



CASE BASED PANEL DISCUSSIONS: LUNG CANCER

EGFR Mutated Adenocarcinoma

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TRANSCRIPT

Dr. Stephen Liu: Out next case here is a 72-year-old never smoking woman, who undergoes primary surgery for a node-negative 4.1 cm left lower lobe, moderately differentiated adenocarcinoma. So, surgery first 4.1 cm testing shows an activating EGFR mutation. But this patient is reluctant to pursue chemotherapy, far more amenable to targeted therapy. So, question: Do you press her to receive post-operative chemotherapy? Osimertinib? Neither, both? Your approaches here. Ana, I think this is a very real-world situation. So, what's your approach there?

Dr. Ana Velazquez Manana: Definitely, very real-world. I think this is something that we all encounter. I would show them the data. My recommendation would be to do chemotherapy followed by also Osimertinib. Again, we're trying to think of what has shown the benefit of overall survival, which chemotherapy would. Also, **[01:24 inaudible]**, I think it's to be shown that we are excited about the potential. And then going through the supplement figures and **[01:35 inaudible]** that we saw from the ADAURA study, in which patients who received chemotherapy had better responses overall, and trying to speak with the patient about what the options or the outcomes here are, and our data shows. I think, in that study, of course, I believe it was around 40% of the patients did not get chemo, which is a limitation. But in those subset analyses, they were able to compare those who got chemo had better outcomes in terms of time to recurrence, which is something that I would explain to the patient, particularly, and try to pursue that route.

Dr. Stephen Liu: Happens quite a bit. I think that chemotherapy is not something that most patients are excited about. Justin, is your approach any different here?



Dr. Justin Gainor: No. I do think one of the challenges when we're talking about all of these different studies is the changes in staging classifications, where we talked about Stage IB, and just remembering that many of the studies we're discussing here – IMpower010, ADAURA – they were conducted under the seventh edition. We're now in the eighth edition. And there was a critical change in IB to IIB in the different staging system. We've encountered this in our tumor board where people are saying one thing; they keep talking about IB, and then, "Wait, wait. Is what you're talking about the same I'm talking about?" So, we have instituted some guidelines in our tumor board around PD-L1 expression. And then around T-stage and which edition we're using, just to keep everyone on the same page. So, I think, in this patient, this would have been in the seventh edition on IB, in the eighth edition of Stage II, this is where I would recommend adjuvant chemotherapy. From my perspective, I think until we get curates higher, we shouldn't necessarily be de-escalating therapy. And chemotherapy is the one agent here that has an overall survival benefit that's been demonstrated. So, I would offer both adjuvant chemotherapy as well as adjuvant Osimertinib. And if at the end of the day, though, the patient said, "You know what? I'm concerned about adjuvant chemotherapy. When I look at the data, only a 5% to 10% absolute improvement in survival. Thanks, but no thanks." I would still give adjuvant as opposed to Osimertinib. There was a follow-up publication in JTO or CCR showing that whether one received chemotherapy or didn't, the hazard ratios look pretty comparable, may be off by a little bit. But I think in that context, I would certainly offer it with all the caveats of toxicity, relapse-free survival, as a surrogate for overall survival, all of those things.

Dr. Stephen Liu: Our approach is very similar. We're just very upfront about the modest benefit. It's a real benefit in a lot of cases. But I think that we all have different values. And if for a modest benefit, some say that's just not something that sort of aligns with their values, then I agree. I don't think that any of us would insist on it. And I think that Osimertinib still plays a role there. So, important marks again in the future. Hopefully, we'll be able to use some sort of biomarker, some sort of test of MRD to really see what people need and don't. But I think that we will acknowledge that adjuvant cisplatin-based chemotherapy can provide a survival benefit in resected lung cancer, but it is not BEP germ-cell tumor. So, it's a modest benefit, and it comes at the cost of some talks. And if someone's got a borderline creatinine clearance, maybe that tips the scales in a different direction. But this is definitely a very real situation, Osimertinib clearly playing a role there. Chemotherapy, it sounds like we're all recommending it, offering it, and then discussing it with the patient.

Dr. Justin Gainor: Stephen, you raise a really good point, which is assessments of MRD. For all of us, we're thoracic spin ahead, in terms of molecular testing and targeted therapies, but the GI space now is much farther ahead than us in terms of incorporating MRD assessments into therapeutic decision-making. They already now have Phase III data that we recently saw at ASCO. So, I think that's something where can we use MRD assessments to either intensified or de-intensified therapy in the right context. I think that's where we need to be moving.