



Bladder Cancer Video Series 2019

Muscle Invasive Bladder Cancer

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Dr. Ramy Sedhom: Welcome to Cancer Grace I'm Ramy Sedhom, a medical oncology fellow at Johns Hopkins, and we are grateful to have with us, Dr. Petros Grivas here for our bladder cancer series. Dr. Grivas is a medical oncologist at the Fred Hutch and Clinical director of the GU program. Thank you, Dr. Grivas for being with us.

Dr. Petro Grivas: Thank you so much, Ramy for having me and congratulations for doing this series.

Dr. Ramy Sedhom: Thank you. So let's just dive right into it. So first, how do we define muscle invasive bladder cancer?

Dr. Petro Grivas: Muscle invasive bladder cancer is defined by the tumor, which is originating in the luminal part of the bladder in the area where the urine is collected. This tumor can invade through the layer of the bladder wall, and it's trying to find the way from inside through the wall to outside of the bladder. And when it invades through the muscle layer of the bladder wall, muscle layer is part of the bladder wall, and is responsible for contracting the bladder. So urine can be produced. When the tumor is invading this muscle layer, we call this muscle invasive bladder cancer. So it represents the depth of how deep invading the bladder wall, how much deep it goes in the bladder wall, the tumor I mean. And that's important because the deeper the tumor is invading. And especially if it invades the blood, the muscle wall and this muscle invasive, then the chance of entering the small blood vessels and what we call in fatty channels is higher.

And that can actually be associated with higher chance of spread what we call metastasis. So it's very important to have a proper diagnosis of muscle invasive bladder cancer, and it's very common to under diagnose it or miss it. That's why it's important to have a good dialogue and communication between the urologist who does the procedure of biopsying the tumor through the urethra, and the pathologist who reads the [inaudible] is out. So, this is important because it's very common to think you have less deep invasion, what we call, not muscle invasive, but actually in reality, in actuality you have muscle invasive tumor. So it's important to have this proper and accurate diagnosis, which might require a second biopsy of what we call T U R B T, which stands



for transurethral bladder tumor resection, which is a way that bladder cancer is diagnosed and also states, meaning we see how deep it goes into the bladder wall.

Dr. Ramy Sedhom: Okay, thank you for that. And you hinted a little bit about the importance of multidisciplinary teams and communication. So on that note, what are the different modalities of treatment for muscle invasive bladder cancer?

Dr. Petro Grivas: So, I agree with you Ramy, that multi-disciplinary approach is very important. And we actually have a multidisciplinary bladder cancer tumor board which is a clinic that happens every Tuesday morning at the University of Washington and Seattle Cancer Care Alliance. So where I practice. And this clinic involves the urological oncologist, the surgeon, medical oncologists, like me and my colleagues, and radiation oncologist, as well as pathologists to review the actual biopsy results. And other information from the tissue analysis under the microscope, as well as radiologist who helps review the cat scans, MRIs, the imaging studies that we use. And overall, I would say that there are two strategies to try to treat muscle invasive bladder cancer, assuming that this is not spread, not metastasized.

And this approach is the following number one, trying to remove the bladder and also the lymph nodes around it. We call this radical cystectomy and as well as removal of the prostate in men. So radical [inaudible] in men, which means removal of the bladder and the prostate, as well as the surrounding lymph nodes. And radical cystectomy with what we call removal of lymph nodes also in women. So surgical approach, and this strategy ideally should be preceded whenever possible with chemotherapy, not with any regimen, but a specific regimen, including cisplatin. Which are very important chemotherapy drugs, and actually to be accurate, we have two different chemotherapy regimens that are being used in this particular scenario with chemotherapy before radical cystectomy, meaning removal of the bladder. And those chemotherapy regimens, both of them, I would say includes cisplatin, which the most important chemo drug we have.

However, about half of the patients may not be able to safely receive cisplatin because of medical issues, not adequate kidney function, not adequate functional status, overall other medical issues. So it's important to have a dialogue with the oncologist in order to see whether the patient is a good candidate to tolerate safely cisplatin. And we use criteria that allow us as medical oncologist to see whether a patient can safely tolerate cisplatin or not. So the first approach to summarize is the removal of the bladder. And we call this a radical cystectomy. We should not do partial cystectomies. This is important. We have to take the entire bladder. That's important point of the patients should know. There are very, very few exceptions in that.



But sometimes a partial cystectomy can be done with very unique scenarios, but the right answer is it's a radical cystectomy, the entire bladder that has to go with the lymph nodes. And ideally if we can, in specific occasions, we give cisplatin based chemotherapy. One of the two regimens I mentioned before overall, the second approach that about one out of five patients maybe a good candidate for an ideal candidate for, is what we call bladder preservation. Bladder preservation is an attempt to try to keep the bladder in place, instead of removing it and bladder preservation is achieved or attempted with what we call a maximum or optimal TURBT, what we call before a resection of the tumor through the urethra, from the urologist to adequately diagnose and stage the cancer. Followed by chemotherapy blast radiation at the same time.

So concurrent chemotherapy and radiation. And as I mentioned, not, everybody's a great candidate to attempt bladder preservation, but it's an important discussion to see which patients may be a good candidate for that. And as I mentioned, some patients may not be ideal candidates, but at the same time may not be good candidates for a radical surgery. So they may kind of default to that option of bladder preservation because they are not good candidates for surgery because surgery may be too risky for a few patients because of frailty and other medical issues. So these are thus, I think to your point, a great example of how important is this multispecialty bladder cancer clinic.

Like the one we have at the University of Washington and Cancer Care Alliance and other areas where the medical oncologists, radiation, oncologists, urologists, pathologists, radiologists, sit down together to discuss what is the best approach for this individual patient based on other medical issues, based on functional status at that particular time point. And choose between these two genetic approaches; removal of the bladder with, or without perioperative chemotherapy before surgery, if possible, or attempt for bladder preservation in those who are good candidates for that based on the overall characteristics of the tumor, as well as other medical issues, etcetera.

Dr. Ramy Sedhom: Okay, perfect. So thank you for walking us through that. The last question that we'd like to ask, we both know a very common question in any medical oncology clinic is whether there's a role for immunotherapy. So at this time what is the understanding of either the efficacy, or where is it immunotherapy with regards to muscle invasive bladder cancer?

Dr. Petro Grivas: So overall one important component of treatment, in addition to the standard approaches, as I mentioned before, is clinical trials. And I think it's very important for the patients to ask about clinical trials every single time to the providers. And clinical trials are a key way to make progress. And it's a key component of how we have made



strides in bladder cancer so far and other cancers too. So it's very important to discuss clinical trials and I would encourage every single patient to ask active with a provider, what are the clinical trials that I qualify for, or you know I'm a good candidate for based on the cancer characteristics, based on my other medical issues, et cetera? In that context, immunotherapy is being tested in multiple clinical trials in what we call localized muscle invasive bladder cancer. And in those scenarios the other cancer is still able to be resected. We call this resectable being able to remove it by surgery.

Localized, meaning, not spread bladder cancer, muscle evasive, as we defined it before. In this scenario, immunotherapy is still experimental. So this is a very important point because immunotherapy has a strong track record and is approved by the FDA in different scenarios. For example, for metastatic bladder cancer, when the cancer has been spread, metastasized to other organs, or it's, we call very advanced and has invaded through the abdominal wall of the pelvis wall near the bladder and cannot be resected. We call these locally advanced and are unresectable. In those scenarios of metastatic advanced unresectable bladder cancer, the FDA has approved immunotherapy with specific indications that can be discussed with individual patients. The results are different indication by the FDA for earlier what we call non muscle invasive bladder cancer, where the blood cancers still in early superficial layers of the bladder wall, has not invaded yet the muscle layer, and has been not responsive to the treatment with BCG.

Which has given us three installations inside the bladder. We call this BCG unresponsive non muscle invasive bladder cancer. And in those patients that treatment is radical cystectomy, removing the bladder. But some patients may not be able to get the cystectomy down because it's not safe for them, or they may still refuse to despite being the right thing in those cases of BCG, unresponsive and muscle with bladder cancer. In this scenario, immunotherapy has also indication, especially with patients. So you can see that immunotherapy has some approvals by the FDA in kind of an earlier stage, and kind of a later stage, but in this particular scenario of localized resectable muscle invasive bladder cancer is still experimental. And there are multiple clinical trials that are being done testing the combination of chemotherapy immunotherapy in those who are fit enough to get cisplatin.

And also, immunotherapy alone in combinations of immunotherapy for those who may not safely tolerate cisplatin. So there are multiple trials and I encourage the patients to discuss with the oncologist about this options, including immunotherapy. And as I mentioned, if the bladder is removed and the patients are done with radical surgery, or they are done with chemotherapy radiation for bladder preservation, there may still be a clinical trial options. And I think it's important to discuss them. When a clinical trial or a treatment is being considered before the surgery, we call those neoadjuvant setting.



So neoadjuvant trials, meaning before surgery, if it is done after the surgery, we call the adjuvant trial. So in either scenarios, or in the context of bladder preservation, I think many trials are ongoing and many of them in immunotherapy. And it's very important to discuss those options with the patients when possible.

Dr. Ramy Sedhom: Perfect. So, we just want to thank Dr. Petros Grivas for his time to discuss muscle invasive bladder cancer. For those patients and caregivers who are listening in, please, we encourage you to also check out our videos on immunotherapy in metastatic bladder cancer, which were featured with Doctors Elizabeth Clinic and Dr. Matt Golinski. Thank you again, Dr. Grievous. And we really appreciate your time.

Dr. Petro Grivas: I appreciate you having me. And the last thing I would say, it's a wonderful organization out there called Bladder Cancer Advocacy Network. BCAN, it's a great resource for the patient is led by patient advocates. BCAN is involved in you know, research is funding Research, is involved in policy advocacy, and can connect patients with each other. So it's important to be a resource available to patients and has a nice clinical trial dashboard that looks at different clinical trials that we discussed before. It's a great conduit and venue for patients to get information. So BCAN, Bladder Cancer Advocacy Network. Among other great resources are out there for the patients as well.

Dr. Ramy Sedhom: Perfect. Thank you for that. We hope you have a wonderful day.

Dr. Petro Grivas: Thank you.

Dr. Ramy Sedhom: Alright, take care.