Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/closing-gaps-nsclc/mechanisms-of-acquired-resistance-to-targeted-therapies-in-nsclc/11227/

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

Mechanisms of Acquired Resistance to Targeted Therapies in NSCLC

Announcer:
Welcome to *Closing the Gaps in Non-Small Cell Lung Cancer* on ReachMD, sponsored by Lilly.

On today's program, we'll hear from Dr. Joshua Bauml, who's a medical oncologist and an assistant professor at Perelman School of Medicine at the University of Pennsylvania. Dr. Bauml joins us to discuss resistance to targeted therapies in non-small cell lung cancer. Let's hear from him now.

Dr. Bauml:
When a patient with non-small cell lung cancer harboring a molecular driver alteration develops resistance to their therapy, it is very important that we identify what the source of that resistance is. Now, this story began when we were looking in the EGFR space where we found that up to 60% of patients receiving a first- or second-generation EGFR TKI developed the T790M mutation. Now, this is really important because it meant that they were likely to respond to osimertinib. Looking at mechanisms of resistance to osimertinib, we're seeing disparate mechanisms which can be targeted in different ways, so in the EGFR space, as well as in ALK, MET amplification is emerging as a critical mechanism of resistance.

And it's important to know that the way you test for MET amplification is ideally with fluorescent in situ hybridization, or FISH. While next-generation sequencing can identify an increase in the gene copy number, it cannot do a comparison between that gene copy number and the amount of centromeres, and so, as a result, its ability to identify amplification is limited. As a result, every patient of mine who's developing progression I will do MET FISH because we now have multiple MET inhibitors that are on the market in the form of crizotinib and capmatinib—crizotinib for the treatment of ALK and ROS1 whereas capmatinib is FDA approved for the treatment of MET exon 14 skipping non-small cell lung cancer.

We've seen MET be important in ALK. We've also seen that in resistant samples for patients with ALK translocated non-small cell lung cancer, that one of the more common mechanisms of resistance, G1202R, its incidence depends upon which ALK TKI was used, and so, which ALK TKI you're going to use in the second-line really depends on what you used first-line and what resistance develops. The other reason it's so important to look for mechanisms of resistance is histologic transformation. If I have a patient who retains non-small cell lung cancer and ALK translocation, I'm going to treat that patient very differently than a patient who has developed small cell transformation where clearly the right answer is not to just continue the TKI and ignore the transformation. There, incorporation of chemotherapy does seem to be critical. And that's why we really need to be thoughtful about your management of patients who are progressing on targeted therapies.

Announcer:
That was Dr. Joshua Bauml discussing resistance to targeted therapies in non-small cell lung cancer. To revisit any part of this discussion and to access other episodes in this series,visit ReachMD.com/NSCLC, where you can Be Part of the Knowledge. Thank you forlistening!