DAVID A. KATZKA: Hello, my name is Dave Katzka, and I'm the head of the esophogeal interest group at the Mayo Clinic in Rochester. And I'm here to discuss a study that we performed entitled "Which Upper Airway Symptoms Respond to Acid Reflux Therapy?"

There are several questions we wanted to answer in this multi-discipline study. The first is, by looking at a group of patients who have high-grade erosive esophagitis, to determine if timing of PPI dose makes a difference as far as their overall healing rate, which is an issue among patients, and particularly patient compliance. The second issue is that, knowing that there are many upper airway symptoms which may be causative from gastroesophageal reflux, is to see what the correlation of healing of erosive esophagitis is to possible resolution of upper airway symptoms, and therefore try, as many others have, to determine the relationship of upper-airway symptoms to reflux esophagitis.

So the next question is how do we do this? And our methods involve randomizing 80 patients in an open-label study to two preparations of bicarbonate preparation of Omeprazole. We used either a morning dose or a nighttime dose, and split this evenly through the 80 patients. We also measured symptom correlations, specifically by typical reflux symptoms as well as upper airway symptoms, by validated scoring systems, and determine statistically the correlation of these symptoms to, again, healing of erosive esophagitis.

So what did we show? We showed several things from the study. Importantly, we demonstrated about 96% healing of erosive esophagitis in patients with grade C and D LA erosive esophagitis, which is rather remarkable. And even more impressive is, despite the high-grade injury, 83% of patients had complete healing with eight weeks of our bicarbonated Omeprazole preparation.

We also found that it didn't matter whether this preparation was taken in the morning or at night, going against some of the prior data suggesting that the greatest benefit of this Omeprazole preparation is nighttime, due to its suppression of nocturnal reflux. So whether this indicates that daytime reflux is more important than we thought, or this preparation has a more sustained effect, even when taken in the morning, in controlling nocturnal reflux, is unclear. But certainly, it makes it much easier for the patient to take this dose, whether in morning or night, according to his or her schedule.

What was also interesting in this study is the fact that many patients were asymptomatic as regards typical reflux symptoms. Specifically, we found that 14 of the 80 patients were completely asymptomatic despite having grade C and D esophagitis, and remained asymptomatic even after healing. And what this suggests to us is that patients are truly asymptomatic with high-grade disease, and not so much that they have subtle symptoms which they don't realize are symptoms, which then resolve after healing of therapy.

This is an important issue because, when patients have such advanced disease and therefore may be at risk for stricture formation or Barrett's esophagus, it's important to encourage them to take their medication to the end point of healing, and not so much that these patients have to eradicate their symptoms, which again, may be nonexistent.

We also obtained interesting data when looking at upper airway symptoms. And when we looked at six upper airway symptoms, particularly cough, throat clearing, sore throat, hoarseness, Globus, we found that some symptoms did correlate with healing of esophagitis as regards improvement, whereas other symptoms did not. And specifically, we found that dry cough, Globus, and sore throat completely resolved when there was complete healing of esophagitis.

So this is important because there's been a lot of controversy establishing whether these symptoms are indeed due to reflux when a patient presents with these type symptoms. At least in our study, it suggests that certainly in patients with underlying severe reflux, these symptoms are indeed reliably due to severe acid reflux.

On the other hand, when we looked at symptoms of nocturnal cough, throat clearing, and hoarseness, we found that although many of these patients did improve with our preparation of Omeprazole, in fact some improved yet had persistent erosive esophagitis, and some had persistent upper airway symptoms yet had healing of esophagitis. So it's important to realize that, despite the fact that we could attribute these latter three symptoms to reflux, it's difficult to attribute them to the same mechanism by which erosive esophagitis is caused.

And this raises the question as to whether these latter three symptoms, again, nocturnal cough, throat clearing, or hoarseness, are due to the same mechanisms of reflux or other mechanisms, for example, non-acid reflux or whether these symptoms arise from much smaller levels of acid reflux, those that cannot be controlled with those required to heal erosive esophagitis. We obviously don't know the mechanism, and certainly further studies with pH impedance would be helpful here.

So, as you could tell, we have many important findings from this study. Again, to summarize, the key points would be the following.

First is that, with Omeprazole preparation using bicarbonate, whether this preparation is taken either in the morning or at nighttime, we still are very successful at healing patients, even with advanced-grade erosive esophagitis, specifically LA classification C and D.

We also found that a sizable proportion of patients, despite advanced erosive disease, are completely asymptomatic as regards typical reflux symptoms, and remain asymptomatic, suggesting that there is still a sizable proportion of patients who are hypo-sensitive. And therefore, treatment for these patients has to be aimed at endoscopic healing and prevention, hopefully, of future complications, as opposed to worrying about symptoms.

As regards upper airway symptoms, we know that there are some symptoms that do correlate with severe acid reflux, particularly that of Globus, cough, and sore throat, and that with healing of high-grade erosive esophagitis, we might be hopeful and expect that the symptoms should resolve.

However, some upper airway symptoms, such as sore throat-- such as throat clearing, nocturnal cough, and hoarseness, do not necessarily correlate with esophageal healing, and therefore suggest to us that either not all these symptoms are from reflux, that perhaps they are from reflux but from different mechanisms of reflux, such as lower levels of acid exposure, or perhaps a reflux arc mechanism mediated through non-acid reflux. Thank you.