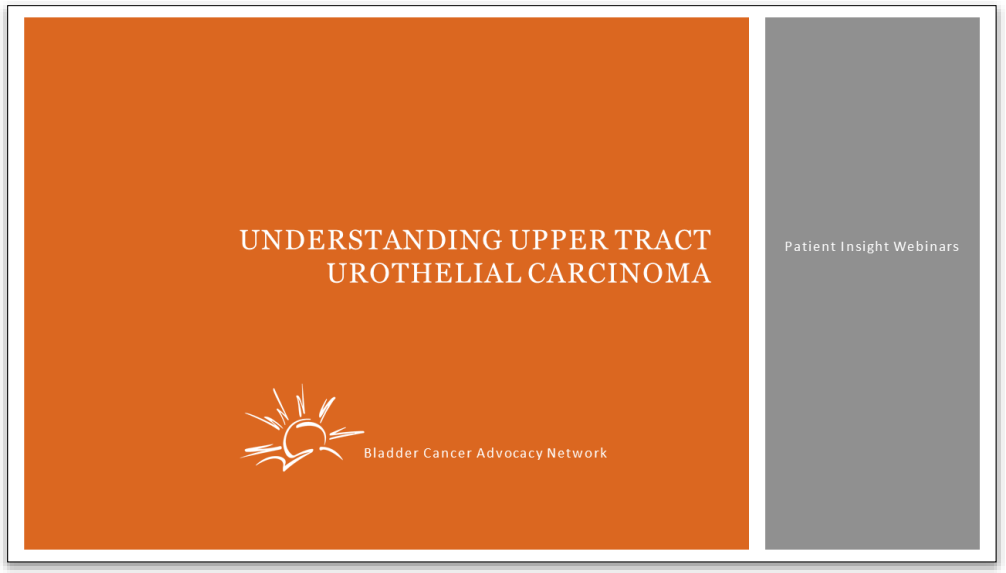

Morgan Stout:

Thank you so much, everyone. That was so insightful and wonderful presentation. We do have some questions that have rolled in, and I know that they've already been answered in the chat, but for the sake of those, maybe just listening in, I'm going to ask one or two of them out loud. The first one has to do with recurrence, which is something on everybody's mind, especially with those nephroureterectomies is, how can we prevent recurrence? What is the recurrence rate for the folks in the different grades?

Dr. Kate Murray:

Sure. Yeah. I think we're talking about, if you have a nephroureterectomy or you've had an upper tract cancer, and so much of this is based on age, but I'm just going to throw out some general rules. The follow up is so important. Up to 40% of patients will end up with a tumor in their bladder at some point in time and up to 5% of patients can end up with a tumor in the other kidney or if you have a kidney remaining in another part of the ureter or something. So often, many of these patients maybe have had a history of bladder cancer and so they're quite familiar with that bladder cancer follow up of having to look inside the bladder in clinic and do those routines. But there also are many patients who are found to have a tumor of the upper tract of the kidney or of the ureter based on an episode of blood in the urine and they've never had anything in their bladder, and so explaining that risk of recurrence in the bladder is so important, in that it's a very similar cancer in some of our treatment bases are based on the similarities based on that urothelium, but as was noted at the very beginning, it's also maybe not the same cancer as we've always historically thought about from a molecular level. There is so much more to come from us in the world of urology from that aspect.

Morgan Stout:

Thank you so much, Dr. Murray. Dr. Matin, Dr. Campbell, anything to add on that?

Dr. Surena Matin:

That was a really good summary of it. I think the one question about the follow up for this, at least in terms of what you read in the papers, it's, in my opinion, a little too intensive. A lot of these papers we

write that you have to, we have to do ureteroscopy or the upper tract endoscopy every three months in the first year. Gosh! That's a lot. It's a lot to put the patient through. It almost always requires anesthesia. There's always a lot of symptoms afterwards because we have to put a stent in. Patients hate stents, I can't blame them. We don't love them either, but the alternative is worse. Anyway, I've actually gotten to the point where I modified that. I don't feel ... I will modify my follow up for patients depending on what the risk of disease is. Basically, I generally don't do that intensive of a follow up, as you might read in some of the papers. I don't know. Dr. Murray, do you modify? Is your follow up modified for those types of things or are you still pretty dogmatic in terms of how you follow them?

Dr. Kate Murray:

I think that you're absolutely right. I think even if you want to be dogmatic and you want to be the most strict surgeon and say every three months, I have to be looking, we also are putting that into patients lives. It's hard to come in for surgery every three months. Every time you go under an anesthetic is impactful. You have to take off work or your children have to take off work, there's lost revenue, lost income, and so I really, if it's somebody I really am worried about, I'll stretch it and I'll do try to get four months, so I get one less a year even. Or if it's somebody who you can see on a scan, I'll alternate it with a CT scan and assuming I don't see a big, large tumor on a cat scan, I'd probably have enough time to wait another three months thereafter, so alternate cat scan and endoscopic direct visualization.

Morgan Stout:

Thank you. We did have a couple of really good questions submitted prior to the program, and they talked a lot about the genetics and gene expressions in upper tract tumors. As the experts here, how important is it to get those genetic screenings and look at just the genetic biomarkers that come off of these tumors? Is that something you recommend for everyone or is it pretty specific?

Dr. Surena Matin:

Yeah, I think, the truth is in terms of, it's really, no, we're not there yet. I actually do it, but that's also because we have a program and we have a clinical trial going on, so I'm trying to see if some of my patients are eligible for the clinical trial. Having said that, outside of that, there really is not a role for a patient with localized disease at the current time for us to look at the tumor genetics. I do want to clarify that I think the question is specifically about the genetics of the tumor and whether they have mutations. The other genetic test is to look at the patient's own germline, and that's different. That's when we're looking for an inheritable syndrome. I just want to clarify that because sometimes it can be confusing about which one we're talking about. In this particular case, we're talking about having obtained a biopsy of the tumor and doing a mutation profiling, looking at the, seeing if there are genetic mutations there.

I don't think we're quite there yet, at least for localized disease. I'll give Dr. Campbell a minute to answer for patients with metastatic disease, they will actually, there is probably some role for that. It may be changing a little bit in those with patients with Lynch syndrome, because there is actually a provision to treat those patients with immunotherapy, even if they don't have metastatic disease. It's very slowly changing, but bottom line is there really is not a role if we're looking at it in an everyday type of case that we might see.

Dr. Matthew Campbell:

Yeah, I would agree. We, for all of our metastatic patients, and I have not gotten in trouble for this yet, but if patients are node positive, I look as well at their molecular profile looking for particularly FGFR3

mutations, since we do have FDA-approved targeted therapy. But to me, it gives me a roadmap of potential clinical trial opportunities and a potential better understanding of how their tumor is behaving. I completely agree with Surena. I think if we could have all patients screened for lymph syndrome with upper tract, that would be ideal. But I understand the concern about potential cost and that we do have the luxury of the ability to do that here that may not be covered in the community though. I think the immunohistochemistry test that we use as a screening tool are relatively inexpensive. Though the ramifications are immunotherapy is extraordinarily active for patients that have this, but it's also important for families to understand risks to relatives, including siblings and children that as this is part of a syndrome that also increased risks of colon cancer, uterine cancer, pancreas cancer, and others, and so it's ideal if we can try to identify that as early as possible.

Morgan Stout:

Absolutely. Thank you so much. I believe we have time for just one more question and Dr. Campbell already wrote the answer, but I want to ask it out loud. What's the protocol for screening for upper tract in patients that have already had a radical cystectomy?

Dr. Matthew Campbell:

Yeah. In general, we're following patients that have had a cystectomy most often for muscle invasive disease, but can be for non-muscle invasive disease with cross-sectional imaging, which is going to be CT scans or depending on kidney function, can be MRIs of the abdomen and pelvis. Depending on how those are done, as long as they're done with contrast, we're able to see the upper tracts reasonably well, and so that tends to be the way that we monitor for recurrence or a new development of an upper tract disease.

Morgan Stout:

Great. Thank you so much.