Gilotrif (Afatinib) in Squamous Non-Small Cell Lung Cancer (NSCLC)

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TRANSCRIPT

This is Vamsidhar Velcheti. I am one of the Thoracic Medical Oncologists at the Cleveland Clinic and I am here to talk about Afatinib in metastatic squamous cell lung cancers.

Afatinib is an EGFR tyrosine kinase inhibitor. This is a drug that has a pan-erbB activity. Like the other tyrosine kinase inhibitors in the family, Gefitinib and Erlotinib, Afatinib has striking activity in patients who have EGFR activating mutations. What we often don't realize with these EGFR tyrosine kinase inhibitors is that even though the maximal benefit is in patients who have EGFR activating mutations, these drugs have activity in the wild type variants. In fact, like the early studies for example the BR21 study where Erlotinib was evaluated in patients who had chemorefractory non-small cell lung cancer when compared to best supportive care there was overall survival benefit in all commas and independent of the EGFR mutation. In those early studies the benefit of EGFR tyrosine kinase inhibitors like Erlotinib was seen in patients who you don't otherwise expect the EGFR activating alteration for example in squamous cell histology of men and heavy smokers.

It turns out in patients with lung cancer, EGFR pathways activated not just by activating EGFR mutations but also by protein expression or overexpression and gene amplification of the EGFR gene. There is a role for EGFR inhibitors in patients who do not have an activating EGFR mutation. There was a trial, the LUX-8 trial, that actually compared Afatinib which has a broader EGFR activity compared to Erlotinib which was already approved for patients who have metastatic lung cancer. Turns out in that study, Afatinib had superior overall survival and progression-free survival compared to Erlotinib in squamous cell histology of patients who had already had prior chemotherapy and progressed on chemotherapy. But, you have to remember that was a trial that was done pre-checkpoint and those patients had chemotherapy and they progressed and were randomized to either Erlotinib or Afatinib.

None of them had prior exposure to checkpoint inhibitors. In that study, even though there was an overall survival benefit, the survival benefit was very modest and it was approximately a month of overall survival benefit. Some would argue that that is very modest benefit, but I would say in patients who have metastatic squamous cell lung cancers even though the landscape of treatment has changed now and we have checkpoint inhibitors now FDA approved used in patients with squamous cell histology.

Checkpoint inhibitors work in only about 20-30% of patients and we have somewhat limited treatment opportunity for these patients. So, any overall survival benefit is clinically meaningful. In that context, even though I would not use Afatinib in the second-line setting, patients who already progressed on a checkpoint using Afatinib would certainly be an option for those patients who are fit and who have already failed frontline chemotherapy and checkpoint. Using Afatinib could certainly be a good choice for those patients.

http://cancergrace.org/lung/2018/05/24/lung-cancer-video-library-gilotrif-afatinib-in-squamous-nsclc/