The Changing Landscape of First-Line Treatment of ALK-Positive Advanced NSCLC

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TRANSCRIPT

My name is Alice Shaw, I am director of the Center for Thoracic Cancers at Massachusetts General Hospital in Boston.

Since 2011, the first generation ALK inhibitor Crizotinib has been the standard first-line therapy for patients who are newly diagnosed with ALK-positive lung cancer. The efficacy with Crizotinib is very significant, certainly better than with standard platinum combination chemotherapy. We typically see response rates over 70% with first-line Crizotinib and a median progression-free survival close to 11 months. So very good activity of Crizotinib in the first-line setting. However, we all know that patients will ultimately relapse on first-line Crizotinib and we have been working very hard the last several years to develop better options for patients who are newly diagnosed with advanced ALK-positive lung cancer.

Over the last several years specifically, we now have randomized trails comparing second-generation inhibitors to standard of care. I would say the most important of these studies are the ALEC studies: The J-ALEC study which was conducted in Japan and the global ALEC study which was conducted worldwide. The ALEC studies are important because they compared for the very first time first-line Alectinib with first-line Crizotinib. These were randomized studies randomizing patients one-to-one to receive either Alectinib or Crizotinib as their first-line therapy and the primary endpoint in these studies was progression-free survival. Now these were separate studies, but they are remarkably similar on analysis of the data. In both studies Alectinib was shown to be significantly superior to Crizotinib over doubling the median PFS (progression-free survival).

As an example, in the Global ALEC study the median progression-free survival with first-line Alectinib was about 26 months based on independent review and that's as compared to 11 months with Crizotinib. And as I said, very very similar results were seen on longer follow-up of the Japanese or J-ALEC study. We also saw very high response rates with Alectinib in both studies and importantly what we saw in both studies is that the intracranial activity of Alectinib is really quite remarkable compared to the standard of care Crizotinib. So, what we observed is that Alectinib was able to treat and control CNS metastases better than Crizotinib and importantly was able to decrease the accumulative incidence of CNS metastases compared to Crizotinib. So, in a way Alectinib was able to prevent the development of CNS metastases and this is a very important point for patients.

The last thing I'll note about these two randomized studies is that in both cases it did appear that Alectinib was overall better tolerated than Crizotinib. Crizotinib already is a relatively well tolerated drug but Alectinib seemed to have fewer serious side effects associated with it. The most common side effects seen with Alectinib tend to be mild such as fatigue, constipation, edema, and muscle aches.

Overall, Alectinib was not only more efficacious than Crizotinib both in terms of systemic and intracranial activity but overall was somewhat better tolerated than Crizotinib as well. These two studies now have really changed the treatment landscape for patients who are newly diagnosed with advanced ALK-positive lung cancer. These patients just a few months ago would have received Crizotinib in the U.S. as their first therapy and I think now with the J-ALEC and ALEC studies both published that we've now moved toward using Alectinib as our preferred first-line therapy for patients with advanced ALK-positive lung cancer.

http://cancergrace.org/lung/2018/04/12/lung-cancer-video-library-changing-landscape-of-first-line-treatment-of-alk-positive-advanced-nsclc/