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Emerging first-line ICI combination regimens in patients with unresectable HCC

Announcer:
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Dr. Abou-Alfa:
This is CME on ReachMD and I'm Dr. Ghassan Abou-Alfa from Sloan Kettering, New York. Today I'll review some of the emerging data on first-line immune checkpoint inhibitor combinations in unresectable HCC.

We all know about the CARES-310 study. The study is now published that looked into the combination of camrelizumab plus the rivoceranib versus sorafenib, looking of course, for PFS and OS for superiority. The patient population were the same as like any of the Phase 3 trials I've been talking about, BCLC B or C, ECOG 0 to 1, Child-Pugh score A, of course.

Many secondary endpoints, including response rate, disease control rate, the duration of response and safety. In regard to the first primary endpoint, the PFS, it showed an improvement in favor of the camrelizumab plus the rivoceranib. As you can see here, PFS median of 5.6 months compared to 3.7 month for sorafenib, with hazard ratio of 0.54.

Impressively, when it comes to the overall survival, it also showed an improvement in survival in favor of the camrelizumab plus the rivoceranib 23.8 months compared to sorafenib 15.2 months. Again, of course, clinically and statistically significant.

The adverse events part of the study, exactly as expected with those kind of combinations, with the camrelizumab plus rivoceranib, or of course, with TKI being sorafenib. We can see here that there was quite apparent Grade 3 adverse events that were probably more present on the camrelizumab plus rivoceranib. And this showed, of course, the well-noted hypertension that required control of the blood pressure.

The other study, which is right fresh off the news, is the Checkmate-9DW that looked into nivolumab plus ipilimumab versus sorafenib or lenvatinib. Key important notes on the study, number one, this is the combination that specifically was followed through the CHECKMATE-040 study, and specifically, the combination of 1 milligram per kilo of nivolumab plus ipilimumab 3 milligram per kilo, given every 3 weeks for 4 doses, then followed by single-agent nivolumab monotherapy. The primary endpoint was overall survival and the key secondary endpoints were response rate, duration of response, time to symptom deterioration.

That study was also reported and showed an improvement in outcome in favor of the nivolumab plus ipilimumab: 23.7-month versus lenvatinib or sorafenib 20.6-month, with hazard ratio, however, of 0.79.

Safety. Same thing as we already expected and see in regard to the two arms of this study, being the checkpoint inhibitor doublet or the single-agent TKI. And obviously, you can see there was a little bit more pronounced, specifically related to the checkpoint inhibitors, like elevated AST and ALT, and increased lipase. But on the other hand, we see a pronounced increase in regard to hypertension, in regard to proteinuria, part of the tyrosine kinase inhibitor sorafenib or lenvatinib.

What do you learn from this data? Number one, give credit to all our colleagues on the continued work to try to improve further on the

survival. Number two, the survival improvement, to be fair, has to be put in context because, after all, these patients have more opportunities for other choices of therapy. And if anything, this improvement in survival, even for the tyrosine kinase inhibitor single-agent, is reflective of that part.

Number three, especially in regard to the CARES-310, we have to remember that this is mainly driven by people with hepatitis B that we know will fare best when it comes to the checkpoint inhibitors.

And number four, in regard to the 9DW, we are definitely eager to hear more data and more details because know that number one, that kind of like, flip of the overall survival Kaplan Meier curves that occurred about one year is that with, in doubt, in regard to why the patient with the ipi/nivo did not fare well in the beginning, and then changed around after 12 months. And number two, why this separation did not happen until much later on? Let alone also, we see that the patient with hepatitis C did fare better than the hepatitis C on the subgroup analyses.

There's a lot to dissect still and digest, but to be fair, this is right of the platform at ASCO. I do have to give a chance then, to see more details.

Well, my time is up. I hope you find this review useful. Thank you for listening.

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