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Emerging and Practice Changing Data in Immunotherapy Strategies for Melanoma

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Dr. Patel:
This is CME on ReachMD, and I'm Dr. Sapna Patel. Here with me today is Dr. John Kirkwood.

Dr. Kirkwood, could you tell us about the emerging data for immunotherapy, really even across the spectrum, neoadjuvant, adjuvant, frontline?

Dr. Kirkwood:
Thank you, Dr. Patel. It's a pleasure to join you for this. I think it's been a very interesting year. I think the year, if we stretch it out to 2024, started with Jeff Weber's presentation of the KEYNOTE-942 trial that showed us really remarkable data on the effects of an mRNA cancer vaccine added to pembrolizumab, which led to a phase 3 study, which was rapidly accrued, and which I think we're all waiting to see the results of because that truly could be transformative.

I think at the ASCO closing session this year, we heard several papers, one of them that involved the cooperative groups, and was therefore, for me, particularly exciting was a neoadjuvant trial of a TLR9, a Toll-like receptor 9 agonist, which uses that signal, which is, if you will, something to stir up the pot of the tumor to induce a response given intratumorally with pembrolizumab versus pembrolizumab alone in the neoadjuvant setting. And this, which was really a randomized phase 2 small study, employed the previously CheckMate and now vidutolimod to test this question with intratumoral therapy, which has been of interest, as we pointed out earlier, for a variety of agents. And I think the results, with a 20% improved complete pathologic response in the tumor, fulfilled all that we expected from the trial. And I think it's now to be decided whether this will go forward in a phase 3. But this is in active discussion, and I think our listeners should be prepared for this. It's something which obviously will be exciting to all of us to be able to give intratumoral therapy to invoke the immune response to a greater extent in the neoadjuvant treatment of our patients.

A surprising study that was presented by Georgina Long, on behalf of the RELATIVITY-098 trial, tested the fixed-drug combination versus nivolumab, proved to be negative. And this was stopped for futility, I think, to all of our surprise, earlier in the spring. And the analysis that was presented at ASCO showed us something in terms of the corollary analysis that we should always be thinking about in all of our trials, to ask what was different between 047, the original phase 3 trial in metastatic disease, and the 098 trial given in the adjuvant setting. And with all of our emphasis on neoadjuvant therapy, it should be no surprise to anyone that it turned out that in the setting of metastatic disease, peripheral blood, cytoplasmic LAG-3 positivity was very clearly expressed, whereas in the 098 trial, it was

not. And so this analysis of corollary endpoints suggests to us that maybe we need to do more in the adjuvant setting than we have in the metastatic disease first line, as in the 047 trial.

So I think we have much to look forward to, and many new things that are coming down the pike, and hopefully we'll be able to see these mature in the next year or 2, to the betterment of all of our patients' therapy.

Dr. Patel:
Yeah, I agree. I think these neoadjuvant regimens, we will see more of them coming, and really more of them emerging as combinations or adaptive strategies. So if we're not already incorporating that into our clinical practice, I think there's going to be no shortage of outstanding trials to try to consider enrolling to.

And one of the regimens we heard, really, last year at ASCO, and we heard a version of it this year, is triplet checkpoint blockade. This may be soon to be confirmed in larger trials, but nivolumab/relatlimab plus ipilimumab, the ipilimumab is at an atypical dose that we're used to in melanoma. But that triplet checkpoint inhibitor, certainly, when we saw the data in the 40 patients treated in Europe, looked remarkable for progression-free survival, had not been reached at 48 months of follow-up. And that really is head and shoulders, beyond what we see with doublet combination immunotherapy. So if that data holds in a confirmatory trial, even if it comes down by a certain percentage, this could be really exciting.

And then the question will be, how do you mitigate the toxicity? And we heard, of course, Jeff Weber's legacy trial, sarilumab added to triplet, might actually not only improve response rates, but importantly, also help with toxicity.

So I think these are great regimens to be on the lookout for. So that's all the time we have today. Thanks everybody for listening.

Announcer:
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