Clinical Trials: Non-Muscle Invasive Bladder Cancer

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Question and Answer Session

Questions Answered by

Yair Lotan, MD is holder of the Helen J. and Robert S. Strauss Professorship in Urology and Chief of Urologic Oncology at the University of Texas Southwestern Medical Center. He graduated from Baylor College of Medicine and did his residency training at UT Southwestern Medical Center. His primary clinical practice involves urologic malignancies with a focus on minimally invasive approaches. His research interests involve biomarkers for urologic malignancies especially bladder cancer. Dr. Lotan has performed multiple studies evaluating urine-based and tissue markers to improve early detection and prognostication of bladder cancer. He also focuses on outcomes research and health economics involving urologic diseases.

Robert Svatek, MD, MSCI attended the University of Texas in Galveston for medical school. He completed his urology residency training at the University of Texas Southwestern Medical Center in Dallas. Following his 3 year fellowship in urologic oncology at the M.D. Anderson Cancer Center in Houston, he was then recruited to the department of urology at the UT Health Science Center San Antonio in 2010, to build a bladder cancer center of excellence. Dr. Svatek is recognized nationally as an expert in the management of superficial and advanced bladder cancer. Dr. Svatek is one of the top five highest-volume bladder cancer surgeons in the United States, performing over 60 cystectomies yearly. He provides robotic-assisted and open approaches, as well as all available urinary diversion options, including ileal conduit and continent diversions (Indiana pouch and neobladder).

Moderator: I'd like to start with a quick question, which I think really is really important for patients. How do I bring up a clinical trial with my doctor? He's never mentioned it, but he's not at a large teaching hospital?
Dr. Yair Lotan: Obviously each doctor is a little different and Dr. Svatek and I both are commonly see patients for second and third opinions in part because many patients and some physicians want to see if there are other options that we have available that maybe they don't. I don't know that there's a perfect way. I think patients have to be proactive because, after all, as much as we're emphatic, the patients really have a lot more at stake than we do. Obviously BCAN's site has a lot of information about clinical trails. The National Cancer Institute actually has every clinical trial online and you can identify a bladder cancer trial. I really think that the best you can do is to, you can print out a list of trials or you can engage your physician with what are their thoughts about clinical trials in general? I'm not sure that there's any real strategy beyond just being honest with your physician that you want to see what else can be done, especially in the case where standard treatments are not working well.

Dr. Robert Svatek: I just want to add to that that there are urologists that are in a community, not in necessarily big academic centers that are really active in clinical trial research. It would just start by inquiring are you participating in any medical trials of bladder cancer, and if so, what are they? To start the dialogue.

Moderator: Okay. Thank you very much. There's another question. What's the value of blue light cystoscopy? If you could speak to that?

Dr. Yair Lotan: Sure, absolutely. Blue light or fluorescent cystoscopy is a method that has been approved primarily for us in operating room up to now, where you instill a substance called hexex which is really short for hexaminolevulinate acids. What it does is, it's a substance that's non-toxic and it gets taken up by cancer cells, but when you look at it under a blue light it looks pink. There have been several randomized trials that have shown that it can improve the detection of cancer by about 10 to 20%, in particular, carcinoma in situ, which is often difficult to detect. Most of the time it's used in the operating room, in patients who have normal bladder cancer to try to identify new lesions, but there's actually a large national trial right now to use in the office with a flexible cystoscope to try to figure out which patients where you don't see cancer might actually have cancer. That you may emit with a white light. They're still lacking evidence that it improves survival and progression, but it did reduce recurrence in several large trials. There is probably a role for it in some patients with bladder cancer, if not many.

Moderator: Great. That's really helpful. Thank you. That sort of segways into the next question: Are there any trials that you know of that are looking at early diagnosis or trial specifically looking at surveillance for recurrent? I think this is a question specifically looking at family members and others who might be at risk for bladder cancer.

Dr. Robert Svatek: You know, actually Dr. Lotan is obviously one of the national leaders in early detection in bladder cancer. He did one of the very few screenings studies ... him and I actually worked together in using a urinary biomarker to aid in detecting cancer early. Generally, we both feel that there's a role for early detection.

Dr. Yair Lotan: There are older studies that have found that detecting bladder cancer early probably will improve survival because you can reduce the chance of finding bladder cancer when it's invaded the walls of the bladder or metastatic. Which unfortunately, about 25% of all patients with newly diagnosed bladder cancer already have muscle invasive disease. One of the biggest problems that we have right now is that a lot of people have microscopic blood in the urine but don't get adequately evaluated until they either see blood in the urine or it happens many times. As Dr. Svatek and I are actually working on
a trial to try to find a certain urine marker will help detect those patients early. As far as the family connection, it's a complicated issue, because in fact, as Dr. Svatek pointed out, the genetics of bladder cancer are very weak.

There are many cancers such as prostate cancer and breast cancer where there's a strong family link. But in bladder cancer, most of the time, whenever genetics are involved, they're not inherited. They're acquired. In other words, something like tobacco smoking caused you to have genetic changes that lead to cancer. As far as I can tell, the biggest risk for family members is if they also smoke or if the parents smoke. We don't usually screen family members unless they have microscopic blood. The only thing that I can recommend is if you have a relative who has bladder cancer and you have risk factors such as smoking, then you can look for blood in the urine or your doctor can. If you find it, then you will need to evaluate it by having someone look in your bladder. But we don't currently screen family members for example.

**Moderator:** Great. Okay, I have another question. Are there any types of trials that are available that you know of that you could speak to, if BCG is not working?

**Dr. Robert Svatek:** This is actually one of the most exciting areas from a clinical trials perspective, for two reasons. One is that there are a lot of new agents that are being developed and this is one area where a lot of those agents are being tested. I can think of three, maybe four trials right now that are in the works for this specific population. The other reason that it's an exciting area is because look, the fact is that this is a really challenging disease. When BCG has failed, most patients get their bladder removed. That seems like a drastic maneuver, but we know that that's one of the only ways that we can prevent it from progressing. The FDA is actually been approached to develop a kind of platform for licensing of new drugs specifically for these patients. It's kind of been spelled out. They've met with urologists and bladder cancer experts and we have a spelled out platform of how we can get licensing for these new drugs in these particular disease stages.

As an example of some drugs that are being evaluated, there's a gene therapy drugs which aims to have the bladder cells make interferon. That's one drug that's being evaluated and that would be built into the bladder. There is a drug, immune therapy. It's a really interesting and exciting agent provider cancers. There is what we call check point inhibitors which are immune therapies that are going to be evaluated in this particular population. There's a few of them out there, so there's different tests, or I say, different trials depending on the agents. This is an exciting time for us in the bladder cancer field, particularity in that disease state.

**Moderator:** Great. Thank you. All right I have another question. What can we learn from atypia in pathology and cytology?

**Dr. Yair Lotan:** This is a bit of a complicated question in some respects. For the most part, it's a meaningless finding in the sense that the pathologists typically have different ways of characterizing cells in the urine. They can be completely normal. They can be atypical. They can be reactive. They can be suspicious, or they can be malignant. Atypia is common. We find it in about 15 to 20% of patients, and it's common because we are constantly doing things to the bladder that irritate it, between looking in the bladder and putting treatments in it. The cells look a little bit abnormal, but not abnormal enough to be suspicious or cancerous. For the most part, these findings should be ignored, but at some intuitions, including ours, we use urine markers, such UroVysion to try to figure out which of those
patients have cancer. That's especially the case when we see something in bladder, because sometimes BCG causes inflammation, sometimes the lining looks a little bit red, and then we don't know if that in combinations with atypia means the patient has carcinoma in situ. Genetic markers often help sort that out. But the vast majority of institutions, atypia by itself doesn't mean anything in terms of cancer and can be safely ignored, unless there is also some finding other, when they looked in the bladder.