

**SPEAKER:** So I think some of the key points from that case are that IV amikacin can be very difficult to tolerate. There are significant toxicities, including the ototoxicity. And I would not minimize the tinnitus that happens in our patients, because that can be incredibly life-altering, vestibular toxicity, and then again, in some patients, renal insufficiency. So to be able to have a topically administered form of inhaled amikacin is very important. We did not see any renal insufficiency in the patients that were in the study who were administered inhaled liposomal amikacin.

The side effects of inhaled therapy are not trivial, but they are side effects that resolve in the vast majority of patients. And so providing reassurance and coaching to the patients is of paramount importance. And even more important, it's setting the expectations that those side effects may be present, but they will get better over time.

And there are some therapies that can help with those side effects. For example, in patients that have a lower IPV1, that have COPD or asthma, they are going to benefit from the pre-treatment with a bronchodilator before administering the inhaled liposomal amikacin. In other patients, it's just giving them information about certain kinds of throat lozenges that might help with a sore throat while they're inhaling the liposomal amikacin. But these side effects, in general, were tolerable, and very few patients had to actually discontinue treatment in the study because of the side effects related to the airway irritation.

And as far as the tinnitus, I wanted to just elaborate on that for a moment. As far as the tinnitus, I see tinnitus quite frequently with intravenous amikacin. The longer someone's on that drug, it's a cumulative effect. Ultimately, they will start to develop tinnitus. They only saw tinnitus in about 7% of the patients that were in the inhaled liposomal amikacin arm. And when checking drug serum concentrations, they were undetectable in these patients. So whether or not it was actually related to the drug, I think, is up for debate.