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Expert Peer Discussion: Integrating Novel HER3-Directed ADCs Upon Disease Progression Following EGFR TKI and Platinum Chemotherapy

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

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Dr. Jänne:
This is CME on ReachMD, and I'm Dr. Pasi Jänne, a thoracic medical oncologist from the Dana Farber Cancer Institute in Boston, Massachusetts.

Dr. Yu:
And I'm Dr. Helen Yu, a medical oncologist at Memorial Sloan Kettering in New York.

Dr. Jänne:
Managing patients with EGFR-mutated, advanced, non-small cell lung cancer upon disease progression following an EGFR tyrosine kinase inhibitor and chemotherapy presents a real challenge.

Helena, how would you integrate HER3-directed ADCs into the management of these patients, if available?

Dr. Yu:
Yeah, I do think later-line treatment for this patient population is an unmet need and a moving space. Patients can have the EGFR TKI and chemotherapy in sequence, or based on the FLAURA2 data, maybe they get the EGFR TKI osimertinib and chemotherapy in combination. But either way, at progression, we do need new treatment options. At that point, I often biopsy patients, looking for a potential mechanism of resistance, whether that be an acquired genomic alteration, looking for histologic transformation, and potentially treating directed on those results. But if not, and hopefully with patritumab deruxtecan soon to be approved, I would definitely think about utilizing that in this third-line setting. I think the efficacy was very strong in this third-line space. And generally the treatment is well tolerated.

How about you, Pasi?

Dr. Jänne:
Yes, I certainly think there is a role for HER3-directed ADCs like patritumab deruxtecan in this space, following EGFR TKI and chemotherapy treatment. It is an area where new therapies and therapeutic modalities are definitely needed. And the data so far for patritumab deruxtecan in this patient subset has been quite good, as you point out.

Dr. Yu:
And one thing that I think is comforting is the data presented to date really looked at different acquired resistance mechanisms to osimertinib, and we did see in a very heterogeneous population with patients with on-target, off-target, and unknown resistance that we

did see efficacy. And then, again, I think knowing that there is some CNS benefit as well, I think, is really important for this patient population, where more than half of these patients will ultimately develop brain metastases.

Pasi, as someone that has had experience with HER3-DXd, are there any sort of unique side effects or dosing considerations that you've noticed when treating patients?

Dr. Jänne:
Well, certainly interstitial lung disease, which is seen with many of the antibody-drug conjugates, also can be seen in patients treated with HER3-DXd. So this is a side effect that I think, when the agent becomes available, we need to be aware of. I think that's the biggest new safety consideration that we perhaps didn't have to think about as much with standard of care chemotherapy.

Dr. Yu:
There is that study ongoing with HER3-DXd with osimertinib, so it'll be interesting to see efficacy there, but also make sure there's no added ILD signal.

Dr. Jänne:
And you mentioned the study combining osimertinib with HER3-DXd. Given that there's efficacy of HER3-DXd in the refractory setting, should we be moving this agent into earlier lines of treatment for patients with advanced EGFR-mutant lung cancer?

Dr. Yu:
Yeah, I'm looking forward too. In that study, there was a cohort that was first line with osimertinib plus HER3-DXd. So I think some of these other novel agents in combination with osimertinib in the first-line setting should be interesting when they read out.

Dr. Jänne:
Absolutely. And having agents that both have activity by different mechanisms in patients with EGFR-mutant lung cancer, I think that gives a great rationale for evaluating them in combination and seeing we would get a better efficacy than what we have historically with osimertinib alone.

Well, that has been a brief but great discussion. I hope we gave you something to think about, and thanks again for tuning in.

Announcer:
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