SPEAKER: So I have mentioned the use of amikacin in patients with MAC lung disease, particularly in patients who either have demonstrated progression because they have cavitary disease or they have demonstrated themselves as treatment refractory. There actually is a long history of, I mean, of amikacin use in the treatment of MAC, in part because it's been known to be a highly active agent in the laboratory setting. And then with clinical experience seeing the benefits of patients, it has become part of the regimen in many of those patients.

Typical approach might be systemic therapy for six to eight weeks after which converting to an inhaled form of amikacin. Now, on the one hand, the question of, well, why would you go systemic and then switch to inhaled? In many cases, it was actually because patients just don't want to tolerate longer, longer courses of systemic therapy because it's given intravenously. It's not a pill. And so inhaled becomes an option.

But actually, the real reason to consider systemic delivery versus inhaled is because you're trying to enhance getting the drug to the site of infection. And there aren't any great tests that you can do to demonstrate which one is going to increase delivery. You can't actually go and get airway specimens to tell you whether you're getting a sufficient amount of drug. You're using systemic levels to predict what might be getting there, but you cannot make the assumption or presumption that systemic therapy is always the best.

Fortunately, in the lung, we have the opportunity to give drug topically by the aerosol route. And actually, we have a very long history of aerosolized antibiotic use in the cystic fibrosis population. And we have drugs that are approved for the use of aerosol therapy, which we typically do. And so using inhaled antibiotics for the treatment of other infections is not foreign to us. We've been doing it for a long period of time.

So we've been using amikacin with great success and in our patients. More recently, we actually now have an approved product, a liposomal form of nebulized amikacin. And so one can ask, well, what's the choice in terms of using an IV formulation, nebulized, or the approved product? And I favor the approved product for a few different reasons.

Number one, when you have an option of a drug which is formulated for the airways, then that would be preferable than one which has been formulated for systemic delivery. And a key reason for that is that the systemic drug has preservatives that you may not necessarily want put into the airways. We went through this whole experience with inhaled tobramycin when we started with IV formulations in the CF population and then developed a formulation which was intended for the airways.

The second is that when you're using IV formulations, there's no pharmacovigilance. Nobody is tracking any adverse events or other consequences that might actually affect the way you think about these medications. And so using an approved product actually offers that potential benefit of having greater pharmacovigilance. Someone is required and obligated to track adverse events as best as possible.

But there's another reason that makes it attractive, and that's the fact that it's packed into liposomes. And so a challenge with microbacterial lung infections is that you certainly have some bacteria which are out in the environment in the open. And then you've got to put drug directly in that space to affect them. But many of those bugs are actually intracellular. And so what you'd like to have is some confidence that drug is getting into the intracellular space.

And the fact that those liposomes are present, they get sucked up into macrophages. And so it has been shown that there is a uptake of those liposomes into the macrophage, and so you are getting a greater concentration of drug in the intracellular space. Now, I confess that we haven't seen the evidence to show that that is associated with greater killing, but at least you have gone one step further to demonstrate that you're getting drug into the vicinity of where the bugs are.