, then the questions like 'What- during what parts of our COVID outbreak has there been a higher incidence of other ethnicities like the Hispanic population, you know, getting COVID? Now is there a reason why that says 87 and not 60- like 66? And we really did delve into that. And, you know, someone who is running to nursing homes, and someone who is related to other things. We know that in the literature that there are certain ethnic groups that, they do not want to get the COVID vaccine. They don't want to give a certain other types of treatment and it was the same thing here. We did see a little bit, maybe not statistically significant, but we did notice that there was patients that were declining it a little bit more in those ethnic groups than in the Caucasian groups. So it- it is- it's always worth taking a- a stop, a pause, and looking at what you can do better.

Dr. Secor:
Mr. Kile, what is the cost of these medications and does insurance cover them?

Mr. Kile:

Yeah. So currently the products are free, you know, the government has bought them and they're available. I guess I'm fortunate in Pennsylvania and at this point I can sort of order the one I want and how much I need. Looking at Dr. Bloch is still stuck to some extent based on allocations from the state, but the thing you have to remind the patients is the fact that they still have- there is still going to be possibly some charges related to the infusion, wherever the infusion is. Again we took a little bit of time because we had to find ways of, like, electronically allocating spaces, slots, that were coded to an infusion and not an ED visit which is much more expensive. Now knock on wood, I have not heard any feedback and usually if there is anything related to cost, we get- we hear about it pretty quick. I have not heard a problem in that relation. So it seems that payers are paying for the infusions. Now I can't say anything about the newest, you know, combination, the bamlanivimab with the atezolizumab. We'll have to wait and see with that one, I don't know.

Dr. Secor:
Dr. Bloch, what have your experiences been with treating COVID-19 patients?

Dr. Bloch:
Can I please have the next slide? So I was so interested to hear about the Lehigh Valley experience, because we took a slightly different tack. We recognized that these are all patients who were infected and infectious, and so we couldn't necessarily use our existing, ah, infusion centers and so we built a free-standing infusion center out of a existing parking garage. It does have heat and light so it is not quite as basic as one might think. But we have 6 chairs, our infusion time is 3 hours each, and so we have 4 seatings or the capacity to do 24 patients a day. And when we opened the center, we were really expecting that you know, broke up quite quickly and I think this slide shows very nicely that there is certainly sort of a startup period. So while we had the resources in place, you know, getting sort of the logistics down, identifying the patients and getting it sort of accepted by the community and by the patients really took a period of time, so I guess my advice would be don't expect to you know, be maximally full one day one.

The other thing we recognized, and I- I alluded to this earlier, we actively screen for patients, so we'll- we'll identify patients and call them but we do encourage our providers to also let them know- let us know about eligible patients. And this slide shows among patients who received infusions who had p- a primary care provider at our institution, there are some real super-users. So, seven per- seven providers accounted for a third of all infused patients and while we love their enthusiasm, we did worry a little bit that perhaps this was sort of skewing and then we wanted to make sure that there was, yeah, equal accessibility and equitable distribution of,medication to all.

So, I'm gonna end this session before the questions with a couple last thoughts. I think we pointed out that what works at one site may not work in another so Mr. Kile's approach may not be the perfect one for my site and neither of ourselves may be perfect for yourselves. So I really would encourage you to sort of think about what works in your community and your institution. We've emphasized the fact that patients need to be treated within that 10-day window so think about whether- how you are capturing patients will accomplish that and then while we've really focused on the benefit to the individual patient which is really important, I think what I haven't emphasized and would like to end with, is that in a period of time where we're in a public health emergencies and our institutions are- are- you know packed to the gills, our staff is stressed and overworked, it's really important not just at the individual level but again at the community level to decrease hospitalizations, and so I think that's one of the unsung benefits of these treatments. Thank you.

Mr. Kile:
Great.

Dr. Secor:
Thank you. So we're gonna take your questions now as we wrap up this session and the first question is for Dr. Bloch. Is there a difference in morbidity and mortality outcomes between convalescent plasma monoclonal antibodies and manufactured monoclonal antibodies, and can convalescent plasma monoclonal antibodies and manufactured monoclonal antibodies be given simultaneously? That's quite a mouthful!

Dr. Bloch:
So that's a bizarre, really good questions and you're getting at an important point which is they're sort of doing the same thing but the convalescent plasma is still in the experimental phase they're doing it, unh, in patients. I'm not aware of any studies looking at on outpatients, there may be. So it's again a different population that's being targeted with these. I think one of the advantages of the monoclonals is we have a much better sense of how much active antibody is in these products, whereas on the convalescent there is incredible variability. Some people who are very sick may have very poor antibody production and that product then may not be as effective as somebody who had a really robust innate immune response and so, I- I think that they're both have a role I think that they have not been studied head-to-head, and I think that they again have slightly different niches in terms of their uses.

Dr. Secor:
Thank you. Next question is for Mr. Kile. Not all hospital outpatient infusion centers are offering these infusions. Are there community resources for persons testing positive, meeting criteria, when the hospital they use isn't providing this service?

Mr. Kile:
Yeah. It- it- it's difficult and again I'm fortunate in the general geography of where I live on the East Coast being within an arm's reach of- a n- some kind of medical institution pretty quickly. It really goes back to that one slide we discussed about, you know, finding the places that it's being distributed to. Again infusion centers are in general, you know, usually there is a lot of oncology patients going there. So, most of those are not doing it for that reason alone and they're finding some other place that they can get patients in and out and keeping them away from those immunocompromised patient populations.

Dr. Secor:
Thank you. This question is for Dr. Bloch and then this'll be the last question. Obviously sooner is better but what is the therapeutic window that monoclonal antibodies will be helpful?

Dr. Bloch:
So I don't think that has been studied, so we do not have a clear answer, and actually the studies didn't look at onset of symptoms, they looked at time since testing which sort of throws a little bit of a wrench in how we use them clinically. It is at least some thought that maybe in some of these incredibly susceptible populations who really are not able to mount their own immune response, that maybe there's sort of a tail end where giving these antibodies might be, useful, but I think that this could only be studied in a, in a clinical trial because right now the EUA is very, very clear that 10 days is sort of that deadline. So certainly if an exception is made for good reason that could be considered but in general we just don't have any data about whether there's a, you know, a benefit to giving it after that 10-day period.

Dr. Secor:
Alright, thank you. Well, that's a great way round out our discussion on neutralizing monoclonal antibodies for the treatment of COVID-19. I want to thank my colleagues Dr. Bloch and Mr. Kile for helping us better understand the key role of physicians, nurse practitioners, PAs, nurses, pharmacists in this challenging topic. It was great speaking with you both tonight.

Dr. Bloch:
It was my pleasure, thank you.

Mr. Kile:
Thank you. Have a good evening.

Dr. Secor:
You too.

Announcer:
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