Are There Clinically Significant Differences Among the Third Generation EGFR Inhibitors?

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TRANSCRIPT
**Dr. West:** We now have two, hopefully very soon, commercially available third-generation EGFR inhibitors, osimertinib, and also rociletinib. These agents really seem pretty comparable in efficacy – some differences in toxicity. What do you see as potentially clinically significant differences? If you had both available, how would you approach a patient with T790m mutation-positive acquired resistance?

**Dr. Horn:** So yeah, I was going to say their similarities are in the T790m-positive patients – there are some differences in the negative patients.

**Dr. West:** We’ll cover that too.

**Dr. Horn:** But, I do think that – I’m going to use their numbers because they’re easier to remember than names, 9291 (osimertinib) is a little better tolerated, in my experience, than 1686 (rociletinib), the Clovis drug. I think that, for patients who are going to be on the Clovis drug, we’re going to have to be very diligent about monitoring their blood sugars because the hyperglycemia is a real toxicity that can be quite significant. Now, 9291 did have more rash, but, for these patents, they’re used to be dealing with a rash, they’ve had rashes for years because they’re been on erlotinib, gefitinib, afatinib, and even the rash of 9291 is less severe than the first and second generation agents.

**Dr. West:** Clearly, these agents will do well with their marketed names, given how hard they are to differentiate based on their names now! Ben, what do you think here?
Dr. Solomon: Yeah, look, I agree. I think they're both very active, they both have response rates of about 50-60% in patients that have progressed on Iressa or Tarceva, but they are different in their toxicities, and rash and diarrhea with the AZD9291 compound, which we believe to be called osimertinib, today, is generally manageable and, for patients, quite similar to the rash they might have experienced, and diarrhea they might have experienced before, or even milder; whereas, hyperglycemia is a completely new toxicity and I think, again, patients need to be vigilant about this toxicity, and doctors need to know how to manage this toxicity with the use of Metformin and monitoring of blood glucose, so it can be a little bit trickier.

Dr. West: I must say that, about a year and a half ago, when these data were first presented, I thought that managing hyperglycemia with some Metformin seemed pretty trivial for cancer patients who have an effective treatment against cancer – but when there's an alternative that doesn't have that, and, in some of my patents I've had challenging nausea and anorexia, you know, just diminished appetite, weight loss, fatigue – my experience has been that it’s not a trivial challenge, at least in a subset of patients. That said, they’re both a real advance.