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Understanding Trial Data

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Samson:

This is CME on ReachMD, and I'm Dr. Susan Samson. Today I'm breaking down the treatment landscape and clinical trial data for acromegaly.

Let's talk a little bit about somatostatin receptor ligands. We can break these down into first and second generation. The first generation would include octreotide and lanreotide, which both bind to somatostatin receptors on the surface of growth hormone tumors to dampen growth hormone secretion, decrease IGF-1, and hopefully shrink the tumor.

Now that is in comparison to second generation, which is really comprised of pasireotide. Pasireotide also is a somatostatin receptor ligand, but it has higher affinity for somatostatin receptor 2 and 5, so this means that pasireotide may work in some patients with more difficult-to-control tumors. And there certainly have been head-to-head trials that have compared how first-generation and second-generation somatostatin receptor ligands work in our patients. For example, there are trials which have looked at medication-naïve patients, so they've never had a medical therapy for acromegaly, and they could be post surgery or just not being able to go to surgery but needing medical therapy. And when those patients were treated with pasireotide versus a first-generation somatostatin receptor ligand, the degree of IGF-1 and growth hormone control was increased in patients on pasireotide.

We also know from the PAOLA trial that patients on octreotide or lanreotide maximum dose that did not have a controlled IGF-1 – in other words, it was over 1.3 times the upper limit of normal – if patients were switched to pasireotide, either 40 mg or 60 mg, their IGF-1 control improved in comparison to those that stayed on their initial first-generation somatostatin receptor ligands. So I do think there is a role for pasireotide in patients who are not fully controlled, and we have to take into careful consideration the tumor characteristics and the patient characteristics when making the decision to use pasireotide after octreotide or lanreotide.

Now there's also some data that has looked at combining pasireotide with pegvisomant. For example, if you wanted to look up the PAPE study. This was a very interesting trial where patients who were on pegvisomant had their dose of pegvisomant decreased by 50%, and if the IGF-1 remained controlled – that is, less than 1.2 times the upper limit of normal – they could be switched to pasireotide. Or if they did not remain controlled, pasireotide was added to pegvisomant. And what we learned from that trial is that the combination therapy of pasireotide and pegvisomant was able to control IGF-1 in many patients, but unfortunately, the addition of pegvisomant did not mitigate the hyperglycemia. But nonetheless, pasireotide was pegvisomant sparing, so if you think about the cost of combination therapy, there was definitely a positive side to that.

The other role for pasireotide is really a nose that you have maximized your first-generation somatostatin receptor ligand, and the patient just has not responded fully or they are unresponsive. Some of the characteristics of those types of patients could be a patient with a sparsely granulated tumor, which can sometimes be seen as a tumor with T2 hyperintensity on MRI. It might be a patient who has a tumor with poor expression of the somatostatin receptor 2. So there are definitely patient characteristics that might point toward the need

for pasireotide in these patients.

So I hope I've given you some tips that you can put into practice. Thank you for listening.

Announcer:

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