



Chemotherapy/Immunotherapy Combinations in Advanced Squamous Non-Small Cell Lung Cancer

**Presented by H. Jack West, MD
Medical Director, Thoracic Oncology Program
Swedish Cancer Institute
President & CEO**

TRANSCRIPT

For a couple of decades now, the standard treatment approach for patients with advanced or metastatic squamous non-small cell lung cancer has been a two-drug combination of chemotherapy agents given as our first treatment to shrink the cancer and help patients live longer. We've also started using immunotherapy – IV treatments to help stimulate the immune system to recognize and attack the cancer. We've got several different agents that have been studied and now FDA approved and commonly used in patients as a second-line treatment after they have received prior chemotherapy. But what about possibly moving the immunotherapy that is proven to be effective as Plan B along with chemotherapy to give the drugs together as a first-line treatment.

We've just seen the first few big trials of chemo combined with immunotherapy for patients with squamous non-small cell lung cancer presented at meetings in 2018 and these are shaping new standards of care going forward. The biggest of these in terms of its influence and how we are going to change treatment going forward is a trial called KEYNOTE-407 which gave a combination of carboplatin chemotherapy with another chemo agent known as paclitaxel or Taxol or a related drug called Abraxane or nab-paclitaxel. One of those two-drug combinations either with a placebo, a nonactive treatment, or with Keytruda. There was a 50/50 randomization, so half the patients got chemo with the placebo and half of the patients got chemo with the immune therapy as a first treatment. This was for patients with any level of PD-L1 expression. PD-L1 is a protein that is sometimes seen on cancer cells in a biopsy. High levels are associated with a better chance of responding to treatment while low levels are associated with a somewhat lower chance of responding to immunotherapy.

This study was presented at ASCO 2018, our biggest cancer meeting of the year, to a lot of fanfare because it demonstrated that there was a significant improvement in the probability of a cancer shrinking in these patients, in delaying of the time before the cancer progressed, and also in how long patients lived if they received the combination of two chemo agents combined with Keytruda (pembrolizumab) chemotherapy. Importantly, in the patients who have high PD-L1 we saw a very good major improvement in how well these patients did and that's typical for what we would expect. These are the patients who we anticipate seeing the biggest benefit from immune therapy. But, it was also very impressive to see that even the patients with low-level PD-L1, that's less than 50% on the PD-L1 test that we use to define PD-L1 expression commonly, that's about a third of patients who are low, a third of patients who have high expression, and another third of patients who have PD-L1 levels that we'd say is negligible or less than zero. All of these patients had a significant improvement in how they did including how long they lived when they received the combination upfront of the two chemo agents and Keytruda.

At the same meeting, there were a couple of other combinations of chemotherapy doublets, or two-drug combinations, with other immune therapy agents such as Tecentriq and Opdivo. These studies have shown that in certain patients you can see an improvement in the time before the cancer progresses, but these studies have not shown an improvement in overall survival. So, we can say as a general principle that there is an improvement for patients with squamous non-small cell lung cancer with chemo combined with immune therapy as a first-line treatment, but the particular regimen of carboplatin with either Abraxane or Taxol and combined with Keytruda is the biggest benefit improving overall survival, progression-free survival which is the time before the cancer is growing, and it gives the best chance of shrinking the cancer. Moving forward, this is going to be a very strong consideration for the majority of our patients with advanced squamous non-small cell lung cancer at least as long as they are fit enough to get all of these treatments together.

<https://www.youtube.com/watch?v=hZTxvQ3LHhc&feature=youtu.be>