Direct from the World Conference on Lung Cancer 2015

What Are the Treatment Choices for EGFR Mutation-Positive Acquired Resistance in Patients Without a T790M Mutation?

TRANSCRIPT
Dr. West: What’s your approach for patients with acquired resistance who do not have a T790m mutation? We’re going to be doing this testing routinely now, and we know that acquired resistance in patients with an EGFR mutation is mediated by this T790m mutation in about 50-60%, which leaves nearly half the patients without that option. Do you think these agents are appealing in this setting, and what would you do outside of a protocol setting for them. Ben, why don’t I start with you?

Dr. Solomon: Yeah, so, with both compounds there are some data to suggest that there are patients who have biopsies that are reported as being T790m-negative may respond. Now, in part, that may represent that fact that the T790m result is a false negative, and that might be due to tumor heterogeneity, but there are responses seen, and the response rate with rociletinib, for example, is about 30%, but it is lower than within the T790m-positive. Off the study, I think my standard practice would be to use chemotherapy in those patients, but given that many of these patients will have tumor tissue available for testing, I think it’s worthwhile looking for other mechanisms of resistance. For example, MET or HER2 which might guide patients to a particular clinical trial that would benefit those patients. There was some interesting data that was presented in the presidential symposium today by Daniel Tan from Singapore, who sequenced a bunch of tumors from patients who had progressed, and in some of those T790m-negative patients, they found a high mutation load, which may predict that this subgroup of patients may be the group that might respond to immunotherapies, but that’s early days, and again, another hypothesis that we need to test and practice.
**Dr. West:** Leora, what’s your approach for the T790m-negative folks?

**Dr. Horn:** So, outside of a clinical trial, chemotherapy, or I do use afatinib and cetuximab in some patients. I do warn them that the rash could be a little bit more severe, but that is a, often, go-to regimen, especially for patients who are not wanting or are not ready to switch to chemotherapy.

**Dr. West:** Right, it’s interesting, I mean, harkening back, it’s now data that are a few years old and have been slow to get corroborated, but the afatinib combination with cetuximab looked encouraging in, not just the T790m-positive, but the negative patients, but as you say, the toxicity issues can be pretty challenging there and we need to get more data in a larger setting than the initial reports were – but interesting.

**Dr. Solomon:** Yeah, I agree, those data look good. In Australia, our issue is, neither of those agents are funded and I think it’s a very expensive combination for our patients to pay for.

**Dr. West:** No question.

**Dr. Horn:** Definitely.
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