Non Muscle Invasive Bladder Cancer (NMIBC) | Experts Discuss Treatment Options

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Part III: Question & Answer Session

Presented by

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Dr. Arlene Siefer-Radtke *is an Associate Professor in the Department of Genitourinary Medical Oncology, the Division of Cancer Medicine at the University of Texas MD Anderson Cancer Center in Houston, Texas. She's a clinical co-leader of the Bladder Specialized Program of Research Excellence, or SPORE, in the executive committee there in Houston, TX.*

Question 1: Does Johns Hopkins typically do a DNA study on the tumors for patients there?

Dr. Bivalacqua: Yeah, so what we have started to do now is all new diagnosed bladder cancer, our goal is to perform the RNA sequencing to look at these gene expression changes that Arlene was talking about. And that is something that actually ... On July 1st, our goal is to start doing that in everyone. As you can imagine, that's a very hefty and very challenge ... Very much a challenge to do, but that is our goal. And I would suspect over the next 12 to 18 months that every new diagnosed and every new tumors that we remove here at Hopkins will be sequenced to look at these gene expression changes.

Question 2: And do they do that at MD Anderson?

Dr. Arlene Siefer-Radtke: We are doing it mostly on patients on clinical trials, trying to understand which patients are responding to which treatments. But I do want to point out that looking for gene

mutations is something that is readily available for all bladder cancer patients. At least those with metastatic disease. So I think at a minimum, every patient who has a stage four or metastatic cancer should be asking for mutation testing since there are clinical trials that are available with different medications targeting these differently mutated tumors.

Dr. Bivalacqua: Just to add on to that, the good news is that a lot of patience with ... Especially with advanced disease, when we look for these mutations or even do some type of sequencing, either RNA or DNA, there are now ... A lot of insurance will cover that. That's something that you can have a conversation with your physician about.

Question 3: Why isn't blue light used in every clinic?

Dr. Bivalacqua: So blue light cystoscopy is currently FDA approved to be used in the operating room. And so obviously my practice, that is what I do on a routine basis in the operating room. As I stated, it does help us detect more carcinoma in situ, papillary tumors, which we know reduces recurrence. We have just finished a multi-institutional trial in which we're now doing flexible blue light cystoscopy in the clinic. In order to do that in our patients for surveillance cystoscopy or, for example, post-BCG or post-intravesical chemotherapy. And that trial just finished, and the results were presented at the AUA last month, which showed that the flexible cystoscopy in the clinic was able to meet its endpoint of more detection of bladder cancers. So, I believe the company is moving towards FDA approval for that, and therefore, if it is approved, then we'll be able to use it in the clinic.

Question 4: Which non muscle invasive bladder cancer lesions require a re-staging TURBT? Is there a category?

Dr. Bivalacqua: Yes. So, it'd be a re-staging exam for anyone that has high grade invasive T1 urothelial cancer. You should undergo a re-staging TURBT. Additionally, if a patient has a high grade cancer, either T1 or Ta and there is no muscle in the specimen, then you should under got a re-staging TUR, and the AUA guidelines now say you should strongly consider performing a re-staging exam if you have papillary Ta disease. And as I stated in my presentation, in my practice, I perform a re-staging exam on all patients that have high grade disease.

Question 5: How do you minimize inflammation from treatment? I went through courses of BCG initially, twelve weeks. And three maintenance treatments before I suffered severely with cystitis. Two and a half years later, I went through six weeks of docetaxel after a recurrence, then two years of maintenance with docetaxel. I still have inflammation and tested negative for an AFB test.

Dr. Bivalacqua: Yeah, so it's a great question. Some patients have really profound sort of local irritative systems in response to either BCG or chemotherapy. And the exact cause of that is really ... It's really dependent on the individual, and potentially even dependent on their immune system. But there is no magic pill, or there's no magic medicine that we can put inside the bladder to help reduce the inflammation. You can think of it one of two ways, you can think of inflammation as potentially good because the same cells or cytokines that are causing the inflammation of the bladder are also helping

potentially fight off the cancer. So I wish we had something that would allow patients to be more comfortable, but the reality is there really ... It's not easy once you develop these local symptoms.

Question 6: Do frequent resections weaken the bladder wall?

Dr. Bivalacqua: The frequent resections do. If a resection is performed and you thin the bladder in the same area multiple times, that is possible. But as you heard from Arlene, these are bladder lining, the mucosa as well as the deep layers. The bladder is able to regenerate and actually grow and from new layers. So the bladder is a pretty resilient organ and it actually regenerates pretty well. So in general, and globally, does it weaken the bladder wall? Yes. But as long as you have ... As long as you're a healthy individual and don't have the resection the exact same spot over and over again, your bladder should be able to sustain it.

Question 7: After say 10 to 15 years, would you stop annual surveillance if there's not been a recurrence for non invasive low grade disease?

Dr. Bivalacqua: I think it's a decision that you have to make with your physician. In my practice, at 10 years, I stretch out the two years. And then at 15 years or at 14 years, I have the discussion with the patient. So I'm comfortable stretching it out at that point.

Question 8: For patients with the CT1 N-O-M-O micropapillary tumor, is neoadjuvant chemotherapy advised if a radical cystectomy is being selected as a primary treatment?

Dr. Arlene Siefer-Radtke: This is something that we've been actively debating even at MD Anderson. So it's a very difficult decision to make. When to give neoadjuvant chemotherapy. And some people will use muscle invasive disease as a definitive factor. I personally think it depends on how your T1 disease is staged. We know there's some T1 disease that are under-stage, they have tumors near the ureteral orifice and there's concern that too deep a resection could damage the ureters. It's also harder to do staging around the bladder neck because they have to retroflex the scope to get tissue. So my personal belief is in an adequately staged T1 micropapillary tumor, where you definitely have muscle behind it, confirming it is a true T1, a cystectomy alone may be very reasonable as the treatment without a need for neoadjuvant chemotherapy.

But if there's inadequacies in staging due to location of the tumor or other features that are worrisome, say it's tumor near a bladder diverticulum. And a diverticulum is like an out-pouching or ballooning of tumor through the wall of the bladder. So by definition, there typically is not a muscle layer behind it. So if there's other features, I would say a T1 tumor with micropapillary may need chemotherapy first. So I think these tumors should be considered on an individualized basis. I wished I had data based upon hundreds of these cases, hundreds of T1 micropapillary tumors where I could say something more definitive, that the answer is yes, or the answer is now. At the moment, I think you need to see an expert medical oncologist and urologist and have this difficult discussion where we look for features and try to best assess each patient's individual risk.

Question 9: I recently had two resections resulting in a benign diagnosis. Does this type of material grow similar to a cancer tumor?

Dr. Arlene Siefer-Radtke: So, I am a medical oncologist, so I don't have a lot of direct experience, but I would say, if what they've resected is truly benign tissue, meaning there's no evidence of cancer or even these PUNLMPs, these papillary urothelial neoplasm of uncertain malignant potential. If it's truly benign, then you haven't been diagnosed with cancer. If it is not benign and these ae are just extremely low grade lesions, well then you still may need additional follow up with your urologist.

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