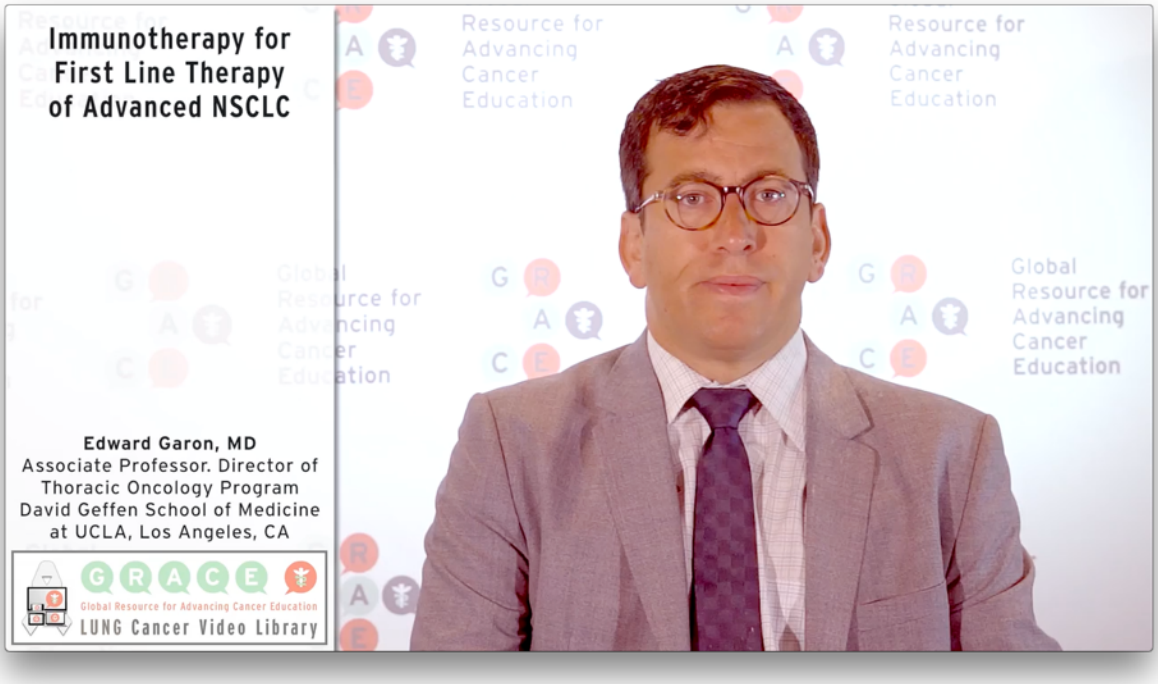
Global Resource for Advancing Cancer Education

LUNG Cancer Video Library

Immunotherapy for First Line Therapy of Advanced NSCLC



TRANSCRIPT & FIGURES

So, initially, development of the PD-1 and PD-L1 inhibitors were in patients who were previously treated, as that is a very difficult clinical scenario. Now, we do know, in the front line setting, that there is data that would indicate that many patients do quite well with chemotherapy, certainly not all, and the toxicities are certainly there, but chemotherapy can be quite effective in patients with non-small cell lung cancer. So, the question when you have a drug that is as effective, or a class of drugs that are as effective, as the PD-1 and PD-L1 inhibitors in previously treated non-small cell lung cancer, is: can those results be moved forward — can patients receive this as their initial therapy, rather than traditional chemotherapy approaches?

This is a place where, in my estimation, evaluation of the biomarker is going to be particularly important. So, there is data that would indicate patients who have higher degrees of staining for PD-L1 are more likely to respond to these immune checkpoint inhibitors. Of course, there is other biomarker work that is underway as well, some of which has been published, and some of which continues to go on, that may also be very helpful in identifying the appropriate set of patients. But, when one is looking at front line checkpoint inhibitors, one has to realize that, if you can identify a group of patients that are unlikely to have a response to a checkpoint inhibitor, that group of patients, probably, would be better off receiving standard chemotherapy in the front line setting, which we know can be quite effective, and, therefore, most of the studies that are looking at front line therapy are selecting patients who have, for instance, high level expression of PD-L1, and that has been, certainly, a major focus — people have taken different approaches. There are some studies that are specifically identifying patients, and only randomizing patients who have a high degree of staining to chemotherapy or

a checkpoint inhibitor in the front line setting. Others are enrolling patients more broadly, but limiting their analysis to the patients who have a high degree of staining.

What I will say is, as somebody who has, for instance, studies in the front line setting that would give everyone a checkpoint inhibitor, as well as studies in the front line settings that would give only selected patients a checkpoint inhibitor, I have been very reluctant, at this point, with the data we have available, to enroll patients on a front line checkpoint inhibitor without knowing their PD-L1 status, because my concern is that, although you can say, well, those patients could always get chemotherapy later, we know that some patients with non-small cell lung cancer don't get to their second treatment, and, in fact, that is not an uncommon scenario. We know, as well, that it does take some time for these checkpoint inhibitors to be effective in many of the patients in whom they are effective.

So, I have some concerns — for instance, if a patient has low level staining, although we don't have all of the data yet, my suspicion is that, for instance, a patient with absent PD-L1 staining would probably be better off getting standard chemotherapy in the front line setting, and I think that it's an important thing for patients to know, and of course the clinical data will sort of lead us there, but it is not clear that this is the absolute best therapy for everyone at every time. I think that there is a group of patients for whom that is likely to be the case — the group of patients in the KeyNote 001 study, which was looking at Keytruda, where they had not previously been treated — the survival in that group was so impressive, in fact, that we couldn't even report on the bottom limit of the 95% confidence interval for survival,

because patients just were staying on, they weren't dying, of the people who had high level staining. That being said, the people who had absent staining – they didn't do as well, and that's a group of people, where my suspicion is, would do better with chemotherapy. We will see when the clinical data comes out.

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