

ROBERT S. ROSENSON: So when we evaluate our patients, I think it's very important to support evidence-based therapy. And that therapy includes maximally tolerated statins. Not everybody can tolerate a statin at the maximal prescribed dose, the high intensity statin. But one needs to try to get them on a high intensity statin.

Why do we use ezetimibe? Ezetimibe is a generic. It's been supported in a clinical trial, the IMPROVE-IT trial. But the question remains, what about individuals who have very high LDL cholesterol levels, where one might anticipate that the LDL cholesterol level would be inadequate? My approach is, I still try high intensity statins and ezetimibe.

Ezetimibe achieves its LDL cholesterol lowering effect in about two weeks, so one doesn't need to wait several months for a high risk individual to evaluate them. And actually, this approach makes it easier for the insurance process, because you're going to get a rejection if you send them a patient who's on a statin and not ezetimibe.

We also need to keep in mind that certain individuals who have polymorphisms on the Niemann-Pick protein that allow for a greater reduction in LDL cholesterol. We see some patients, maybe about 1% to 2%, who have a 60% reduction in LDL cholesterol with ezetimibe, so one needs to try. I think that this process allows for efficiency and also keeps health care costs into perspective.

Now, what about health care costs with the PCSK9 inhibitors? There were insurance agency evaluations that were saying that, based on the FOURIER trial, based on the ODYSSEY Outcomes study, that the therapy was too expensive. Recently we've seen a reduction in the price to meet these ICER guidelines.

Another population that we might consider for PCSK9 inhibitors are those who have failed multiple statins, and statins at the lowest dose, as well as ezetimibe-- the statin muscle intolerant individual. In a paper that was led by Colantonio that I participated in, health care expenditures for patients with a myocardial infarction who have statin muscle intolerance are about \$14,000 more in the first year after their event.

So one needs to consider the bigger picture. Spending money on medication is one factor, but avoiding the recurrent hospitalizations or recurrent myocardial infarctions, the increased visits that occur when you try and evaluate or achieve LDL cholesterol lowering in a statin intolerant patient needs to be balanced against these higher health care expenditures.

So I think that we're really in a changing environment with regards to the PCSK9 inhibitors, based on the cost reduction and the ICER recommendations and the pharmaceutical companies that have met those expectations based on cost effectiveness, so that we've seen a synergy in this partnership related to health care economics. And that will allow more patients to benefit from this highly effective therapy.