Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/pivotal-data-supporting-first-line-durvalumabtremelimumab-in-unresectable-hcc/26330/

Time needed to complete: 19m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Pivotal data supporting first-line durvalumab/tremelimumab in unresectable HCC

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Abou-Alfa:
This is CME on ReachMD and I'm Ghassan Abou-Alfa. Today I'll provide a brief overview of some pivotal data supporting the use of first-line durvalumab and tremelimumab in unresectable HCC.

The data is emanating, understandably, from the HIMALAYA study, which, as you can see, recalls a comparison of this STRIDE regimen, which is what we call, now, STRIDE for tremelimumab single-dose 300 milligram plus durvalumab, which is on monthly basis. And this was compared for superiority versus sorafenib, the standard of care therapy.

There was a third arm, though, that looked into durvalumab single-agent comparing sorafenib, looking for noninferiority. This study, understandably, was available for patients with advanced HCC, Child-Pugh score A for liver performance, BCLC B or C, and good performance status ECOG 0 to 1.

The primary endpoint, as we said, is overall survival, looking for this STRIDE regimen tremelimumab anti-CTLA-4 plus durvalumab anti-PDL-1 versus sorafenib. And the key secondary endpoint, exactly as I also mentioned, is overall survival looking for noninferiority of durvalumab anti-PDL-1 versus sorafenib, also look at progression-free survival, overall response rate, and safety.

The data, as you know, was positive and proudly, we presented it 2 years ago, and now we are into further updates and, as you can see, the HIMALAYA now has 4-year overall survival. Continuation of the same survival that was positive to begin with, but now, as we can see, at many landmark analyses, there's continued improvement in survival.

We can see at 18-month, we can see at 24-month, we can see at 36-month, and now, even at 48-month, 4 years, survival is still noted for the STRIDE regimen, tremelimumab plus durvalumab in 25.2% of the patients, while for sorafenib in15.1% of the patients.

Ideally, we'd would like to know that the analyses using the landmark is critical because, as we all know, the immune system continued to evolve and provide further support for the therapy that were provided.

And here we see the 4-year overall survival for durvalumab versus sorafenib. Please remember this was a noninferiority component of the study. And if anything, this kind of equivalence between the durvalumab single-agent versus sorafenib continued to be present 19.3% alive at 4-years for the durvalumab versus 15.1% for the sorafenib.

If anything, this is one more proof for the criticality of that one single-dose tremelimumab that we gave 4 years for the patient who were on tremelimumab plus the durvalumab.

What about the responses? Understandably, the responses were there. If anything, the overall response rate for this STRIDE regimen was 20% compared to sorafenib 5%. The durvalumab by itself still can improve response of 15%, and interestingly, we had complete response in 3% of the patients on the STRIDE regimen, and 1.5% for the durvalumab. Understandably, most patients had stability of

disease plus about 40%.

Safety. No doubt that adverse events will occur, especially in view of the different interventions here being the checkpoint inhibitors or the TKI in the sorafenib arm. And you can see over here, that, the Grades 3 and 4 were present, almost equaled in regard to the arms, and equivalent, especially between the STRIDE regimen and the sorafenib. And if anything, the hepatic treatment related adverse events were mildly noticeable in the checkpoint inhibitors dual regimen being the STRIDE and the single-agent durvalumab. And of course, I mean, we did have adverse events, of course, that were mostly noticeable in the STRIDE regimen with the doublet being the anti-PDL-1 plus anti-CTLA4 of 12.6%. And in the durvalumab, 6.2%, and sorafenib understandably, not existent 2.4%.

What else is going on these days? We have the SIERRA study, a Phase 3B single-agent, multicenter study of tremelimumab plus durvalumab for first-line treatment for advanced HCC. The coprimary endpoints are as said. This is Grade 3 and 4 adverse events, possibly related to treatment, and investigator-assessed overall response rate.

The other one is MONTBLANC which is randomized two-arm Phase 2 study of durvalumab plus tremelimumab and bevacizumab in patients with advanced HCC, with two arms. The first one, the STRIDE regimen plus the bevacizumab upon progression or lack of response by 4-month, and arm B is STRIDE plus bevacizumab. And of course, primary endpoint is response.

Well, we just heard about the STRIDE regimen improvement and outcome. This is, no doubt, is an appropriate and applicable therapy in first-line treatment for patients with HCC. We are mostly delighted by the ease of the regimen. One single dose of tremelimumab and only one month dose of the durvalumab. Number two is, we're, of course, thrilled about the continued improved survival. Even now, we are reported for the first time ever in any study, 4-year overall survival.

Even at four years, we're showing still a value for the addition of the two checkpoint inhibitors being, tremelimumab plus durvalumab. And lastly, the adverse events clearly are noticeable but not significant concern. This is, yes, of course, is the standard of care.

Well, this is my time and time's up. I hope you'll find this update useful. Thanks for listening.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Total CME, LLC and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.