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

Case Application: Patients With EGFRm Resistance Post 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 from the Dana Farber Cancer Institute in Boston, Massachusetts.

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

Dr. Jänne:
Let's start our discussion by looking at a case. So this is a case of a 56-year-old male who presented with chest pain and shortness of breath. CT imaging demonstrated a left upper lobe lung mass and metastases to the pleura, mediastinal lymph nodes, to the right adrenal gland, and several bone lesions. A biopsy demonstrated an EGFR exon 19 deletion mutation. He began single-agent osimertinib treatment and had a rapid symptomatic improvement and an excellent radiographic response that lasted for 15 months. However, at that time, progressive liver lesions were found on restaging scans. A repeat biopsy was performed and showed the original exon 19 deletion in EGFR, but no other new genomic alterations.

At that time, carboplatin and pemetrexed was added to osimertinib. After 2 cycles of chemotherapy, repeat imaging demonstrated a reduction in his liver disease and no new sites of disease were noted. Following 4 cycles of combination therapy, the patient was switched to maintenance pemetrexed and osimertinib. And after 6 cycles of maintenance therapy with that combination, the liver lesions had started to grow, and a new left-sided adrenal mass was also noted.

At that time, if all options were available, which one would you choose as the next line of treatment?

And I'll ask Dr. Yu as to her thoughts on the case and how she would manage this case.

Dr. Yu:
This is a pretty common case where the patient got the standard of care first-line treatment, osimertinib monotherapy, followed by chemotherapy. He did appropriately have a repeat biopsy at the time of progression on EGFR TKI, which did not show any acquired genomic alterations. If all options were available, if we did have patritumab deruxtecan available, that would be what I would choose.

And that's really primarily based on the efficacy data from HERTHENA-Lung01. HERTHENA-Lung01 was a phase 2 study looking at patritumab deruxtecan exactly after EGFR TKI and after chemotherapy for patients with EGFR exon 19 L858R or exon 19 deletions, and did show that HER3-DXd, patritumab deruxtecan, had a response rate approaching 30% with a median PFS of 5.5 months. And so that clearly, in my mind, is an improvement on second-line chemotherapy. So would definitely choose that.

How about you, Pasi?

Dr. Jänne:
Yeah, similarly. And I will add that we also know that a phase 3 clinical trial, HERTHENA-Lung02, has been conducted which randomized patients a little bit earlier in their treatment journey, only after an EGFR TKI but without prior chemotherapy, randomized patients to receive patritumab deruxtecan or platinum-based combination chemotherapy. And we know from the press release that the study met its primary endpoint of PFS prolongation in patients who were treated with patritumab deruxtecan. Although the data is not available yet, but we know that the study is positive.

So I do think that looking for alternatives to current standard of care second-line chemotherapy with agents like patritumab deruxtecan, or other antibody-drug conjugates that are being studied in this context, offer a new therapeutic approach for patients with EGFR-mutant lung cancer, and unfortunately, most of our patients will be in this situation at some point in their disease journey.

Dr. Yu:
Yeah, looking forward to hopefully having patritumab deruxtecan approved and available.

Dr. Jänne:
Absolutely.

With that, our time is up. We hope you found this brief case review useful. And thank you so much for listening.

Announcer:
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