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Emerging Clinical Evidence for B7-H3–Directed ADCs in ES-SCLC From WCLC 2025

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Dr. Paz-Ares:
This is CE on ReachMD, and I am Luis Paz-Ares.

Dr. Byers:
And I'm Lauren Byers.

Dr. Paz-Ares:
Lauren, we just attended the World Lung Cancer Congress 2025 in Barcelona. And would you review for us the latest clinical data that were presented on B7-H3–directed ADCs?

Dr. Byers:
Absolutely. So I think there was a lot of excitement around some of the updated data and some of the new data coming out for B7-H3 antibody-drug conjugate targeting. And so there was actually a session that was devoted specifically to these antibody-drug conjugates, and 2 that were really highlighted included the I-DXd study, as well as another therapeutic also targeting B7-H3, which is QLC5508.

And I think just to kind of give a broad overview, what we're seeing with these B7-H3 antibody-drug conjugates is that they're demonstrating a strong signal of response, and also patients are having very rapid responses to these.

So for example, in the updated data that was presented from the I-DXd trial—this is again targeting B7-H3 using a Topo-1 payload—the response rates overall were around 50%, and the duration of response for the data that's available to date was around 5. 3 months, with a PFS of around 5 months. And I think something that was especially encouraging was the median overall survival of around 10 months for these patients, who are relapsed patients with small cell lung cancer.

With the second B7-H3 ADC, the QLC5508 which was presented by Dr. Zhou, this also showed a similarly encouraging level of activity, with a median progression-free survival of 6 months and a median overall survival around a year again, which is very exciting to see that level of durability.

And just in general, some of the common toxicities include hematologic toxicities with the Topo-1 payload, which again is not unexpected but generally was well tolerated. So there are now phase 3 trials proceeding to see if these could become new standards of

care.

Dr. Paz-Ares:
This is really good news, having the updated data from those 2 trials. And I think today there are at least 5 of these ADCs directed to B7-H3 that have presented data.

I must say that, for most of the cases, the data are pretty similar one to each other in terms of efficacy. As you said responses around 50%, median PFS 5 to 6 months, and median OS 10 to 11 months.

So I know it is not clear to me, apart from some slight difference in toxicity, particularly pneumonitis, that it is not going to be really easy to make a clear difference.

On the other hand, it is unclear today what is the role of biomarkers in this setting. It looks like expression is not a great predictor. And we didn't see—I mean, at least I'm not aware about—any biomarker related to the payload. What do you think about how the field will move in those respects, in terms of predictors?

Dr. Byers:
Yeah. So I think those are really great points. We see that across the small cell lung cancer subtypes, for example, that B7-H3 is consistently expressed at relatively high levels, and so it is a very common and consistently expressed target.

I agree that thinking about the payload will be important Many of these antibody-drug conjugates for a variety of targets are using similar payloads, and I think we expect that we will see mechanisms of resistance similar to what we've seen to some extent with prior chemotherapy studies. And understanding that better and sort of how we can anticipate what might be the mechanisms of resistance or ways to combine these antibody-drug conjugates targeting B7-H3 with other agents, I think, will be things going forward that will be really interesting to think about and to see how those might be combined.

Dr. Paz-Ares:
Absolutely. Okay, so I think it's been a great micro discussion, I could say. But our time is up right now. So thank you very much for this conversation and thank you very much for listening.

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