



GRACEcast

Immunotherapy as First-Line Treatment



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TRANSCRIPT & FIGURES

A class of agents known as immune checkpoint inhibitors has really incredibly invigorated the field of lung cancer and many other cancers over the last year or two. These agents are given intravenously and essentially take off a braking mechanism for the immune system and by doing that, can stimulate it to recognize and attack your own cancer. These agents, at least a couple of them, have been approved by the FDA as of now, in late 2015, and the question is whether they should be used earlier than the second line setting where they've already been approved.

Two agents, one known as Opdivo or nivolumab, and another known as Keytruda or pembrolizumab, are approved in patients who have already demonstrated progression after receiving a first line chemotherapy. So the question is: should these treatments be given earlier in therapy? There are two leading considerations in how we might do this. One is that we might give an immunotherapy in combination with standard chemotherapy. There are other ways to do this that might give the immunotherapy instead of standard chemotherapy. There are studies looking at various combinations being done with any of the many immune checkpoint inhibitors that are in development right now.

An interesting trial that is being done now is with pembrolizumab, or Keytruda – this is the KEYNOTE-189 trial that is looking at whether the addition of Keytruda to standard chemotherapy improves outcomes for patients when they get it first line. Specifically this trial is for patients with a non-squamous cancer and these patients can have any level of PD-L1 expression, the protein that tends to be associated with better activity of the immune checkpoint inhibitors – there's no restriction on PD-L1 expression

and patients just have to have not received prior therapy for advanced lung cancer. These patients are then randomized to receive the two drug chemotherapy combination of cisplatin or carboplatin with Alimta, or that same chemotherapy combination with Keytruda (pembrolizumab). That study is being done now and we hope to learn more about it in the next year or two, to learn whether it is beneficial to give these immunotherapy agents in combination with chemotherapy, compared to giving them sequentially.

Another very similar study, though looking at squamous lung cancer, is called EMPOWER 131 – this is with an immune checkpoint inhibitor known as atezolizumab. This agent is being looked at in combination with either carboplatin and Taxol, or carboplatin and Abraxane, a very similar agent. There are two arms of this study where a patient gets a combination of chemotherapy and the immune therapy, and the third arm is just carboplatin and Abraxane alone. We should learn more about the potential benefits of combining immune checkpoint inhibitors with chemotherapy in the first line setting from this, looking at both patients with squamous and non-squamous histology in different trials.

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