

### 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/what-to-consider-when-testing-for-oncogenic-drivers-in-nsclc/11229/>

### ReachMD

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

---

## What to Consider When Testing for Oncogenic Drivers 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 the Perelman School of Medicine at the University of Pennsylvania. Dr. Bauml joins us to share the opportunities and challenges in targeting oncogenic drivers in non-small cell lung cancer. Let's hear from him now.

Dr. Bauml:

In recent years we have seen the emergence of many targeted therapies for the treatment of metastatic non-small cell lung cancer. These are for patients with specific molecular abnormalities in their tumor that really make their tumor behave like a tumor. So, the most common targetable alteration at this time is the EGFR mutation. The most common alterations are the exon 19 deletion or L858R occurring in exon 21, but there are others. We now have FDA approval for ALK translocation, for ROS1 translocation, for BRAF V600E, for NTRK. We now have an approval for RET fusion. We have an approval for NTRK fusion. This is enormously overwhelming. And so, what is the critical thing that we must remember for patients with non-small cell lung cancer? It is that we must test every single patient with metastatic, at least nonsquamous non-small cell lung cancer. And some of those newer targets, such as MET and RET and NTRK, can occur in squamous cancers and sarcomatoid cancers, so just limiting it to nonsquamous may not be appropriate moving forward.

And then beyond that, it's really important that we know exactly what test is being done. Doing single-gene assays is neither tissue-efficient nor, based on recent ASCO data, is it cost-efficient, so panel-based next-generation sequencing is really critical in this space because we have so many molecular driver alterations to check for and we don't want to miss one and miss out on the opportunity to give a patient a treatment with a fantastic response rate as well as a very good tolerability profile, so it's really important that we do that testing and then identify what are the limitations of that test. So, many of the NGS tests that are being performed are DNA-based, and what that means is that they are not as good at identifying fusions or translocations. So, if I have a patient who comes to me who had a biopsy and had a DNA-based NGS and I clinically suspect a molecular driver alteration even if we don't find one, I will send off for an RNA-based fusion assay like the one that we have at the University of Pennsylvania—as well as there are also commercial ones which are available.

Another critical thing to remember when you're doing molecular testing is that the site of the biopsy is really important. So, we want to make sure that, first of all, this biopsy contains adequate tumor sample to get tumor DNA, and second of all, that we don't use bone biopsies. The decalcification process from a bone biopsy can degrade the DNA and decrease the sensitivity of the assay.

Finally, I think it is absolutely critical that for patients receiving targeted therapy, we do molecular testing at the time of progression. We are now seeing across the panel of molecular driver alterations that resistance develops in a heterogeneous fashion, and we must look for exactly what is driving that resistance so we can give the patient the best possible treatment. Here we can use liquid biopsies if the tissue biopsy is inadequate, but it's important to remember that a liquid biopsy will not identify histologic transformations, such as small cell transformation and squamous cell transformation, both of which have been reported in the targeted-therapy space.

Announcer:

That was Dr. Joshua Bauml talking about how we can target oncogenic drivers 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](https://ReachMD.com/NSCLC), where you can Be Part of the Knowledge. Thank you for listening!