



GRACEcast

Immunotherapy Combinations



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TRANSCRIPT & FIGURES

The class of agents known as immune checkpoint inhibitors have really invigorated our study of lung cancer, and many other cancers over the last few years. Agents like Opdivo, also known as nivolumab, and Keytruda, known as pembrolizumab, are now commercially available, FDA approved as a second line therapy for patients who have progressed on first line standard chemotherapy. We are now actively asking the question of whether we might be able to move these immunotherapies into the first line setting and also asking whether we might do well by giving a combination of immune therapies, rather than just one treatment at a time.

So these agents, immune checkpoint inhibitors, are largely categorized into PD-1 or PD-L1 inhibitors, and those are just targeting two separate sides of an interaction between two receptors. The PD-L1 is on the tumor cells, PD-1 is on the immune T cells, and so blocking either side of this can lead to a beneficial effect because this effect leads to a braking mechanism on the immune system – you take away that braking system and you turn off the brakes and lead things to move forward, and that's what we often see.

There are other agents that can also lead to braking mechanisms and that have been studied in other cancers. An agent such as Yervoy, which is known as ipilimumab is a CTLA-4 inhibitor and this is an agent that's been approved in melanoma. In fact, the combination of Opdivo (nivolumab) and Yervoy (ipilimumab), as two different ways of blocking the immune system, have been shown to be beneficial as a combination in melanoma compared with either one on its own. Because of that, we're looking at combinations of immunotherapies compared with single immunotherapy approaches, or standard chemotherapies.

One interesting study being done right now is called CheckMate 227 and it is looking at first line treatment of patients with advanced lung cancer that is either squamous or non-squamous histology. It does not require any level of PD-L1 expression on the tumors, the protein associated with tendency toward better efficacy of immunotherapies, partly with the thought that the combination of two immunotherapies may make even the cancers that don't express PD-L1 respond well. This trial is looking at first line therapy with either standard chemotherapy of cisplatin or carboplatin with Alimta for non-squamous cancers, or Gemzar (gemcitabine) for squamous cancers, compared with either Opdivo alone or a combination of Opdivo and Yervoy – Opdivo being a PD-1 inhibitor, Yervoy being a CTLA-4 inhibitor – and asking the question of whether immunotherapy is as good, better, or worse than standard chemotherapy as a first line treatment, and whether the combination of two immunotherapies is better than first line therapy.

I should mention that there are other trials looking at very similar versions of this question using different combinations of immunotherapies. There are many companies looking at several different immunotherapies in development and they are overall really very comparable and all quite exciting.

You can learn more about this specific trial from the link on the screen,

[CheckMate 227 Clinical Trial](#)

but I would encourage you, if you talk to your doctor and they recommend a trial with an immunotherapy in the first line setting, potentially comparing it

to chemotherapy, to carefully consider it – it does not have to be this specific trial to be of interest.

We're going to learn more about this in the coming years and we're going to figure out the best way to integrate immunotherapies with our standard treatment approaches today.

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