GRACEcast

Direct From ASCO 2015:

Highlights & New Approaches in Kidney Cancer

Immunotherapy for Metastatic Kidney Cancer Shows Increased Survival

TRANSCRIPT

Dr. Pal: Well, it's a great honor to be here today with Dr. Toni Choueiri, from the Dana-Farber Cancer Institute. I consider him to be a real legend in the field of renal cell carcinoma, so it's great to get his perspectives on the disease. So, Toni, just to begin, you'll actually be discussing some data related to PD-1 on Monday — can you shed some light on that; tell us what you'll be discussing that day?

Dr. Choueiri: Yeah, we do have some exciting data regarding nivolumab, which is a PD-1 inhibitor, in metastatic renal cell carcinoma. We have conducted a biomarker-based study where we collected tissue at baseline, just before nivolumab, with a biopsy and, while on nivolumab, trying to figure out potentially any mechanism, any biomarkers of response or resistance to nivolumab and, on the other hand, try to reproduce, as much as possible, the previous experience with nivolumab in the same setting. We did find overall survival, which will be presented for the first time, to be quite interesting — exceeding two years in some cohorts, as well as we found some interesting biomarker data related to T-cell infiltrates in the tumor that correlate with better outcome. There were no signals of toxicity, nothing new that we did not know before regarding PD-1 inhibition or nivolumab, so this is exciting. It provides some framework to base our next study, next biomarker study, related to mechanisms of resistance to nivolumab, or in case we would want to add another drug to nivolumab in metastatic renal cell cancer.

Dr. Pal: Yeah, I think that's going to be really exciting data and it really lends itself to one of the struggles that I have from day to day in the clinic — every patient discussion entails some talk of PD-1, but we don't know who to pick. Right now, are any of these markers that you've discussed — PD-L1

expression, T-cell expression; are they ready for primetime, or do we need further study?

Dr. Choueiri: They're not, but we are getting very close, and the thing I want to mention here is that data in one disease setting may be different from another disease setting. I think there's a lot of variability in calling what is positive by PD-L1 immunohistochemistry, which is what we use currently.

The cut off remains unknown at this point. Folks are looking at 1%, 5%, 10%. There are different antibodies in the field which are used by different companies and different academic centers, and there is always the problem in renal cell, as well as other tumors, of tumor heterogeneity. You can look at the same tumor, in the same site, and some areas will be PD-L1 positive, some will be PD-L1 negative.

We just reported very recently on a study from our institution with Dr. Signoretti and colleagues, that tumors tend to have tumor with higher Fuhrman grade around the area of highest Fuhrman grade — that's where PD-L1 expression tends to be the highest; we did not find a major difference between primary and metastatic side, but I think the story continues to evolve. What we found interesting in the study is that, even the patient we called PD-L1 negative still have relatively very good outcome. So, at this time I do not think you can choose a biomarker in metastatic RCC [renal cell carcinoma] to guide your therapy with an immune checkpoint blocker, at this time — things may change next year, at next year's ASCO, perhaps.

Dr. Pal: That's very well said, I appreciate that. I'm going to ask you a very provocative question right now, but something that I think emerges in many of our discussions, probably in yours as well, at City of Hope. So, if you've got a patient who says to you, "look Doc, I know the data is still pending, we don't know the results of the phase-3 study yet, but I'd like to get nivolumab right now, off-label." Is that something that you support, or what are your perspectives on that?

Dr. Choueiri: Well, I'm blessed to work at an institution where I always have — not always, but, a lot of times, availability for clinical trials. I do think the data, from the pivotal trial of nivolumab in second-line, finished accrual, and hopefully the result would be available soon. It's not unreasonable to recommend, but you know, in our current system, there's a lot of unknown, like: who is going to pay, what is going to happen, is this an optimal patient, what kind of kidney cancer do they have, is there a clear cell or non-clear cell — all these trials were done in clear cell, so what if you have, in front of you, a patient with non-clear cell, and actually what type of therapy did they have — if someone comes to you and wants a PD-1 inhibitor today, I mean, there is really very little data.

So what I want to mention is, the field may change in a matter of weeks, with what's happening with the emergent results from trials that we're waiting for. What I can tell you, it seems that the drug is well tolerated overall, and it helped a subset of our patients — there is no doubt.

Dr. Pal: Great, well, Toni, as always I learned a lot from chatting with you, and thank you so much for your time.

Dr. Choueiri: Absolutely, thank you Monty.

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