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NSCLC Care: Evaluating Durvalumab in the First-Line Setting

Dr. Sands:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and joining me today to discuss her research evaluating the safety and efficacy of durvalumab as a first-line therapy for patients with advanced and metastatic non-small cell lung cancer is Dr. Liza Villaruz. She's an Associate Professor of Medicine at the University of Pittsburgh School of Medicine.

Dr. Villaruz, it's great to have you with us today.

Dr. Villaruz:
Thank you so much, Dr. Sands. It's a pleasure to be here.

Dr. Sands:
So to start us off, can you give us a little background on your study and what the primary objectives were?

Dr. Villaruz:
Yeah. So our study was a first-line study of the checkpoint inhibitor durvalumab in previously untreated patients with metastatic non-small cell lung cancer, and it was specific to a population of patients with an ECOG performance status of 2, so these are patients that are functionally impaired at baseline that are up and about about half of their day. And that in general would not have fit criteria for many of the clinical trials that evaluated checkpoint inhibitors in the first-line setting. So the objective of this study was really to establish a survival benefit with regard to checkpoint inhibition in this clinical population and also to establish the safety and tolerability of durvalumab.

Dr. Sands:
And with that in mind, what methods did you use to achieve those objectives?

Dr. Villaruz:
So when we designed this study, we set out to enroll a population of patients, about 50 patients, who had an ECOG performance status of 2 with newly diagnosed metastatic non-small cell lung cancer. All the patients on the clinical trial were treated with durvalumab monotherapy, so a once-monthly injection at a flat dosing schedule, and they were able to continue this until disease progression or toxicity up to about a year. We followed these patients very closely, and one of the key secondary objectives of this clinical trial was to assess quality-of-life measures, so patients were administered quality-of-life measures at the beginning of the study and routinely during treatment so that we could assess not only if we were helping patients with regard to survival, but also with regard to their quality of life.

Dr. Sands:
Now checkpoint inhibitors have obviously become a huge part of our management really across multiple different tumor types, and certainly, we've seen this within non-small cell lung cancer and durvalumab after chemoradiation for Stage IIIB. Moving into the first line now is a new setting, and it's exciting to hear about a quality-of-life trial within that setting as well. Can you discuss a bit more about the quality-of-life aspect and what measures you are using within that quality-of-life objective?

Dr. Villaruz:
Yeah. So we measured quality of life using a FACT-L questionnaire, which basically is a composite questionnaire looking at the physical and emotional well-being of a patient, and then specifically also looking at the lung cancer scale, so symptoms specific to lung cancer that many of our patients experience, such as shortness of breath, chest pain, and difficulties with regard to their day-to-day. What we found was that patients who are treated with durvalumab who remained on study and were able to fill out the questionnaires had essentially stable quality of life over the course of their treatment, which is encouraging, right? Because these are patients with

borderline performance status. And so the ability to demonstrate that treatment doesn't adversely affect their day-to-day I think is actually quite impactful, especially in particular for this patient population where their day-to-day can have its inherent challenges based on their performance status.

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. Liza Villaruz about her research on durvalumab for the treatment of advanced and metastatic non-small cell lung cancer.

So, Dr. Villaruz, we've discussed a bit of the background on ECOG 2 performance status first-line non-small cell lung cancer use of durvalumab with some attention to quality-of-life outcomes. Can you give us more of an overview now on the results that you found within that trial?

Dr. Villaruz:
Yeah. So we were able to demonstrate that durvalumab within the metastatic and non-small lung cancer population with impaired performance status was associated with modest survival benefit overall. It's important to note that when we designed this clinical trial several years ago, durvalumab was being evaluated in the first-line setting in a number of different clinical trial settings, and it was being evaluated in a number of different PD-L1 expression cut-points. We enrolled an all-comer population, so a population of patients with any level of PD-L1 expression—PD-L1 non-expressors to high expressors—and patients both with squamous and nonsquamous histology.

What we demonstrated is that it was associated with a modest survival benefit, and that benefit was most pronounced in patients with PD-L1-positive tumors, so a survival benefit approaching about a year, which is comparable to the survival benefit that we see in the advanced and metastatic setting. For patients with high PD-L1 expression, particularly in patients with impaired performance status, we were also able to demonstrate that this was a safe strategy within this population. In terms of our historical reference point for the PS2 population, there's a very robust body of literature spanning decades of platinum doublet versus single-agent therapy in the PS2 population. What we found with durvalumab is that it was actually likely to be much more tolerated than a platinum doublet in the PS2 population, which is quite impactful.

Dr. Sands:
It is very interesting to look at that. And I remember, this is now more than 10 years ago, there was a study looking at ECOG 2 performance status doublet chemo versus single-agent chemo, and it really showed that the doublet outperformed, even though we get nervous about these borderline functional status scenarios. But now with a drug like durvalumab and some of the other checkpoint inhibitors, it seems like there's this option that continues to treat the cancer at full dosing while also generally being better tolerated. Can you speak a bit to just the side effect profile of durvalumab as compared to chemotherapy?

Dr. Villaruz:
Yeah. So the side effects are different, right? And I think, in general, checkpoint inhibitors as monotherapy are going to be better tolerated than platinum doublet. The typical platinum doublet side effects that we experience in terms of myelosuppression, fatigue, and the platinum toxicities like the metallic taste, these are things that can be quite bothersome for patients. Checkpoint inhibition, as I like to explain to patients, is generally overall better tolerated. You don't experience a lot of the typical platinum doublet side effects or the chemotherapy side effects that are associated with traditional chemotherapy. It's not without side effects, right? And the patients that can experience these side effects typically get side effects on sort of the spectrum of inflammatory disorders, right? And what I like to explain to patients is that while it can happen in a severe enough grade, typically, severe immune-mediated toxicities associated with checkpoint inhibitors are actually quite rare, about 5 percent. So in general, this class of medications actually tends to be generally better tolerated than a platinum doublet.

Dr. Sands:
Now given all of that context, what you would you say are the implications of the data that you and your coauthors have published and how that might impact clinical practice?

Dr. Villaruz:
I think that, in general, there is a paucity of literature within the borderline performance status population, and much of that resolves around the registrational trials that have led to the approvals of checkpoint inhibitors in the first-line setting. And these trials have formerly excluded patients with borderline performance status, so a performance status of 2 or more, so this is an active area where I think the applicability of registrational trials to the real-world population, there are some limitations there.

I think the other side of the question is that, thankfully, it's getting better. This is one of a number of different studies that have evaluated checkpoint inhibitors in the performance status 2 population in the first-line setting now. There's the IPSOS trial, which evaluated

atezolizumab; there's a clinical trial of nivolumab and ipilimumab; and then there's single-arm trials about the same size as our trial looking at pembrolizumab in the PS2 population. So it's a growing area, and the body of literature is actively being enriched, and I think that this helps to add to the enrichment of that body of literature and also helps to support the safety of checkpoint inhibition in the first-line setting in this impaired performance status population.

Dr. Sands:
Before we close, Dr. Villaruz, do you have any final takeaways that you'd like to leave our audience with today?

Dr. Villaruz:
What I hope that this clinical trial contributes to the literature is not to undertreat our patients with borderline performance status. These are oftentimes patients that can't necessarily travel to large academic hubs, which is a strength of our study. We actually treated a lot of our patients within the community clinics, which are part of the overall UPMC Hillman Cancer Center here in Western Pennsylvania, and so many of these patients were treated in rural areas. So the ability and the reassurance that we can treat these patients with effective first-line therapy and reassurances that we shouldn't necessarily be undertreating them just purely based on their performance status.

Dr. Sands:
Well, that is a very appreciated final point on this interesting discussion on durvalumab in the first-line setting for patients with advanced and metastatic non-small cell lung cancer. I want to thank my guest, Dr. Liza Villaruz, for joining me to share her research findings.

Dr. Villaruz, it was a pleasure having you on the program.

Dr. Villaruz:
Thank you, Dr. Sands. It was a pleasure to be here.

For ReachMD, I'm Dr. Jacob Sands. 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.