MET as a Target in Advanced NSCLC

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TRANSCRIPT

So this is Vamsidhar Velcheti, I am a Thoracic Medical Oncologist at Cleveland Clinic and I am here to talk about MET in lung cancer.

For the past couple of decades, we have investigated MET as a target for treatment in patients with lung cancer. MET is often upregulated or the protein expressional MET is increased in a lot of patients who have lung cancer. We have had multiple clinical trials and studies looking at various drugs that inhibit MET in lung cancer including Crizotinib.

We know Crizotinib as an ALK inhibitor, but initially it was actually first developed as a MET inhibitor. There were other drugs including antibody-based treatments like MetMAb that targets MET. In those clinic trials, investigators have used protein expression or increased levels of the protein MET as a biomarker for response to these drugs. Unfortunately, all those trails were negative, and we did not see much benefit with using these drugs in patients who have increased protein expression of MET. However, some of those trails the challenge was to identify the right cutoffs of the protein expression and the biomarker related issues that actually lead to the failure of those trails.

However, there are other mechanisms of upregulation of the MET pathway in lung cancer including MET amplifications and certain mutations in MET that activate the MET pathway like EXON 14 skipping mutations. When you have these genetic or genomic alterations in the RET gene, that activates the MET pathway. More recently we have seen some interesting data using Crizotinib which is a small molecule inhibitor of MET tyrosine kinase. Crizotinib has a very strong MET activity. Patients who have MET EXON 14 skipping mutations, Crizotinib appears to be a very actionable drug in those patients.

However, we need more data in patients who have MET activating mutations and there are a lot of clinical trials which are currently ongoing including the NCI Match Trail that has an arm for patients who have a MET EXON 14 skipping mutation. So, I highly encourage patients who have a MET EXON 14 mutation to consider participating in some of these clinical trials to help our understanding of how those patients should be treated with targeted therapy targeting MET. There is a lot of promising new MET inhibitors in clinical development and hopefully we will see more positive news on that front.

http://cancergrace.org/lung/2018/04/14/lung-cancer-video-library-met-as-a-target-in-advanced-nsclc/