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Applications of Emerging Data in Resectable NSCLC

Announcer:
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Dr. Liu:
This is CME on ReachMD. I'm Dr. Stephen Liu, and today I'm here with my colleagues, Dr. Joshua Sabari and Dr. Susan Scott, to talk about resectable non-small cell lung cancer.

Let's begin with discussion on the integration of immunotherapy. Susan, how has the integration of perioperative immunotherapy reshaped your approach to managing resectable non-small cell lung cancer?

Dr. Scott:
Thanks, Stephen, absolutely. This has completely reshaped our approach in the past couple of years. We are now needing earlier molecular testing to determine which patients are appropriate for perioperative immunotherapy. We're needing a multidisciplinary approach up front, where medical oncologists are becoming involved in the care before surgery, where sometimes we were consulted after surgery. And we're starting to use kind of a sandwich approach for many patients, where we give systemic therapy both before and after surgery. So it's really changed a lot in the past couple of years.

Dr. Liu:
Yeah, I think all for the better. Josh, can you start by summarizing the findings of the CheckMate 816 study, looking at the addition of neoadjuvant nivolumab, a PD-1 inhibitor, to chemotherapy in patients with early-stage resectable disease?

Dr. Sabari:
Yeah. These are patients with untreated, resectable stage IB to IIIA disease. Large randomized controlled trial, phase 3. Patients got standard chemotherapy, carboplatin, pemetrexed, plus nivolumab at the 360-mg dose versus chemotherapy alone. And as Susan mentioned, chemotherapy alone has not been a successful sort of neoadjuvant or really adjuvant strategy, in my opinion. Primary endpoint here being event-free survival, as well as complete response rates.

And we saw dramatic improvements in event-free survival, 31.6 months for nivolumab versus about 21 months for chemotherapy. On the heels of these impressive complete response rates, or pathologic complete response, seeing no viable tumor post-resection. So if you received chemo plus nivolumab, 24% of patients achieved this complete path response, versus only 2% for chemotherapy alone.

And what was really exciting in ASCO 2025 is we saw some of the updated 5-year OS data. And not only is it an improvement in event-free survival or an improvement in complete path response, but there also is a dramatic improvement in overall survival. And I think that's really the name of the game in this patient population.

Dr. Liu:
Yeah, I think a really important update there, that improvement in OS, very impressive long-term numbers there.

Susan, though, what about perioperative approaches we saw with pembrolizumab? KEYNOTE-671 also showing a survival benefit. What are the data from that study?

Dr. Scott:
Yeah, so KEYNOTE-671 added pembrolizumab to chemotherapy both preoperatively. This was 4 cycles of chemo/pembro compared to 3 cycles with nivolumab in CheckMate 816, and then a year of pembrolizumab after surgery. This showed a dramatic improvement both in event-free survival and pathologic complete response, but importantly, overall survival as well. So it was a significant benefit, though small at 24 months, 80.9% with pembrolizumab versus 77.6%. But we were looking at possibly curing more of these patients with the sandwich approach or with any kind of perioperative immunotherapy. So really exciting for our patients. There was a modest increase in treatment-related adverse events with the addition of a third treatment regimen or treatment arm, but that is to be expected. So this is another option for perioperative control.

Dr. Liu:
Yeah. Absolutely. And that survival benefit, really important. But it's not the only perioperative study that we've got approved in the US. CheckMate 77T looking at nivolumab, the AEGEAN trial looking at durvalumab. Susan, how do these compare to this KEYNOTE-671 study?

Dr. Scott:
So very similar. CheckMate 77T is much like CheckMate 816, with the extra year of nivolumab on the back end. We see a dramatic improvement in event-free survival with the addition of the pre and postoperative nivolumab, improvement in the pathologic complete response from about 5% up to 25% as we saw with CheckMate 816. And then a bit higher treatment-related adverse events, again, with the addition of immune checkpoint inhibitor to the chemo. This has, again, really improved event-free survival.

The AEGEAN study is similar with the addition of durvalumab to chemotherapy. Again, a perioperative approach, pre and post resection with chemotherapy in the neoadjuvant setting, improving event-free survival, improving complete pathologic response, and again, slightly increased treatment-related adverse events.

So these are all options for our patients, and I'm tending to use nivolumab and pembrolizumab most, but it's nice to have a wealth of options to choose from.

Dr. Liu:
Yeah, agreed, and yeah, I think we're on board with this neoadjuvant approach. There still remains an open question as to is the adjuvant component necessary? How much is that adding? And these studies aren't really designed to answer that specific question.

But Josh, there was an exploratory analysis from Dr. Patrick Forde at WCLC 2024 that looked at CheckMate 816 and CheckMate 77T, looking at patient-level data. A unique comparison because all these patients did receive neoadjuvant nivolumab and chemotherapy; 77T, they're also getting that adjuvant component. Josh, can you discuss the findings of that study, and importantly, how that sort of influences your practice?

Dr. Sabari:
Yeah, it's great question. And this is a question of do you need the adjuvant therapy or not? We're looking a lot at ctDNA to see whether a patient's clear, and that seems to correlate with lack of recurrence. And again, still experimental. But this was an analysis — and really an exploratory analysis essentially taking the data from CheckMate 816 and comparing it to 77T in absence of a head-to-head clinical trial. And what we saw here was a 40% reduction, or 39% reduction, in the risk of disease recurrence or death after surgery, observed in patients who received greater than or equal to one dose of adjuvant nivolumab following the neoadjuvant nivolumab plus chemotherapy, compared to those who did not receive adjuvant nivolumab alone. So it's interesting to think about the addition of nivolumab maybe does improve sort of durability of outcome in this patient population. Again, we'd likely need a head-to-head trial here to parse that out.

Dr. Liu:
And we'll have those soon enough. And I think today, when we're making decisions, what we know from a lot of subset data from CheckMate 816 is that those patients that do achieve a pathologic complete response have excellent 5-year survival numbers. Is that a group where maybe we can spare the adjuvant component? I think especially if there was any toxicity, I wouldn't hesitate to do that. We also saw other clues. We're putting together a story where PD-L1 negative, those patients didn't do nearly as well as PD-L1 positive.

So I think we're still learning a lot about this space. It's good to have options. We want more, but I think these are great insights, Josh and Susan, to really wrap up this brief discussion. Thanks everyone for listening.

Announcer:
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