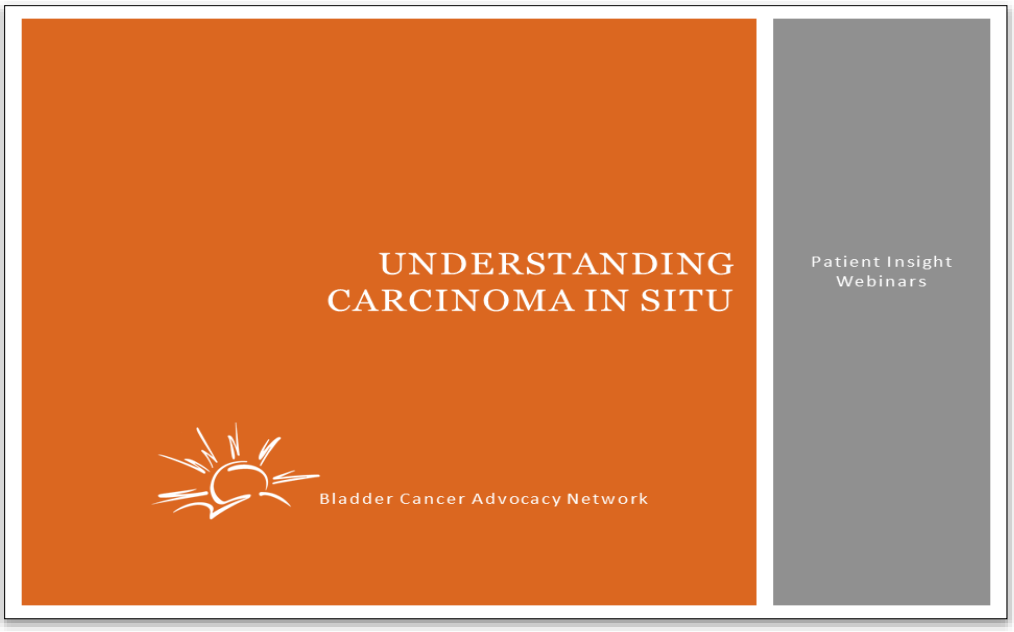

Stephanie Chisolm:

Well, thank you both so much. That was very insightful and informative, such great information. So easy to understand and a lot of good questions. I'm going to just go right into those questions if you don't mind. One of the... actually, two of the questions are about the same as far as is it better sometimes if you're at risk to just go ahead and have a cystectomy and have your bladder removed or could that be done too early? Is there ever a point where you take out a bladder too soon?

Dr. Peter Black:

Yeah. It's a very good question, and it's something we as physicians and with our patients really struggle to come to terms with sometimes. It's really relevant for... it's also for T1 and Ta carcinoma in situ. I think if a patient comes in with a first diagnosis of carcinoma in situ, I think ultimately the risk of progression and especially sort of a surprise progression that we didn't anticipate coming is very low, and I think cystectomy would be overtreatment and the risk of a major complication with cystectomy would make us say that it's potentially bad care and that really was done too soon. But as soon as you have a high grade recurrence after BCG or while on BCG, then I think the balance shifts and there it's really an individual decision. I have plenty of patients who have carcinoma in situ after their induction maintenance BCG who say, "Yes, please take out my bladder," and many who want to try something else before we take out the bladder. It's an individual decision.

Stephanie Chisolm:

So instead of going through the BCG induction, which can be very toxic for some patients, they have a really hard time handling it, what is your take on just monitoring that's used in case... the case you described, the 87-year-old. Would this have been something maybe you would've discussed just monitoring with him and just keeping an eye on it over time?

Dr. Peter Black:

Yeah, so I think for sure we do that. I think if this patient had had a high grade Ta tumor, so a defined pathway tumor that we completely resect, we probably would've said, "Well, let's monitor it. If it comes back, we can do BCG, but let's find a balance of less treatment burden in an older patient with significant medical problems." Here, the motivation to treat was really the fact that it was carcinoma in situ and certainly had the discussion. Carcinoma in situ is at risk for progressing to something more invasive, but it's not really short-term risk, it's over a few years. If you have an 87-year-old patient with a lot of medical problems, you might say, "Well, let's see what happens," but it's very unpredictable. This patient certainly was motivated to try and prevent that.

Stephanie Chisolm:

If you were to find carcinoma in situ in a small area like in the diverticulum, have you ever considered doing a partial cystectomy? I know that's really rare to do that, but is that something that would come up if it was really contained in one spot or is CIS so pervasive that you might not know that you're not seeing it everywhere, as you showed very succinctly with the two enhanced images, you could see it much better with the enhanced imagery? Would you ever consider a partial cystectomy?

Dr. Peter Black:

Yeah. The official answer is no, because you know specifically with carcinoma in situ that it's a diffuse disease and you would anticipate that it's not only in the diverticulum, and so you wouldn't be treating it adequately. I can say from personal experience, I did it once in a patient who had a lot of medical problems. And one other issue about a diverticulum is that you don't necessarily think that the BCG's going to work well. You don't know how it's going to get into that diverticulum and is it actually going to work? But this patient had really a prohibitive risk for doing a cystectomy, so I did a robotic partial cystectomy for his carcinoma in situ, and six months later, he had recurrent carcinoma in situ in the rest of his bladder. I demonstrated what we would say would probably happen and we would definitely not encourage it.

Stephanie Chisolm:

Okay. There's a lot of research into potential causes of bladder cancer. We know that it could be exposure to chemicals, whether it's in your environment or occupational exposures. Is there anything known that's specific as a risk factor for CIS that makes you more prone to this sort of flat type of a tumor rather than any other type of bladder cancer tumor?

Dr. Peter Black:

Yeah. Hikmat, I don't know if you want to comment on that.

Dr. Hikmat Al-Ahmadie:

Yeah. I mean, I don't think it has kind of been studied that way. It's grouped with all the different bladder cancers, and with the known risk factors, but I'm not aware of any particular exposure pattern or a professional exposure or something that can produce CIS per se, versus a more invasive disease. I don't know. Do you have any other insights, Peter?

Dr. Peter Black:

Yeah, no, I think we think of them as all being relatively the same and that we think of muscle-invasive bladder cancer, for example, and probably T1 as well, that may have started as carcinoma in situ, and so we think the risk factors are the same.

Stephanie Chisolm:

Okay. Thank you. That's really helpful. So you have shown very clearly how you as the urologist are working very closely with the pathologists to understand what's going on with this particular tumor. Is it normal to perhaps get a second pathology opinion on the samples or are you in a relationship with the pathologist that you're using that you really trust that they're doing a really good assessment of what comes next for that patient in terms of understanding that cancer?

Dr. Peter Black:

I would say yes and yes. You tend to trust your pathologist, but it's still probably worthwhile getting a second opinion. Now, if you're at a place like Hikmat's place, where you have top of the line, GU dedicated bladder pathologists, maybe you don't need a second opinion. I'm speaking for Hikmat here, but I imagine that Hikmat gets his own second opinions from his colleagues if he needs them. But I think for sure we know if just in general, community practice compared to what an expert pathologist like Hikmat would say that you would find things that the first pathologist didn't see. Maybe Hikmat can comment more on that.

Dr. Hikmat Al-Ahmadie:

Yeah. I mean, I think it's encouraged honestly, because it's a field that relies on visual, identifying abnormal features in the tissue, and the more you see of something, the better you get at it. So that's one thing. And also, patients now are more engaged, more involved in their care. They read. They always feel like maybe I wanted to be sure before I embark on something. So there are different things that can prompt a second opinion. We do see, as I said, we do see a fair share of cases. Good news is most of the times, we agree. Whatever that initial pathologist found, most of the times we can confirm. There are some times when there are things that are subtle in some cases that are more subtle than others.

Dr. Hikmat Al-Ahmadie:

Sometimes we may have more history than the outside community hospital, so that can help us identify things that might have been overlooked or missed by an outside pathologist. So I think the key to always lower the threshold of asking for another opinion, and I have to say also, admit that we do get sometimes our cases sent out for another opinion. It's not like we're immune. Again, this is a very important decision that a patient wants to make, and they want to always make sure that nothing has been overlooked, so people ask for it and it goes to someone else and most of the times of course they agree with us, but yes, it happens both ways. The main thing is always when something doesn't make sense, especially you're a treating physician and then they get an unusual pathology report that does not necessarily fit the clinical picture, that can also prompt a second opinion. And sometimes it's unusual for a reason and sometimes it could be over-called or a misdiagnosis. So, yeah, these are multiple scenarios, but it's always better to have another opinion.

Stephanie Chisolm:

Especially in pathology, because I don't think people think about that. Like, "Well, can you send this for some other expert to take a look at it?" They sometimes ask for a second opinion from the treating physician, but I don't know that they necessarily think, "I should get a second opinion on my pathology report." That's really good information. I know we're just about at time, and I don't want to keep you too long, but let's see if I have one more question. There was a question about biomarker monitoring as

far as things like Cxbladder to monitor and clarify if there's any atypical cytology. Is that ever used to monitor for CIS?

Dr. Peter Black:

It's a good question. I would disclose that we don't use any of these markers in Canada because they're not routinely available. So my own personal experience is limited, but I think that cytology is used universally. I did see the question about... basically the question what's the sensitivity of cytology? How likely is it going to reveal that there's cancer there? Then it was pertaining to a case where the cytology was what missed a cancer, but so from a sensitivity point of view, it's not very good, but it's very specific, so if the cytology is positive, we're confident there's something there, and so we use it as an adjunct to make sure we're not missing something. Something like Cxbladder is much more sensitive, so it's more likely to detect something, but it'll be less specific, meaning you could end up at a lot of false positive tests that you subsequently are working up. But in general, I think a patient with carcinoma in situ, there's potentially more value for biomarkers because it can be invisible.

Stephanie Chisolm:

Thank you so much. This has been wonderful. I really appreciate it.