



2022 Case Based Panel Discussion

Treatment Options for EGFR+ NSCLC

Speakers:

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TRANSCRIPT

Dr. Dagogo-Jack: Just to move to the next aspect of this this patient's presentation. And so same slide, new data in the blue. So the molecular testing that she has shows an EGFR L858R. And so this is one of the most common EGFR mutations. And so if we recall, that's one of those mutations that was highlighted as being excluded from participating in the chemo plus nivolumab study or receiving this particular regimen. And so I'm going to ask Natalie, in the context of finding this mutation, how do you tend to proceed in stage three?

Dr. Vokes: I think this is a really important point and something that is coming up more and more now that we have this regimen approved. So we had talked at the beginning of this session about sending molecular testing and how important that can be for metastatic patients. And historically, we didn't have it wouldn't change our guidelines or our treatment when we had that information for earlier stage patients. But now that we have this approval in several other studies, we do actually use this genetic testing information to vary our practice.

So as you highlighted, Checkmate 816 excluded patients with EGFR mutations. And in general, I think most of us think of patients with EGFR mutations as being less sensitive or responsive to immunotherapies, and we tend not to use immunotherapies before we use EGFR directed drugs. So for this case, I would proceed. I would talk closely with the multidisciplinary team and see if the surgeons felt that preoperative treatment would help them have a better surgery.

And if that's the case, then we might go ahead and do neoadjuvant chemo. But holding the nivolumab, if they felt that they could take her to surgery safely and effectively up front, then we might do chemotherapy afterwards and I think We'll talk a little bit more about EGFR drugs in that setting as well.



Dr. Dagogo-Jack: Yeah, I think since you brought it up, I think it's worth talking about. Right. And so, so far we've been talking about chemo and immune therapy, but there's a different type of therapy called a targeted therapy. And one of these targets, or actionable mutations, as Kathryn mentioned, is EGFR. And so we do have a proof therapies for both advanced meaning stage four, as well as surgically removed EGFR lung cancer with EGFR mutations. And so, Natalie, you started talking about that a little bit.

And so do you mind just catching all of us up to speed?

Dr. Vokes: Yeah. So we had an important study that came out a couple of years ago that looked at giving EGFR drugs after patients had their surgery, had their tumor surgically resected, then they received standard of care, post-surgical chemotherapy. And then they looked at whether giving an EGFR drug for three years would help. And they looked at basically whether or not the disease was coming back. So that event free or recurrence free survival. And then they also looked at overall survival. And we're still learning some of that data.

But there was a very dramatic effect in terms of preventing the cancer from coming back that led to the approval of giving the drug in in the post-surgical setting. So I think a lot of us have now adopted a little bit of a immunotherapy targeted therapy treatment for if a patient has an EGFR mutation, will preferentially give them chemo and an EGFR drug. And if they don't have one of these targetable alterations, then we put them on the chemo immunotherapy pathway.

There's a lot of complexity as to which targets fall into which of those forks. I can see on the bottom of this slide you said, what if molecular testing showed a RET fusion? So there's a lot of complexity as to which patients get funneled away from immunotherapy. But EGFR is the clearest cut example because we do have that approval for the EGFR inhibitor in the post-operative setting. It is worth adding that we don't have an approval to give EGFR pre surgery the EGFR inhibitor pre surgery.

I will say that that is something that is under current clinical trials. And in my own practice I have every so often managed to do it up front. And I do that in patients who have a big bulky tumor where I really want to maximize my upfront response in those patients. I have kind of worked to get insurance approval to do it in that setting. But that is not strictly according to the FDA label.

Dr. Dagogo-Jack: And I think that that's important, that sometimes we we individualize therapies if we're able to get the insurance to give us the therapy. But I think one key area to stay tuned is this new Adaura study, so similar-ish design to the Checkmate 816. But instead of using chemotherapy



immunotherapy here, you're using that EGFR targeted therapy called Tagrisso or Osimertinib. And so I don't want us to get bogged down in the details of this study, but just this is a similar population of patients who have stage two or stage three lung cancer.

So this is our modern staging system and some patients will get placebo plus chemo, so the standard of care. Some will get Tagrisso or Osimertinib plus chemo, and some will just get Tagrisso or Osimertinib by itself. We're looking at some of those key endpoints that Josh mentioned already. So pCR, MPR, which is a kind of a less robust version of kind of having all of the tumor killed off by the treatments. And then we're looking at the survival endpoints as well. And so this is an area to keep an eye out for.