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/ret-fusions-vs-ret-point-mutations-understanding-the-difference/11232/

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RET Fusions vs. RET Point Mutations: Understanding the Difference

Announcer:
Welcome to *Closing the Gaps in Non-Small Cell Lung Cancer* on ReachMD, sponsored by Lilly. Joining us on this program is medical oncologist and assistant professor Dr. Joshua Bauml from the University of Pennsylvania's Perelman School of Medicine. Dr. Bauml joins us to explain the differences between RET fusions and RET point mutations. Let's hear from him now.

Dr. Bauml:
When we're looking at targeted therapies in non-small cell lung cancer, it's really important to understand the difference between a mutation and a translocation. A mutation means that at some point in the genetic code there is a change in the DNA, whether it's an insertion, a deletion, an insertion and a deletion, but that is just a change of a couple pieces. A translocation, or a fusion, is when a piece of a chromosome breaks off and it gets attached to another chromosome in a different location. This creates a highly dysfunctional protein and can lead to bad outcomes from a biologic perspective.

If we think about the gene RET, it actually has both options occur in cancer biology. In hereditary cancer syndromes that involve medullary thyroid cancer, RET can have mutations. And there are multiple drugs that are approved for the treatment of RET mutations in medullary thyroid cancers, drugs like cabozantinib, vandetanib. These drugs are multikinase inhibitors. When we've tried to use them in RET fusion-positive disease—and this is more common in non-small cell lung cancer as well as papillary thyroid cancer—the drugs don't work very well, and in addition to that, their toxicity is quite limiting.

More recently there have been 2 drugs that have been in development; one which recently gained FDA approval is selpercatinib. The other drug in development is pralsetinib. Now, these drugs have remarkable response rates in patients with RET fusion-positive disease, both papillary thyroid cancer as well as non-small cell lung cancer. This is a real targeted therapy with excellent response rates, duration of response, CNS penetrance, as well as a good duration of response and toxicity profile. So, these were drugs that when they were in development, if I met a patient with RET fusion-positive disease, I would say, "Absolutely the best approach is a clinical trial so you can get one of these drugs."

Announcer:
We just heard from Dr. Joshua Bauml about the differences between RET fusions and RET point mutations. 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 for listening!