Pathology Driving Decisions

Part IV: Questions & Answers

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BCAN Patient WEBINAR SERIES

Presented by:

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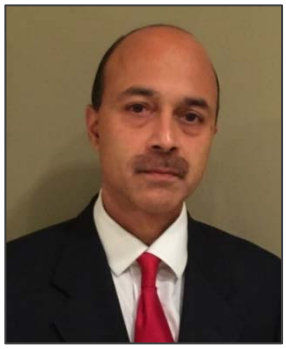

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Question 1: A patient asks about their pathology report and they say they have low grade and high grade, both, in the report.

Dr. Mossanen: That's a good question. I think that in situations like that it emphasizes the need to really rely on that big team. Which means that I would suggest the Urologist and the Pathologist, the person that makes the report, have a discussion and sort of come to an agreement. And then connecting with the Urologist to get the final recommendation is probably best. I don't think there's a black and white answer to that question. In a lot of situations patients might typically be treated as having high grade disease, but again it really depends.

Question 2: Talk little bit about the efficacy of trimodal therapy vs. radical cystectomy.

Dr. Mouw: Sure. So the question is about comparing trimodal therapy which, again, consists of a TURBT performed by a Urologist, followed by concurrent chemotherapy and radiation as an alternative to radical cystectomy or bladder removal surgery. And this is a question that comes up frequently. These two treatment types, the trimodal therapy and the radical cystectomy, have never been compared in a randomized trial, and so it's a bit difficult to compare them. But what we can say is that patient selection is critical in choosing patients who are good candidates for trimodal therapy. And so the list that I went through are some of the characteristics that I consider when I'm meeting with patients and considering whether or not they may be well-suited for trimodal therapy. And we think that if we select the patients who we think are best suited, we think that trimodal therapy has outcomes that compare favorably to radical cystectomy. But again, I think the key is that it is really a patient-specific choice and you need to

rely heavily on the team who speak with one another, who go in-depth on your pathology report, to really understand which treatment option might be best for each individual patient.

Question 3: A patient is wondering if they do get trimodal therapy, is a cystectomy and either a conduit or a neobladder a possibility after trimodal therapy?

Dr. Mouw: Yeah that's a great question. So follow-up, as I described to trimodal therapy, involves frequent cystoscopies where the Urologist goes and takes a look around. And in a subset of patients there's a chance that the tumor will come back. If that happens and the tumor is invasive, then likely the next step in the care is referral back to the Urologist to discuss the possibility of what's called a salvage cystectomy which is surgery to remove the bladder after having received concurrent chemotherapy and radiation. That surgery is possible in a subset of patients and maybe I'll pass it back to Dr. Mossanen to talk about some of the details regarding how that surgery might be the same or different than a radical cystectomy in the upfront setting.

Dr. Mossanen: That's a great point. I think in each patient it'll be a case-by-case basis. What's most commonly done is an ileal conduit, I will say. But again, there's no 100% correct answer. So it will really depend on meeting with your whole team and having a discussion.

Question 4: If a patient has muscle-invasive disease, is it possible to predict the likelihood of actually having metastatic disease in that setting?

Dr. Sonpavde: Right. So it's difficult to answer if a certain patient with muscle-invasive disease actually has metastasis. What we know is that we don't really follow this patient without treating them, but we know that once we treat this patient with either removing the bladder with or without giving the chemotherapy before or after, we know that in patients where it grows back in other organs like the liver or lung, it tends to grow back within a year or within two years. So it tends to be in a time span of a few months that you start seeing it growing in other places. But most of the cases, we feel our cases where these cells were already hiding at the beginning and then started growing later. So it's really difficult to say whether the cells started spreading out when the cancer first arose, or whether it spread later when the cancer was still in place. So there still needs to be a lot of work done to answer that.

Question 5: One of the patients is asking a little bit about getting a CT scan and how accurate that is in determining if the lymph nodes are involved.

Dr. Mossanen: So the CT scan is a useful tool, but it's not 100% right. So it can usually tell us if a lymph node is, for example, bigger than it should be or if it doesn't have the normal shape that it should have. And those things make us suspicious, but sometimes lymph nodes can actually have cancer in them on the cell level and that might not be caught or realized or seen with the imaging studies that we get.

Question 6: Are there any contraindications or reasons why people cannot have immunotherapy?

Dr. Sonpavde: Right. So these immunotherapy drugs, they're the PD-1 inhibitors or PD-L1 inhibitor class of drugs, like pembrolizumab or atezolizumab, and there are three others. They are generally quite tolerable. Their toxicities and side effects are quite favorable compared to chemotherapy. However, around 15%, one five, that is, percent of patients may have a severe what's called an immune adverse event because these drugs are boosting the immune system to eradicate the cancer and therefore when the immune system is boosted up, it can sometimes attack certain organs like the liver, intestine, lungs,

and cause inflammation in these organs. So really what you would expect from this is if someone has an autoimmune disease like Lupus or Rheumatoid Arthritis. And if they're not well-controlled, you really want to stay away from these drugs. But short of that, if you have a controlled disease like controlled psoriasis is a good example of a disease where we might feel comfortable giving these drugs because it's a skin disease and generally does not flare up significantly despite treatment.

Question 7: Why might a patient need another resection if they have high grade T1 in the first bladder biopsy or the first bladder tumor resection?

Dr. Mossanen: That's a good question. The reason for that is because high grade T1 is risky and we get concerned that in maybe around 20% of patients, a certain subset will actually have muscle-invasive disease and that carries important treatment implications. In other words, if you have high grade T1 you might need a second resection of that tumor to make sure that it's not in the muscle because we find that in about one in five cases or so, there may actually be involvement of the muscle.

Question 8: A patient is wondering why patients with CIS cannot have bladder sparing therapy.

Dr. Mouw: Yeah so that's a great question. So CIS, just to review, stands for carcinoma in situ. What it means is that there are tumor cells in the urothelial lining, that inner layer of the bladder. And I want to be clear that CIS is not a strict contraindication to bladder preserving therapy with chemotherapy and radiation; however, what makes us concerned is that we know that the more tumor can be removed prior to starting chemotherapy and radiation, the higher the likelihood of tumor control is following chemotherapy and radiation. And we know that CIS can be sometimes difficult to detect and difficult to remove completely. And so we think of it as sort of a sign to us that there may be more cancer than can be appreciate and can be fully removed prior to chemotherapy and radiation. And so it's not a strict contraindication, it's one of the things that goes into our calculus and it's one of the things that we talk about with the patient and with the other providers as we're making the decision on which type of therapy to pursue for muscle-invasive disease.

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