SPEAKER: Whereas a three-drug regimen is the recommended regimen for a great many of your patients, then adding a drug or more than one drug becomes an opportunity in some of your patients. And those are typically defined by in the guidelines those with more progressive disease, meaning they already have evidence of cavitation, or this is a relapse after a previous treatment, or, as I've defined, those patients who are seemingly refractory to treatment.

And so there are several opportunities that one can look at. Again, I recommend using susceptibility testing to look at what those options are, whether something like linezolid, or tedizolid, clofazimine, bedaquiline, amikacin, and which would be appropriate in your particular patient. That's what you're trying to decide. Now, if a patient presents with cavitary disease, we are already starting with that as an option. I'm going to talk a little bit more in the next module about different strategies of treatment using amikacin because it's the one drug that can come in different formulations for either systemic or topical delivery.

But one thing you have to look at aside from other aspects of the patient in terms of drug interactions or potential toxicities, QTc prolongation, perhaps, liver disease, you also want to know, what's the challenge of getting drug to the site of infection? And this is one of the challenges we see with cavitary disease because it's awfully difficult to know if you're getting a sufficient amount of drug into that cavity.

So one way of looking at success in your patients is looking at the cultures. And you will see in the literature numbers that are broadly describing expected success rates. So in nodular bronchiectasis, for example, you will see eradication rates, culture conversion rates that will be reported as high as 85%. But in many of the papers, what you find is that they are reporting their per-protocol treated patients as opposed to the intention to treat all the patients who participated. And so it might be that a more accurate estimate of actual culture conversion in many of those patients might be as low as 50%. And that's why you need to be able to look at susceptibility testing.

In those patients who are not responding-- and keep in mind that those patients who have cavitary disease will have a lower rate of culture conversion than those patients with nodular bronchiectasis. In those patients who are not achieving culture conversion, repeating that susceptibility testing might give you some clues as to whether-- what drug you might want to add. And what I mean by that is if you have a patient who is taking a good regimen of systemic therapy, say all oral drugs, and they're still growing the bug and yet the bug is remaining susceptible to all of those drugs, well, either your patient's not taking the medications or maybe that medication isn't quite getting to the site of infection. And so in that case, adding a topical agent, such as inhaled amikacin, might be preferred than to adding another systemic drug.

On the other hand, if you clearly have susceptibility changes, then you might need to pull in a drug that would give you perhaps a better combination of approach. So we take a much more aggressive approach to looking at microbiology, culturing our patients with great frequency, and sending them off for susceptibility testing to know if, in fact, they should respond to the therapy that they're on.