Are There Clinically Significant Differences Among the First and Second Generation EGFR TKIs (Iressa, Tarceva, Gilotrif)?

TRANSCRIPT
Dr. West: What’s your sense of whether there are clinically significant differences among the first or second generation EGFR tyrosine-kinase inhibitors – that is, Iressa, Tarceva, Gilotrif. Are these agents that you consider to be really interchangeable, does it matter what actual mutation the patient has, or do you think it’s really completely a dealer’s choice? Ben, why don’t I start with you?

Dr. Solomon: Yeah sure, so there’s certainly differences at the clinical level – the second generation inhibitors, afatinib and dacomitinib, do have a lot more toxicity. They’re very potent inhibitors of both mutant and wild type, or normal, EGF Receptors – so skin, nail toxicities, diarrhea, are more common with those drugs than with Iressa or Tarceva. In terms of the question of efficacy, I think we’re all waiting to hear the results of a head to head study; it’s very difficult to compare different phase three studies, but there is some interesting data that has been presented with afatinib from, actually, a couple of different studies, which, admittedly, was a subgroup analysis, which suggested that in the subgroup of patients that had exon 19 deletions, as opposed to the group that had LA58r mutations, there was a survival benefit. But, it’s not clear whether that same difference might have been seen in the other studies with the other drugs, as well, if it was looked for in sufficient numbers. So, to my mind, it’s an open question about whether there’s increased efficacy. I guess the other point Leora alluded to – occasionally, you do see responses to afatinib in patients who have progressed on Iressa or Tarceva, which may suggest some differences in efficacy.
Dr. West: What are your thoughts on whether there are clinically meaningful differences between them, and whether there is a significant difference between the main activating mutations for all EGFR TKIs, or for afatinib.

Dr. Horn: So, I completely agree with Ben that the toxicities are clinically meaningful and different between the different agents. LUX-Lung 7 is close to accrual, and so, hopefully –

Dr. West: That’s a trial directly comparing afatinib to gefitinib (Iressa) in EGFR mutation-positive patients, first-line.

Dr. Horn: And it’s primarily in Asia because gefitinib, up until a few weeks ago, was not available here.

Dr. West: I just learned that it’s actually half Asian and half European, which will be helpful to know because we do struggle with the question of whether the results out of Asia are completely generalizable to non-Asian populations. So, I think we’re going to be getting the results of that in the first half, hopefully, of 2016, at least some of the results, and, so, that will hopefully, provide – shed some light on this controversial question.