Dr. Eddie Garon, UCLA, reviews the controversial question of whether PD-L1 expression is a reliable enough biomarker to be used to select patients to receive or not receive immune checkpoint inhibitor therapy in lung cancer.

Download Transcript

Please feel free to offer comments and raise questions in our Discussion Forums.

Transcript

So, the role of PD-L1 as a biomarker may be among the most controversial areas in the
checkpoint inhibitor story. So, in melanoma, they have seen tremendous results with the check- 
point inhibitors, and early on in the development, the melanoma physicians were very 
dissimissive of the role of a biomarker, in general, because they were seeing such good 
responses. Nonetheless, many of the studies in non-small cell lung cancer have specifically 
sought out the biomarker and there have been many different biomarkers that have been 
assessed, but the one that has been assessed most strongly in a clinical setting is the 
expression of PD-L1.

Again, PD-1 inhibitors are blocking the interaction between PD-1 and PD-L1, so it seems 
reasonable, perhaps, that the degree of expression of PD-L1 would correlate with the response 
to drug. And, in a very large study, in which we required all patients to have a biopsy around 
the time of therapy, looking at Keytruda, we saw that there were tremendous differences with 
respect to response rate, progression-free survival, as well as overall survival, with patients 
who had a high degree of staining for PD-L1, doing significantly better than patients who had a 
low degree of staining. When that data was published, there was some concern because there 
certainly were patients who had low level of PD-L1 staining, or even absent PD-L1 staining, 
who did have responses to the drug, and the thought was, how could you leave people 
behind? How could you not give patients the PD-1 or PD-L1 inhibitors, for instance, if you are 
in a situation where there are some patients who have no staining, who still respond — and 
that’s a very fair criticism. However, when you look at the data from the CheckMate 057 study, 
what you see is that there, again, now, in this case, they actually weren’t treating everyone 
with Opdivo, they were randomizing patients to receive either Opdivo or Taxotere, and they did 
identify one cutoff where, if you look, there was tremendous benefit in patients who had high 
level staining, but in patients who had lower level staining, those patients did equally well, 
whether they were on Taxotere or Opdivo; and the data from the POPLAR study with 
atezolizumab, where they look at it slightly different — they look at not only tumor cells, but they 
also look at the PD-L1 expression on infiltrating immune cells. In that study, again, they 
identified patients who had higher degrees of staining who did particularly better, and at least 
numerically, when you look, there was a group that they were able to identify where it looked 
like they did a little bit better if they got Taxotere.

So, this is still an area that is under active investigation, it is quite controversial, and the 
additional thing that’s important for patients to know is that it’s going to be a very hard 
situation, because, the way drug development currently is, one essentially gets credit, 
additional credit, for developing a biomarker along with the drug. And, so, for instance, in 
Keytruda, even though they had just a phase 1 study, that phase 1 study which showed clear 
correlation with a biomarker, may hasten that drug being available for patients. But, the 
challenge in that is that each company has their own diagnostic test, and it can be confusing 
because the tests are not identical. As I mentioned, atezolizumab evaluates both tumor cells 
and immune infiltrating cells, while the other tests really evaluate tumor cells alone, and 
similarly, the sensitivity and specificity of the antibody can differ — now that, I know, gets very 
technical, but I think what a patient could take from it is that 30% staining for PD-L1, for 
instance, with one antibody, doesn’t mean that you would have 30% staining for PD-L1 with 
another antibody. And, so, to some extant, each company has looked at their own antibody 
with their own drug, and I think this is going to be something that is confusing to patients as 
these things roll out. And, there are many efforts underway of sort of harmonize this, and
hopefully we will be able to get to a point where it is easier for patients and clinicians to interpret the data.