Immunotherapy Combinations: Is this the Future for Treating Lung Cancer?

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TRANSCRIPT & FIGURES
So, as a research community, I feel like we’ve come a long way. It used to be, even not so long ago, that you would have a new drug, and that the first thing you would do is try to figure out how to add it to all of the established regimens that we were using. Now, that is not the initial development of the checkpoint inhibitors – the initial development has been looking at the single agent, and looking at checkpoint inhibitors as an alternative to chemotherapy. That being said, in this development, we’re sort of now moving back to that, where we’re seeing an effort to incorporate the immune checkpoint inhibitors, along with other approaches – things like chemotherapies, targeted therapies, and those are clinical trials that are under way.

Now, there is certainly some biologic rationale for this, in that, one thought is that if you are able to destroy cancer cells, that you basically would, it’s sometimes described as free-up an antigen, or free-up targets, for the immune system, and that therefore, it would be a more effective approach. There certainly are a host of studies underway, looking at adding checkpoint inhibitors to standard chemotherapy, and to most of the targeted therapies that have been developed – that is something that you are certainly seeing.

So, one of the areas that people have been interested in looking at is actually combining PD-1 or PD-L1 inhibitors with other immune checkpoints, and the ones that has been most extensively evaluated have been inhibitors of CTLA-4, and some of the reason for this is actually practical – there is a CTLA-4 inhibitor, Yervoy, that is clinically available because it’s used to treat metastatic melanoma, so any drug company can run a study with Yervoy. Yervoy is an expensive drug, and so it’s an expensive study to run, but it can
be done. Also, Bristol-Myers Squibb who makes Opdivo also makes Yervoy, and MedImmune is a drug company now owned by AstraZeneca, that is developing both an inhibitor of PD-L1, as well as CTLA-4.

There has been some intriguing data looking at that combination specifically, and there have been some indications that, perhaps in patients who have low level of staining for PD-L1, that you can effectively treat those patients with the combination of agents. I'm a little cautious on those studies, in that the toxicity is clearly higher when you combine a CTLA-4 inhibitor with a PD-1 and PD-L1 inhibitor, and although the numbers to date look quite good, I'm concerned that that may be in a more robust group of patients, as not everyone who I would feel good about putting on a single agent PD-1 or PD-L1 inhibitor study, would I also feel good about putting on one of these combination studies. So, I am very eager to see if some of the promising data that has been seen to date with this combination of a PD-1 or PD-L1 inhibitor with a CTLA-4 inhibitor can be shown on a broad scale, in a larger group of patients.

In addition, our understanding of immunology has certainly increased over time, and there are other immune checkpoints, as well as vaccines, and other immune-based approaches that people are starting to look at in the setting of clinical trials. I think there are a host of exciting clinical trials out there – it will be interesting to see the outcome, I'm sometimes concerned that maybe the clinical trials are getting ahead of where the science are, and that some of these can be associated with harm, but on the other hand, it will be interesting to see what the results are, and it is an exciting time in immunotherapy, certainly.