

## **The evolving role in immunotherapy for lung cancer**

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Current immunotherapy for lung cancer can be broken into four main categories: checkpoint inhibitors, monoclonal antibodies, therapeutic vaccines, and adoptive cell therapy. Because of limited time, this abstract only introduces checkpoint inhibitors in the treatment for non-small cell lung cancer (NSCLC). Immune checkpoint inhibitors work by “taking the brakes off” the immune system, allowing it to mount a stronger and more effective attack against cancer. Several different types of checkpoint inhibitors are currently in use: PD-1/PD-L1 checkpoint inhibitors, CTLA-4 checkpoint inhibitors, and combination checkpoint inhibitor approaches.

In 2015, two new immunotherapy drugs, nivolumab (Opdivo®) and pembrolizumab (Keytruda®) were approved by the FDA for the treatment of lung cancer after standard chemotherapy has stopped working. Nivolumab was approved for the treatment of squamous and non-squamous NSCLC and pembrolizumab was approved for the treatment of PD-L1-positive NSCLC. Both nivolumab and pembrolizumab are being tested for PD-L1-positive NSCLC in randomized phase III trials compared to standard-of-care chemotherapy as first-line treatment.

Current research suggests that blocking PD-L1’s ability to bind PD-1 is an effective way to block the PD-1 checkpoint pathway. Atezolizumab (MPDL3280A), made by Genentech/Roche, and Durvalumab (MEDI4736), made by AstraZeneca/MedImmune, are both antibodies targeting PD-L1. They are being tested in a variety of trials for patients with lung cancer.

In addition, Ipilimumab (Yervoy®), made by BMS, and Tremelimumab, made by AstraZeneca/MedImmune, are checkpoint inhibitors that targets the CTLA-4 checkpoint on immune cells. Although there is limited clinical development of CLTA4-targeting drugs in NSCLC as single agents, combination approaches with PD-1 and PD-L1 antibodies have demonstrated encouraging data, such as nivolumab + ipilimumab and durvalumab + tremelimumab being tested in phase III trials versus standard-of-care chemotherapy in first-line treatment for both PD-L1-positive and PD-L1-negative NSCLC. We will go into detail in this talk.