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Current and Emerging Biomarkers of Response to Immunotherapeutic Regimens

Announcer:

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Dr. Saba:

Hello, this is CME on ReachMD, and I'm Dr. Nabil Saba. Here with me today is Dr. Barbara Burtness.

Dr. Burtness, let's talk about biomarkers of response in head and neck cancer. Which biomarkers do you think should be used in the selection of anti-PD-1/PD-L1 checkpoint inhibitor therapy?

Dr. Burtness:

That's a great question. I think, you know, the first thing to say is no PD-L1 drug has gained approval in head and neck cancer yet, so that remains investigational, although biomarker selection is probably similar for PD-1 and PD-L1 agents. The 2 biomarkers that I think are validated are PD-L1 expression and microsatellite instability. And so pretty uncommon to have a microsatellite unstable head and neck cancer, but you see a few of them, and clearly, they respond extremely well to immune checkpoint inhibitors and you can use it as monotherapy there.

The other is PD-L1 expression. And what's best validated in head and neck cancer is the use of a combined positive score where you're scoring both tumor cells and immune cells. If you're using pembrolizumab monotherapy there, it does not appear to be very active in the CPS less than 1. There's probably increasing activity as the CPS for PD-L1 goes up. We've seen a lot of studies in head and neck cancer exploring the CPS 20 cut-point. But I'd be curious to know how CPS 10 performs. But if you look at the 1 to 19s, or the 20s and higher, pembrolizumab is superior to chemotherapy in all of those groups. There's some question, do you really need chemotherapy if you have a CPS of 20 or higher? But you do see higher response rates and better 5-year survival in that CPS 20 group when you add chemotherapy. So for the right patient, I think chemotherapy can still be used in the CPS high. For a frail patient, you might try pembrolizumab alone in the 1 to 19s. You should not be trying pembrolizumab alone if CPS is less than 1.

So, Nabil, I'm curious how you use chemotherapy in the HPV-associated cancers? You know, do you integrate it with CPS? Do you never use chemotherapy in the HPV positive? How does that factor into your decision-making?

Dr. Saba:

Certainly, I would not say never use it, for sure. I think I'm always, you know, thinking about the data in nasopharynx cancer when I think about HPV-related disease, and I cannot help to think that for these virally mediated cancers, chemotherapy may really be playing a major role even though we think of them as better responsive. And looking, as you know, Barbara, on the 048 analysis specific to HPV-related and, I think, others as well, the 651, there is a suggestion there that when you add chemotherapy, you actually may be producing good results for these patients. Outside of a clinical trial, I tend to think about adding chemotherapy for these patients, even though, as you very well said, the trials don't really tell us for sure what is the right approach. And I'm really waiting for 048 to have a more detailed

analysis as far as outcome based on HPV-related, because we have not seen this analysis published yet. And so I very much look forward to that.

Dr. Burtness:

I completely agree.

Another question for you, Nabil, is have you found that there's a CPS threshold where chemotherapy is not indicated? What do you do in the PD-L1 less than 1 population?

Dr. Saba:

I would say chemo is not indicated in every patient. Yet, the CPS score is not also the only driver for this decision. Certainly, between CPS 1 and 19 chemo ought to be considered, given the suggested meager benefit to single-agent pembro in this group.

I would say that for CPS less than 1, I would strongly recommend including chemo in any first-line combination. Whether the PD-1 inhibitor here is adding anything, it is approved after all, so I perhaps tend to give the benefit of the doubt and give a PD-1 inhibitor. But certainly for this group of patients, I would always give chemotherapy.

And I guess for the takeaway from the session I would clearly advise to check PD-L1 by CPS score when trying to make a decision on using PD-1 inhibitors with or without chemo in patients with recurrent disease. You may find that tumor mutation burden is beneficial in certain instances where you have a high value. In general, however, I would say tumor mutation burden is mostly not your guide in decision-making. So keep your eyes and ears open to possible novel markers related to T-cell infiltration or other markers in head and neck cancer.

And this has been a great bite-sized discussion. And unfortunately, however, our time is up. Thank you for listening.

Announcer:

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