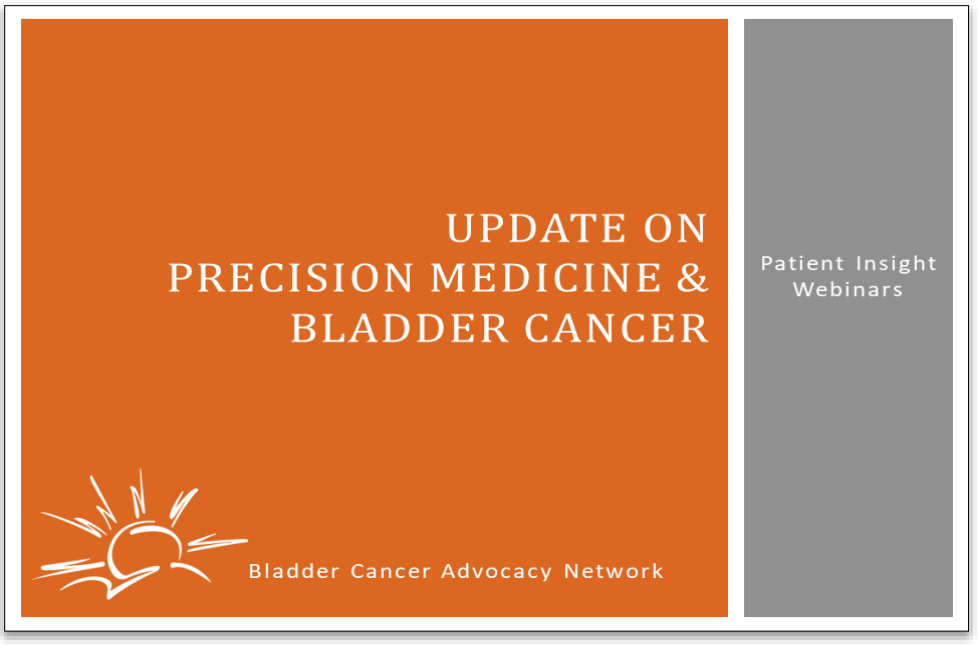

Stephanie Chisolm: We did get a couple of good questions from our group. Some are relevant and some are maybe not so much, but there wasn't a key question. It seems like a regular, everyday urologist, or even people in clinic urologists does not have the knowledge or advocates for any of this. When you talk to them they don't necessarily suggest it, or perhaps they suggest that your insurance doesn't cover it. I know Dr. Iyer, you mentioned the BCGC, the Bladder Cancer Genomics Consortium, that was funded by BCAN research. We actually put out over $1,000,000 to support that research. So how does somebody get genetic testing if their doctor's not even suggesting it, or they're not affiliated with a large institution like either at Memorial Sloan, Kettering or Baylor?

Dr. Gopa Iyer: Sure, I can maybe jump in quickly on this one. I think that's a question and that it's tough. Some of this may depend just as an FYI and the clinical situation that we're dealing with as well, because many times with, with bladder cancer, and as Dr. Lerner can certainly speak to this, most patients with bladder cancer will initially present with sort of non muscle invasive disease or very localized superficial disease, for those patients we're not necessarily always pushing to do clinical genetic sequencing right away, because we don't actually have yet targeted therapy specifically for the early stage patient population, certainly in patients who have more advanced disease, it would make sense to do genetic sequencing. And now with an FDA approval, we should be doing that routinely.

Some companies will do that for you. And so what, one of the companies that many of my patients and many others have sort of sent their tumor tissue to is Foundation Medicine, and you could actually reach out directly to them. They're actually very helpful in terms of helping to coordinate obtaining the tissue. You may not necessarily need, your treating physician to be involved very much in that process. They can certainly also guide you in terms of insurance approval processes as well. So going to the commercial companies is actually not unreasonable. And a lot of them have very friendly websites in which they can at least go through the process with you.

Dr. Seth Lerner: And I think, probably the most important point that Dr. Iyer just mentioned is, it really does depend on the sort of stage of your cancer. So there's a couple of questions that are reflecting, non-invasive cancer, for instance. But if you have, and there's a question that just popped up

about, papillary tumors in a solitary kidney and being treated with Jelmyto. So this is a thermoreversible gel that has mytomycin C, that's FDA approved. I think the issue there would be, is it possible that that individual has a Lynch syndrome and, because that's more common in patients with upper tract tumors. There's very specific criteria, but if... And enriched, for instance, if you have a strong family history of colon cancer or upper tract tumors for that reason, that would be the thing to look at in that patient.

And that can be done actually on the tumor tissue. There's very easy tests that the pathologist can do on the tumor tissue. Now, the people that Dr. Iyer sees, and there was a question about what is the advanced disease? And that's typically say a large tumor in the bladder that's grown through the muscle or might be growing into other adjacent organs, or spread to other sites like that case to the patient that I presented at the very beginning. I think a lot of medical oncologists are advocating, doing this kind of sequencing early on, even though it might not dictate or inform treatment at that time, it could be useful down the road, because as you've heard still quite frankly, the majority of patients are not responding or benefiting from these different treatments, we're getting there.

And I'll just give you one other example, for instance. And the only conflict I have here is I'm an investigator on this trial. So there's a company called QED that has a trial where they're using their drug, which targets this FGFR gene. And this is primarily for upper tract tumors, but it's also for lower urinary tract. If you have an advanced tumor, let's say you had surgery, and there was a muscle invasive cancer, and you have an FGFR3 alteration, you'd be eligible for this trial, potentially. So that would be a reason to maybe get your tumor sequenced. So I think it is stage dependent, whether it's upper tract, or urinary tract. Look, the reality of it is that, it may very well evolve to a standard of care that you come in the door, you get your biopsy and you get sequenced, and then you get plugged into genomic specific, personalized treatment. We're not there yet, but those are... That's the future, right? I mean, would you agree Gopa?

Dr. Gopa Iyer: For sure, 100%. I don't think we're quite there yet, but that's where we're heading to, for sure. The other thing that I would point out, I think, potentially with the person who might've asked that question about insurance issues too. I mean, as an oncologist, I'm certainly guilty of kind of saying upfront, we should go ahead and do the sequencing, do it right away. But especially if you do have a patient who has, let's say stage two or stage one bladder cancer, there may be more in the way of insurance issues since the FGFR3 at the FDA approval was for patients who have more advanced or metastatic disease. So just something to keep in mind.

Stephanie Chisolm: Sure. So I have a question for you. If somebody were to have say, genomic sequencing on a TURBT tumor that had been removed, and then they have disease progression down the road, are there any studies that are showing that mutations change over time or are those mutations consistent?

Dr. Seth Lerner: Yeah, well, it's a very wise question from Harley and she knows the answer to. And, yeah, no, if they do evolve overtime. And even within an individual tumor, if you take a piece from here, here, here, and here, you may get very different results and that's referred to as tumor heterogeneity. And it's actually one of the promises of circulating tumor DNA, which Dr. Iyer explained, because theoretically that is representing the tumor at its current state. Right? And it could be that these so-called liquid biopsies will be informing us of that point in time, because the question that you raised Stephanie is really important, because now what you have to now acknowledge is that these clones of cells that get out into the circulation and say land in the lung, right? Started down in the bladder.

But then the other thing that can happen is the tumor up in the lung can evolve and shed cells out, and then it gets more complicated. But this is the best we have right now. So ideally if you were unfortunate and had spread of the cancer, maybe you could get a biopsy of that lung leash, or maybe you could get a circulating tumor DNA test in the future and have that guide your therapy, as opposed to the tumor that you had in your bladder or tumor that you had up in your kidney, three years ago, for instance. Gopa what are your thoughts about that?

Dr. Gopa Iyer: Yeah. I'm in very much agreement with that, I think that whenever feasible, I oftentimes will talk with patients about whether we could sort of get a biopsy in a patient who let's say, unfortunately does have progression or a new metastatic site. A lot of times it's not feasible, or honestly, we don't have the time to do it, because of the logistics of getting a biopsy, in those situations, we will go with whatever was available from the archival tumor tissue. And if sequencing is available from that, we'll oftentimes use it. But this is where just to underscore sets point, I mean, this is where circulating tumor DNA would be extremely helpful. I think, especially in the patient who unfortunately has maybe rapid progression of their disease or where it's in a site that's just not easily biopsiable, can we do it from a blood sample? And we're getting there. Yeah.

Stephanie Chisolm: So as you mentioned, this is a really exciting advancement in disease treatment and understanding, we appreciate the fact that there's brilliant minds like yours working on this. And this is obviously an evolution. Like I said, we did this program four years ago, it was due for an update. And we'll probably end up with another program in a year's time, because now that you guys are really on this, it's changing the field and you're learning so much more. I want to thank everybody for joining us for today's program.