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TRANSCRIPT

Transcript Details
This is a transcript of an educational program accessible on the ReachMD network. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/closing-gaps-nsclc/how-keynote-189-transformed-clinical-practice-overnight/10285/

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How KEYNOTE-189 Transformed Clinical Practice Overnight

Announcer:
This is ReachMD, and you're listening to *Closing the Gaps in NSCLC,* sponsored by Lilly. On this episode, titled *The Impacts of Keynote-189,* we will hear from Dr. Howard Jack West from the Swedish Cancer Institute in Seattle, Washington.

Dr. West:
KEYNOTE-189 is a randomized Phase III trial with over 600 patients with advanced non-squamous, non-small cell, and without a driver mutation, such as EGFR or ALK, but who could have any degree of PD-L1 from 0 to 100% and who are randomized 2:1 to receive platinum doublet chemo with a cisplatin or carboplatin and pemetrexed backbone along with either pembrolizumab or a placebo every 3 weeks, and then after those 4 cycles of doublet chemo with either immunotherapy or placebo, go on to receive maintenance pemetrexed with pembrolizumab or placebo.

The study was very highly positive with a hazard ratio for overall survival of 0.49, and that benefit was seen across a wide range of subgroups that were clinically defined or defined by something like PD-L1 expression, so the patients with high PD-L1 got a tremendous benefit, but even those with PD-L1 that was low or negative got a meaningful benefit from the triplet combination with pembrolizumab. There

was also a benefit in progression-free survival that was quite substantial and again seen across the spectrum of PD-L1 expression. There was a higher response rate and a longer duration of response and not any untoward or unsuspected toxicity issues. And so I would say that this trial result, which came out in the *New England Journal* by Dr. Gandhi and colleagues in mid-April and was simultaneously presented at the AACR Meeting in Chicago in mid-April, changed practice overnight and redefined a new standard of care for patients with non-squamous, non-small cell lung cancer if they didn't have a driver mutation.

We could still give pembrolizumab monotherapy for those with high PD-L1, but a combination of chemo with pembro, specifically a platinum/pemetrexed combination, became also a very strong choice for the high PD-L1 patients and the leading choice and new standard of care for patients with low or negative PD-L1, as long as these patients are fit. And it was an option to consider. It was FDA approved provisionally based on the smaller KEYNOTE-021G trial that we first heard about in late 2016, but many of us were not particularly inclined to broadly use this for our patients until we saw Phase III data, and those data were delivered in force with KEYNOTE-189 as a not just statistically significant, but crushingly clinically significant benefit for this combination, and I would call this chemo backbone the most attractive and widely used one for non-squamous, non-small cell, not just for lung cancer specialists but in the general oncology community as well, favored for its good therapeutic index, and pembrolizumab, also an appealing immunotherapy agent that oncologists have growing experience with.

Announcer:
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