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Biomarker Breakthroughs: A Look at What's Next for Kidney Cancer Care

Ryan Quigley:
Welcome to *Project Oncology* on ReachMD. I'm Ryan Quigley, and joining me to discuss his presentation at the 2025 American Society of Clinical Oncology Annual Meeting, titled *Blood, Guts, and Tumor: The Search for Kidney Cancer Biomarkers Continues*, is Dr. David McDermott. He's the Chief of Medical Oncology at Beth Israel Deaconess Medical Center in Boston. Dr. McDermott, thanks for being here today.

Dr. McDermott:
Great to be with you, Ryan.

Ryan Quigley:
To start us off, Dr. McDermott, can you give us a brief overview of your session from ASCO and the inspiration behind it?

Dr. McDermott:
Sure. So my session was kind of a sandwich. The first speaker in the session who focused on, as you said, kidney cancer biomarkers was actually Dr. Kim Rathmell, who was the most recent head of the National Cancer Institute and is a kidney cancer researcher. She was back to join us to give an introductory talk, which essentially was a summary of the history of the development of kidney cancer biomarkers, so if you're interested in that story, Kim lays it out quite well. It's on the ASCO website. That was followed by four new presentations from investigators who are trying to develop the next wave of kidney cancer biomarkers, and there was some interesting data presented there, which I hope we can talk about. And then I was brought in at the end to summarize that work and point us to the future of where this work was going to go and how this might lead to better outcomes for our patients, new therapies, and getting us closer to things like early detection of kidney cancer and assays that might help us with clinical decision-making.

Ryan Quigley:
And as a quick follow-up to that, why are biomarkers so difficult to come by, particularly in regard to kidney cancer?

Dr. McDermott:
There are multiple answers, and it's a great question, but the main reason is that as we've known for probably 10 or 15 years from the work from the folks at the Crick Institute, they've defined kidney cancer as a very heterogeneous tumor, meaning that when you look at primary kidney cancer—and they're often large tumors—there are different aspects of the tumor that are different both genetically and appearance wise. And then when you compare the primary tumor to the metastases, they often bear little resemblance to one another. They have maybe some basic mutations in common, but they're often very different. And when you're sampling either a primary or metastases, your view can be different based on how you sample them—so where you put the needle or how big a specimen you get—and that heterogeneity between primary and metastases probably explains the major driver for the difficulty because we're often basing our biomarker analyses on the primary because it's banked and available and not the metastases, which in so many of these settings—both the metastatic setting and, to a certain extent, the adjuvant setting—we're treating the mets, and they look and feel and are genetically very different often than the primary.

Ryan Quigley:
Now, in your session, you mentioned how integrated models are the future of biomarker discovery, so can you describe what these models are and how they can help identify key biomarkers for kidney cancer?

Dr. McDermott:

Given this complexity that we were just talking about, many of us believe that it's likely that numerous biomarkers are going to need to be put together to develop a predictive tool that's as useful as other predictive tools for other tumors—for example, in lung cancer where they're much better at developing and using biomarkers in clinical practice. And what do I mean by integration? Well, that can occur at several levels. That can occur at the source level, so what sources are you obtaining to develop your biomarkers? Is that from blood, or is that from the tumor, for example, and putting those together? There was a couple of good examples of that during this session, but also different platforms. You know, putting together increasingly more sophisticated platforms, for example, RNA analysis with histology or immunohistochemistry or DNA analysis. But even something that was discussed as part of this was different interpreters. So we obviously have the human interpretation of this data, but there was at least one example of the integration of machine learning into biomarker prediction from the CheckMate-9ER story, suggesting that when using machine learning, you might be able to integrate more data and actually come up with a better prediction tool. So the integration happens on multiple levels. It does sharpen our focus, but we're still not quite there yet with defining tools that people can use in clinic. We're getting there, but hopefully, integration is the key to that future.

Ryan Quigley:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Ryan Quigley, and I'm speaking with Dr. David McDermott about his recent ASCO presentation that focused on the continued search for kidney cancer biomarkers.

Now, Dr. McDermott, all of these models you mentioned earlier certainly show promise, but are there any particular limitations keeping them from large-scale utilization?

Dr. McDermott:
Well, the main one is most of the models that we have enrich for a response. So, for example, PD-L1 staining, which is used in other tumor types, enriches your chances of finding responders to immune therapy—and for the most part, I was talking about immune therapies and biomarkers for them during this session, but they don't reliably predict. So, for example, there are a lot of patients who have PD-L1-negative samples that have responses to PD-1. In fact, they're more numerous in many of these trials, which gets to the point that I was mentioning. So depending on where in the tumor you sample, you may sample a section that's cold, meaning not infiltrated with immune cells or not expressing PD-L1, whereas the mets in the patient may be and may be sensitive. So the bottom line is some of these assays—whether it's PD-L1 staining, gene signatures by RNA, or in the case of VEGF-targeted therapy, mutations like PBRM1, which are all associated with increased chance of responding to those individual treatments—are not precise enough to use in the clinic yet.

Ryan Quigley:
And to expand a little further on that, what additional work needs to be done in order to find more of those elusive biomarkers for kidney cancer?

Dr. McDermott:
Well, I think larger data sets, continued application of some of these novel technologies which provide more information, sampling from metastases as opposed to primaries, and getting larger samples will all be helpful. I think the other exciting area for kidney cancer biomarkers is the success we're seeing with blood-based biomarkers: both DNA and, specifically in this session, protein-based biomarkers, which seem to get you a better global sense of what's going on in the patient. They're obviously far less invasive, so patients are more willing to be considered for those blood-based biomarker tests. Ultimately, we need prospective trials to confirm some of these findings. And the exciting thing about the field of kidney cancer is those are starting to emerge, meaning trials, for example, that assign treatment based on a biomarker or try to confirm the ability of a biomarker to predict outcome. Those are all either in development or actually accruing, so that's the kind of thing we need going forward.

Ryan Quigley:
Now, before we close, Dr. McDermott, are there any closing thoughts you'd like to leave with our audience today?

Dr. McDermott:
I think the main point is we're making progress. We need to continue to fund this work, and that's a particular concern where funding for translational research is—at the moment in kidney cancer—harder to come by than it was most recently. We're on the verge of progress, so we can improve outcomes and limit therapy to those who need it so as to avoid, for example, complications that are unnecessary. I think the best example of this is in the adjuvant setting where we now have PD-1 blockade as the standard of care for many patients who have surgery, but we know some patients don't need it because they're not going to benefit. They're already cured by the surgery. There are some patients who are going to have serious toxicity, which can be long-lasting in some patients, and obviously, you don't want to be treating patients who are already cured with therapy that could produce long-lasting or even life-threatening toxicity. In that same scenario, there's also patients who probably need more than just PD-1. So who are those? And to me,

that's where this blood-based biomarker work could make a big difference because we've now seen in three separate trials—both the ASSURE trial, the CheckMate-914 study, and, in this session, the IMmotion010 updated data—that the KIM-1 protein-based biomarker does give us a sense of who is at highest risk for progression in the future and excitingly, in the case of atezolizumab, who might be more likely to benefit from that drug. It's not quite ready for use in community practice, but in my opinion, the KIM-1-based biomarker is certainly ready to be tested in a variety of settings, including adjuvant therapy, so that we can get to a world where we're treating the right patients with the right medicine for the right amount of time. And that's particularly important in the immune therapy world where we're currently overtreating some patients.

Ryan Quigley:
As those comments bring us to the end of today's program, I want to thank my guest, Dr. David McDermott, for joining me to share the key takeaways from his 2025 ASCO presentation on kidney cancer biomarkers. Dr. McDermott, it was great speaking with you today.

Dr. McDermott:
Yes, it was a pleasure, Ryan. Have a great day.

Ryan Quigley:
For ReachMD, I'm Ryan Quigley. To access this and to other episodes in our series, visit *Project Oncolo*gy on ReachMD.com where you can Be Part of the Knowledge. Thanks for listening.