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Incorporation of guidelines-concordant immunotherapy in the perioperative setting of NSCLC

Announcer:
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Dr. Gubens:
This is CME on ReachMD, and I'm Dr. Matt Gubens.

Dr. Yu:
And I'm Dr. Helena Yu.

Dr. Gubens:
Let's start our discussion by looking at a case. I recently had a 69-year-old fit female with a 30 pack-year tobacco history, with persistent cough after she had a diagnosis of a COVID-19 infection. CAT scan showed a 5.4 cm left upper lobe mass and some modest lymphadenopathy. We did a PET. This showed FDG avidity just in the left upper lobe mass. She went for bronchoscopy with EBUS. The left upper lobe mass showed squamous cell carcinoma, but fortunately all the lymph nodes samples were benign. PD-L1 was at 95% expression and there were no actionable mutations, and so we staged here at stage 2B T3N0M0. Her PFTs were favorable for resection, and our surgeons agreed with the plan to do neoadjuvant therapy. We went ahead with pembrolizumab along with carboplatin and gemcitabine for 4 cycles. A CAT scan before surgery showed a partial response. She went to surgery, and pathology after surgery showed a major pathologic response. There was residual 5% viable tumor.

We discussed options at that point, and she elected to continue pembrolizumab after surgery to complete 1 year total. So we give her credit for the first 4 cycles, and then she finishes out a year.

Dr. Yu, what's your impression of this case, and how are you approaching this really exciting emerging field of perioperative therapy?

Dr. Yu:
Yeah, I think that it is an ever-changing space, where we had adjuvant therapy first and then neoadjuvant, and now, really, perioperative options as well. I mean, it sounds like a bread-and-butter case that many of us see in our practice. I think with a large tumor size, it obviously makes sense to proceed with neoadjuvant therapy, and this would be exactly what I would do. I think, maybe I might slightly favor taxanes, so I would give that. But I think the pembrolizumab absolutely makes sense.

And I guess I'm curious for you. Is there any change in your management when you see the path report in terms of whether somebody had a major pathologic response, a complete response, or no response? Does that at all change what you do in the adjuvant setting?

Dr. Gubens:
That’s an excellent question, and unfortunately, we don't have so much head-to-head data against these opportunities in this space. Because I think the 2 big choices, really, are perioperative. We have 3 great choices there. But also, there's the opportunity for neoadjuvant alone, and the FDA-approved approach, there is nivolumab plus chemotherapy of course, but we could always stop

therapy after surgery in the right setting. I admit in my practice, I'm swayed to think that when patients have a complete pathologic response, I do, obviously in a shared decision-making situation, talk about discontinuing therapy at that point and saying that you had a remarkable immunotherapy response; you've had resection as appropriate; maybe it's actually okay to forego the ongoing therapy. Whereas if there is any viable tissue or short of a major pathologic response, I tend to maybe want to do the belt-and-suspenders approach and offer more therapy, but I think that's such an emerging area to try to understand what additional therapy is needed, especially when the path responses aren't as robust.

What's your approach here?

Dr. Yu:
Yeah, I would say pretty similar to you. I think the challenge is we have this new data of being able to see the surgical resection sample, and you're absolutely right. I think it just doesn't feel great when somebody has a residual tumor to say you're done with therapy. Although, again, that's not necessarily evidence-guided because I do think neoadjuvant therapy alone is appropriate. I would imagine that our sort of next-generation of perioperative studies are certainly going to take into account kind of MPR and complete path response, as well as ctDNA and looking at MRD. I think we have sort of the next iteration coming up. But without prospective data to guide me, I would do exactly like what you said. I think if there's any residual tumor, I'd definitely discuss with my patient the idea of continuing out for that year of therapy.

Dr. Gubens:
I'm curious. In the NCCN it's mentioned that aside from checking PD-L1, that we should at least check EGFR and ALK. I'm curious your take on that and how you use that in your decision-making at your institution.

Dr. Yu:
Also a great question. I think that we do have rapid assays fortunately for EGFR and ALK at our institution, and I definitely do check that for all cases, I think. We have different clinical trial options that those patients might be eligible for should they have a driver mutation.

And if someone does need neoadjuvant therapy after tumor board discussion and happens to have an EGFR mutation, the way that we typically proceed right now, without NeoADAURA other data, is to actually proceed with chemotherapy up front and then surgical resection if appropriate. And then, based on ADAURA, I would give adjuvant osimertinib afterwards.

What about you, Matt?

Dr. Gubens:
Completely agree.

But with that, our time is up. We hope you found this brief case review helpful and thanks so much for listening.

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