Are There Distinctions Among Currently Available Oral EGFR Inhibitors for EGFR Mutation-Positive NSCLC?
For patients who are diagnosed with EGFR mutant lung cancer, there’s a choice of initial therapies. There are three FDA approved EGFR tyrosine-kinase inhibitors – these are gefitinib (with the trade name Iressa), erlotinib (with the trade name Tarceva), or afatinib (with the trade name Gilotrif). These three drugs have been developed over the course of the past 15 years or so, and they have a great deal of similarity in that all of them target wild-type, or regular EGFR, the EGFR protein that’s found throughout your body, and they all have different doses – I think that’s probably the difference that we see among them, is largely related to dose. If we look at clinical trial data, and to talk with physicians who have given all three drugs, I think the general consensus is that, at their recommended dose, the FDA approved dose, that the side effect profile, particularly with regard to rash and diarrhea, is probably the lowest with gefitinib, rash and diarrhea is a bit higher with erlotinib, and finally, with afatinib, it’s the highest.

Now, for a given patient, this is largely irrelevant, given that we adjust doses to make it so the patient has a tolerable side effect profile, so that if we’ve given erlotinib at the FDA approved dose and found that it causes too much rash, we generally back down the dose. Similarly for afatinib, we will reduce the dose of afatinib to make the rash and diarrhea more tolerable.

So, when taken together, picking the right EGFR tyrosine-kinase inhibitor, or picking the one that works for a given patient, is a lot about what the physician is comfortable with, and finding the right dose for that patient.

Now, importantly, I’ll contrast these first or second-generation EGFR tyrosine-kinase inhibitors like gefitinib, erlotinib, and afatinib, with the newer
tyrosine-kinase inhibitors like rociletinib, or mereletinib, the so-called third-generation, or T790M specific drugs – these have a very different profile of activity, and we still have yet to learn as much as we need to know about their side effect profile.
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