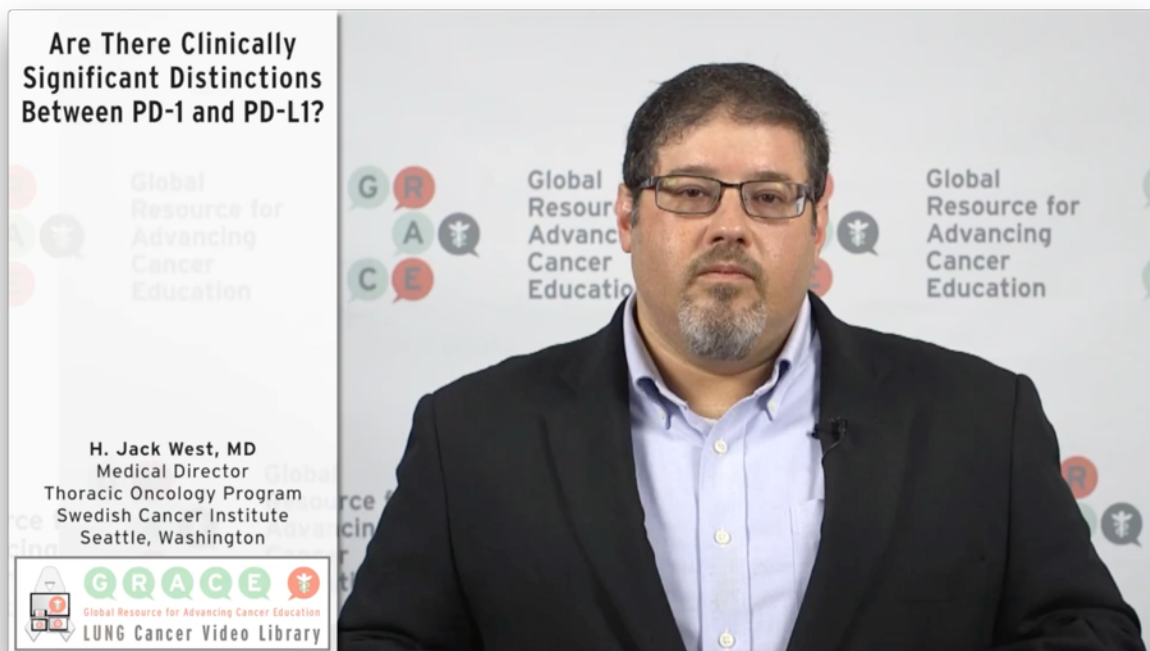




Are There Clinically Significant Distinctions Between PD-1 and PD-L1?



TRANSCRIPT & FIGURES

Among the most exciting developments in lung cancer over the last few years has been the introduction of immune checkpoint inhibitors – agents that are given by vein that help to stimulate the immune system, really by turning off one of the braking mechanisms. There are two main treatment approaches that are used, they're called PD-L1 inhibitors and PD-1 inhibitors. These PD-1 and PD-L1 are receptors that attach to each other, and when they work together they lead to a braking mechanism for the immune system. These antibodies can block either the PD-1 or the PD-L1 side of that and turn off that braking mechanism, much like taking off the emergency brake on a car and leading it to roll ahead.

PD-1 is on the T cells of the immune system, PD-L1 is on the tumor cells, so there are different agents and they block different sides of this interaction. The question is: does it matter which one you get or are they all pretty much the same? There are two agents as of now that are FDA approved in advanced lung cancer and those are Opdivo, known as nivolumab, and Keytruda, known as pembrolizumab, although there are other agents that are likely to become FDA approved in the future.

These two agents, Opdivo and pembrolizumab, are both PD-1 inhibitors. Others such as atezolizumab and others are known as PD-L1 inhibitors. Does it matter which one you get – do the results differ? Well we don't absolutely know because we have not yet seen the results or even done a trial that directly compares how patients do when they get one over another, but the results are remarkably similar regardless of which agent is tested in the same setting. Specifically they all seem to produce response rates of about 15% to 20% in the broad population, and if we look at patients who have

significant PD-L1 expression, the protein that is associated with the more inhibitory effect, we see better results with any of these.

It remains to be seen whether you can treat a patient with a PD-1 inhibitor like Keytruda, like Opdivo, and then get a good result once they show progression because you've given them a PD-L1 inhibitor, but for all intents and purposes, the results in terms of efficacy and also side effect profiles are remarkably similar and most specialists feel they are really essentially interchangeable until we see evidence showing otherwise.

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