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Optimizing Immunotherapy for Advanced NSCLC: How to Manage Immune Toxicities

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Bristol Myers Squibb. Here's your host, Dr. Jacob Sands.

Dr. Sands:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and joining me to share her insights on optimizing immunotherapy-based regimens for patients with advanced non-small cell lung cancer is Dr. Christine Bestvina. She's an Associate Professor of Medicine in the Section of Hematology and Oncology at the University of Chicago Department of Medicine. Dr. Bestvina, it's wonderful having you on the program today.

Dr. Bestvina:
Thank you so much for having me here today, Jacob.

Dr. Sands:
To start us off, how has the evolving use of immunotherapy in advanced non-small cell lung cancer shaped our focus on managing immune-related adverse events?

Dr. Bestvina:
So as immunotherapy has moved into the frontline setting, most patients, both with resectable and metastatic disease, are now receiving immunotherapy. It can be given as monotherapy, chemoimmunotherapy, or in dual IO combinations. And this success has helped patients to live longer and often live better, but it does also bring new challenges, such as balancing survival with the risks of immune-mediated toxicities.

With the Skoulidis data that we saw this year showing the benefit of CTLA-4 inhibition for patients who have STK11 or KEAP1, we may see an increased use in dual checkpoint blockade, necessitating us having better vigilance as far as immune-mediated toxicities and intervening earlier for these patients.

Dr. Sands:
So if we break down these immunotherapy regimens a bit more, how do the safety profiles differ between monotherapy and dual therapy?

Dr. Bestvina:
Pretty consistently across different single-agent checkpoint inhibitors we've seen lower rates of irAEs—somewhere around 10 to 15 percent of patients experience a grade 3 or higher immune-related adverse event.

With dual immunotherapy, however, we see higher rates of grade 3 to 4 adverse events, typically around 30 to 35 percent, and those can include events such as colitis, pneumonitis, skin toxicity, and even more rare events such as adrenal insufficiency.

Dr. Sands:
So related to that, overall adverse event rates in real-world studies are pretty consistent with clinical trial data, but recent cohort analyses have found that immune-related adverse events, such as pneumonitis and myocarditis, may be slightly more common in everyday practice. So why might we be seeing these differences? And how does the data shape your approach to patient selection and

counseling?

Dr. Bestvina:
I do think that there can be small differences between real-world populations and clinical trial populations. As an example, most clinical trials that involve immunotherapy exclude patients who have an autoimmune disorder. In the real world, for patients who have well-controlled autoimmune disorders without recent flares, we may consider still giving these patients immunotherapy. And so that may be a reason why we're seeing higher rates of immune-related adverse events in the real world as opposed to a trial population.

Additionally, in the real world, there may be patients who have, let's say, early signs of interstitial lung disease on imaging but haven't carried a formal diagnosis. These patients are at higher risk for pneumonitis if they have exposure to immunotherapy.

Additionally, one difference in the real-world population versus the trial population may be rates of prior radiation. Clinical trials have quite strict inclusion criteria about prior palliative radiation or radiation washout, and these patients may go on to receive immunotherapy in the real world. Radiation pneumonitis can sometimes be mistaken for immunotherapy-related pneumonitis, and there may be some confusion about what actually caused the pneumonitis. Again, in clinical trials, we're very strict about attribution of immune-related adverse events, whereas in some of these real-world populations, it may be in more of a gray zone.

So I think all of this really underscores the critical need to select patients well, even in the real-world setting, to be thoughtful about who we're offering immunotherapy to, as well as to give a balanced view of risks and benefits to the patient so that they can make an informed decision about their treatment course.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and I'm speaking with Dr. Christine Bestvina about safety considerations for immunotherapy-based regimens in advanced non-small cell lung cancer.

So, given the importance of early identification of immune-related adverse events, Dr. Bestvina, what monitoring protocols do you rely on to catch immune-related toxicities before they escalate?

Dr. Bestvina:
So when we start a patient on immunotherapy, we'll have our nurse as well as our physician's assistant do long teaching visits with the patient about some of the different immunotherapy-related adverse events that can occur, as well as red flags that they should look out for.

We really stress to the patient that we want to hear from them early if they're having any symptoms that they may not be sure what's causing it. Or particularly, if they end up needing to go to the emergency room for any symptoms, we would want the outside emergency room to contact us so that we can screen for different immunotherapy-related adverse events.

Dr. Sands:
As a follow-up to that, how important is the role of a multidisciplinary collaboration? Who do you typically involve when managing adverse events?

Dr. Bestvina:
I do think when managing some of these adverse events, it's critical to have key partners identified who have an interest in immunotherapy-related adverse events from these other subspecialties who are willing to see the patients quickly, get involved in their workup, and also potentially help co-manage these toxicities long-term.

So at our center, we have an identified pulmonologist who's interested in immunotherapy-related pneumonitis. We have a GI person who's interested in colitis and enteritis related to immunotherapy. And additionally, we're very fortunate to have a rheumatologist, Dr. Pankti Reid, lead an immunotherapy-related adverse event clinic. We've been very fortunate to have her play quarterback for many of these patients as they longitudinally experience these immunotherapy-related adverse events and help in our ability to take patients off chronic, long-term steroids, transition to steroid-sparing agents if necessary, and help minimize the impact on patients' quality of life as they're living longer.

Dr. Sands:
It really is such a blessing to have such a highly specialized group that is supporting some of these. And I know we both benefit from that. And for those in the community who are tuning in that don't have that, of course, sometimes that's also the reason to loop in someone from the academic center if there's not that subspecialist that can really help with some of this management.

But before we wrap up, Dr. Bestvina, what best practices are most critical for balancing efficacy with safety as we continue to expand the use of immunotherapy in advanced non-small cell lung cancer?

Dr. Bestvina:
I do think that one area that we continue to improve on is how to talk to patients about these issues. So patient-related visual decision guides—how can we improve our ability to communicate scientific knowledge to the patients in a way that they can understand and help weigh that risk-benefit for themselves?

I also think we can improve on patient education and engagement past just the first infusion. So unlike chemotherapy—which has a predictable onset of different adverse events—with immunotherapy, the timing of onset can be much more unpredictable and can happen months, even years occasionally, into them being on immunotherapy. So continuing that open education and engagement with the patients I think will be critical.

Dr. Sands:
With those best practices in mind, I want to thank my guest, Dr. Christine Bestvina, for joining me to discuss these adverse event management protocols for immunotherapy-based regimens in advanced non-small cell lung cancer. Dr. Bestvina, it was wonderful having you on the program.

Dr. Bestvina:
Thanks so much for having me today, and thank you to our listeners.

Announcer:
This episode of *Project Oncology* was sponsored by Bristol Myers Squibb. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!