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

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

TRANSCRIPT

For many years, our standard treatment approach for patients with advanced or metastatic non-squamous non-small cell lung cancer has been a two-drug chemo combination. We have recently begun to introduce immune therapies, agents given IV to help stimulate the immune system, to better recognize and attack a cancer as a second-line or later treatment. These drugs were introduced several years ago as Plan B, after patients have responded and then had progression or just demonstrated progression on first chemotherapy. It was an obvious question to ask whether patients could benefit more from getting chemotherapy combined with immune therapy as a first treatment.

Now some patients who have high levels of a marker called PD-L1, a protein on some tumor cells that is associated with a high chance of response to immune therapy, that about a third of patients with high-level PD-L1 expression can get Keytruda alone as a first-line therapy and do very well. But, two-thirds of patients don't have this high-level PD-L1. There was a very important study presented in the first half of 2018, a study called KEYNOTE-189, that tested the combination of chemotherapy drugs alone or with placebo versus chemotherapy combined with pembrolizumab or Keytruda as first-line treatment for patients with advanced non-squamous non-small cell lung cancer. The chemotherapy being studied was a platin, so cisplatin or carboplatin, which is really a cornerstone of our chemo treatment for lung cancer. One of these drugs with Alimta (pemetrexed) and then as I said chemo with placebo or with Keytruda. These drugs are given IV every three weeks and then after several cycles one of the drugs, the cisplatin or carboplatin, is dropped and patients can continue on a maintenance therapy of the Alimta with Keytruda if they continue to do well.

This study was a large and well done trial that generated a great deal of excitement and was published in the New England Journal of Medicine, one of our most influential journals, because it showed results that really should change practice. Specifically, what it showed was that the patients who received a combination of chemo combined with immune therapy, Keytruda, at the same time had a significantly better chance of their cancer shrinking, also a prolongation of the time before the cancer tended to demonstrate progression and had a longer survival. This study enrolled patients who had any degree of PD-L1 expression that could be the third of patients with high PD-L1 expression, the third of patients with low-level PD-L1 that we define as 1-49% with high being 50% or greater, and then about a third of patients with essentially PD-L1 negative or less than 1%. Across this whole spectrum, the patients who received the combination of chemo and immune therapy with Keytruda had the better survival compared to chemotherapy alone. This is really likely to change and increase our enthusiasm about giving chemo and Keytruda as a first-line treatment for these patients.

Importantly as I mentioned, Keytruda alone is also a good option for the patients with high-level PD-L1 expression. It's also an option that can be considered for patients with lower PD-L1 expression though the results don't look as favorable as chemo combined with immune therapy in the patients with lower PD-L1 of 1-49%. As I said, this includes patients with PD-L1 zero or negative disease who are really not good candidates at all for Keytruda as a single drug first-line or later. This is really going to be a high priority option and really the best one for many of our patients.

Now importantly there are some other studies that look at different chemo combinations. There's one called IMpower150 that looks at carboplatin and Taxol (paclitaxel) actually with a third agent called Avastin (bevacizumab) which blocks the tumor blood supply. This three-drug combination with or without an agent called Tecentriq which is another immune therapy showed an improvement in progression-free survival and overall survival as well with the four-drug combination. But I would not consider this to be as attractive for the majority of patients with non-squamous non-small cell lung cancer because it's four drugs instead of three and the Taxol that is a component of the trial with Tecentriq causes numbness and tingling in the fingers and toes in some patients and hair loss in the vast majority. It's overall a little more challenging.

There is certainly other trials that are looking at various combinations, but at this point the one to beat is going to be what is called the KEYNOTE-189 trial and most patients will be getting carboplatin, Alimta, and Keytruda together. It is already FDA approved based on a small study that lead to the FDA approval in early 2017, but now with the results from this larger study it has convinced many of us who were prior doubters that this is really the way to go for a lot of our patients who are eligible.

https://www.youtube.com/watch?v=PUeVvjxdYLw&feature=youtu.be