

# Neoadjuvant and Adjuvant Chemotherapy

Dr. Matt Galsky



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## Stephanie Chisolm:

Bladder cancer, patients with muscle invasive bladder cancer diagnosis often go through systemic chemotherapy either before, known as neoadjuvant, or after, adjuvant, their bladder removal surgery. And that's really to clean up rogue cancer cells that may be elsewhere in their body.

And systemic chemotherapy is used to decrease the risk of any cancer coming back after surgery, but it may come with some side effects and other considerations that you might want to keep in mind before you agree to different types of treatments.

BCAN is honored to host this important conversation to help you understand neoadjuvant and adjuvant chemotherapy. And we've invited Dr. Matt Galsky. Dr. Galsky is professor of Medicine at Mount Sinai. He's the Director of the Genital Urinary Medical Oncology program and co-director of the Center for Excellence in Bladder Cancer at the Tisch Cancer Institute. Dr. Galsky, it's always a pleasure to see you. Thank you so much for doing this and I am going to turn the screen over to you.

## Dr. Matthew Galsky:

Thank you. Thanks for that introduction and it's my pleasure to be with you all today and I just want to make sure I'm sharing my screen, okay. So, today, I'm going to talk about what we refer to as perioperative systemic therapy for bladder cancer.

The title of the talk is chemotherapy and historically the discussion's been limited to chemotherapy, but now there's actually additional systemic therapies that are employed in the perioperative setting, so we'll be discussing those as well and I'll explain what I mean by that.

So, the whole concept of perioperative systemic treatment, the whole concept of giving

medication for what seems to be a local problem, a tumor in the bladder can sometimes be hard to wrap one's head around. And I don't want to make any assumptions about what the audience knows and what they don't know.

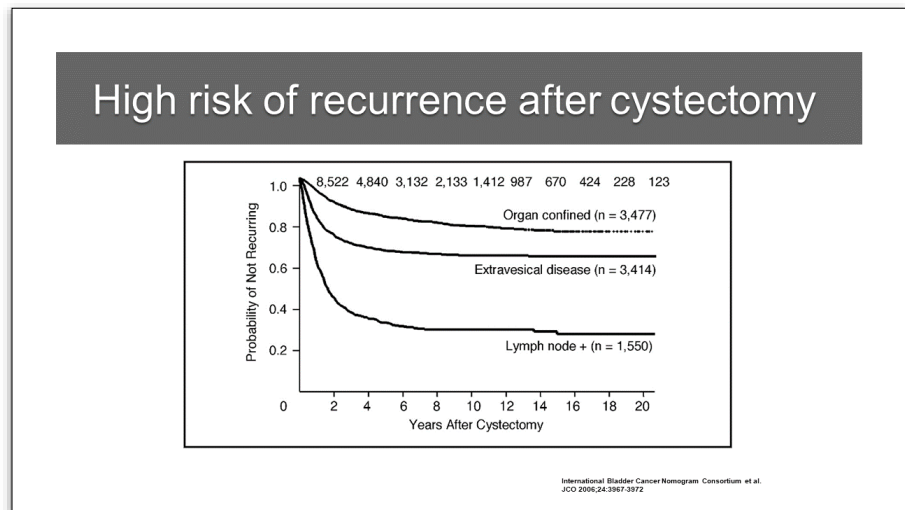
So, some of this might sound a little bit simplistic, but I want to make sure that we're on the same page. So, we know from large series that have been published from individual hospitals and from multiple hospitals pooling their data together that radical cystectomy surgical removal of the bladder can be curative for what's known as muscle invasive bladder cancer, bladder cancer invading at least the muscle layer of the bladder.

And that can be a curative procedure in a large subset of patients. But we know that unfortunately some individuals despite undergoing that surgery months to years later have the cancer show up somewhere in the body that's called metastatic cancer.

Of course, when cancer has showed up somewhere else from the site that it started. So, how does cancer show up somewhere else if the bladder is already removed? Patients often ask me this. And it's not that cancer of magically appears in another organ.

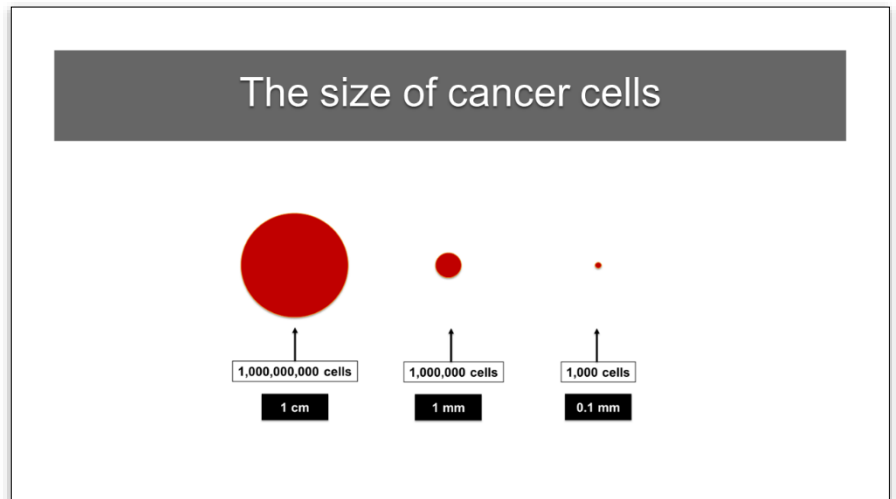
Of course, what happens is that even prior to surgery or even prior to radiation, if radiation is being used as the primary modality for treatment of bladder cancer, even before that happens, cancer cells spread. And they can spread or they do spread in a way that is initially represented by very small clusters of cells.

And so, someone might say, "Well, I had a CT scanner, I had a PET scan prior to surgery and there was no evidence of cancer and then I had my bladder removed." And then, six to 12 months later, something showed up in the lung. And so, it wasn't that that cancer magically appeared in the lung after surgery, but it's that those cancer cells had spread to the lung even before surgery took place.



## Dr. Matthew Galsky:

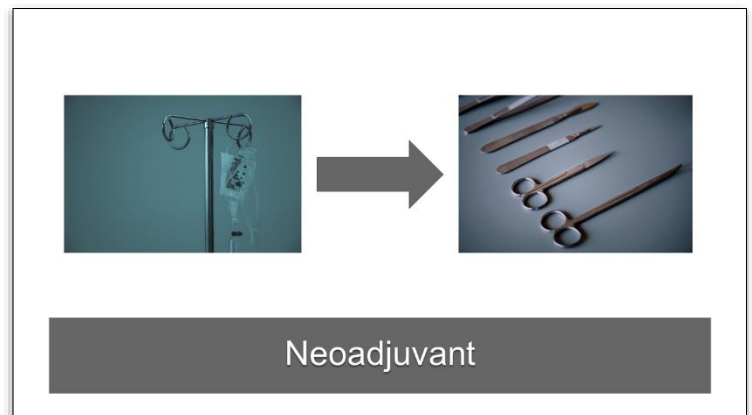
They were too small to be detected on the scans with the technology that we have available. And so, to put this in some context, CAT scans, PET scans, they've gotten pretty good, but we can only detect macroscopic evidence of cancer and our scans are not good enough yet to detect microscopic evidence of cancer. And so, if you see from this figure, it takes about a thousand cancer cells to make a 0.1 millimeter focus and it takes about a billion cancer cells to make a one centimeter focus. And our limit of detection on most scans is probably somewhere between the one millimeter and one centimeter range.



And we're pretty uncomfortable still calling things abnormal when they're less than a centimeter. And so, you can see the amount of cancer cells that need to accumulate until we actually see something on a scan, and then it becomes obvious how cancer can spread not be seen on a scan.

But over time, those cancer cells grow to the point that they can be seen on a scan. So, recognizing that that can occur about 20, 30 years ago, doctors started to think about combining medication, systemic treatment we call it, but medication, to try and eradicate cancer cells that might be outside of the bladder in conjunction with surgery to remove the cancer that is known to be present cancer in the bladder.

And when we do that before surgery, as Stephanie pointed out, it's called neoadjuvant treatment. When we do it after surgery, it's called adjuvant treatment. So, why would someone have chemotherapy before surgery? Why would they have chemotherapy after surgery?



And what's the relative benefit of one approach versus another? And there are both some practical and maybe some scientific benefits to the sequence of treatments. In terms of treatment with chemotherapy before surgery, a few potential advantages.

One is that surgery to remove the bladder is not a minor procedure and there's a recovery period involved. And so, the ability to initiate the treatment is oftentimes more efficient in the setting prior to surgery, initiate chemotherapy is more efficient prior to surgery.

## Dr. Matthew Galsky:

And then, after surgery, when individuals might have a delay in started treatment because of recovery from surgery. Along those lines as well if we are indeed trying to treat microscopic cancer cells that have spread, then there is some rationale for getting that treatment started sooner rather than later.

One of the major... another potential advantage to giving treatment in the presurgical setting is that there's actually a

measure, an indirect measure of how effective the treatment might be in an individual patient. And that is what happens to that primary tumor when it's removed and analyzed under the microscope.

And we know that when you give chemotherapy prior to surgery and you analyze the extent of tumor that's left over in the bladder, that does correlate with long-term likelihood of curing cancer, not because of what happens in the bladder itself because that tumor is removed surgically, but because it might represent a surrogate for eradication of microscopic cancer cells elsewhere.

So, those are the major advantages to the approach giving systemic therapy or chemotherapy prior to surgery. The probably major downside to giving chemotherapy before surgery is that our ability to understand the stage of bladder cancer prior to surgical removal of the bladder is actually fairly crude.

The stage of bladder cancer, what's called the T stage or the stage of the primary tumor, is measured by the depth of invasion of a tumor into the wall and through the wall of the bladder. And it's very difficult to assess that on imaging like CAT scans or even MRIs.

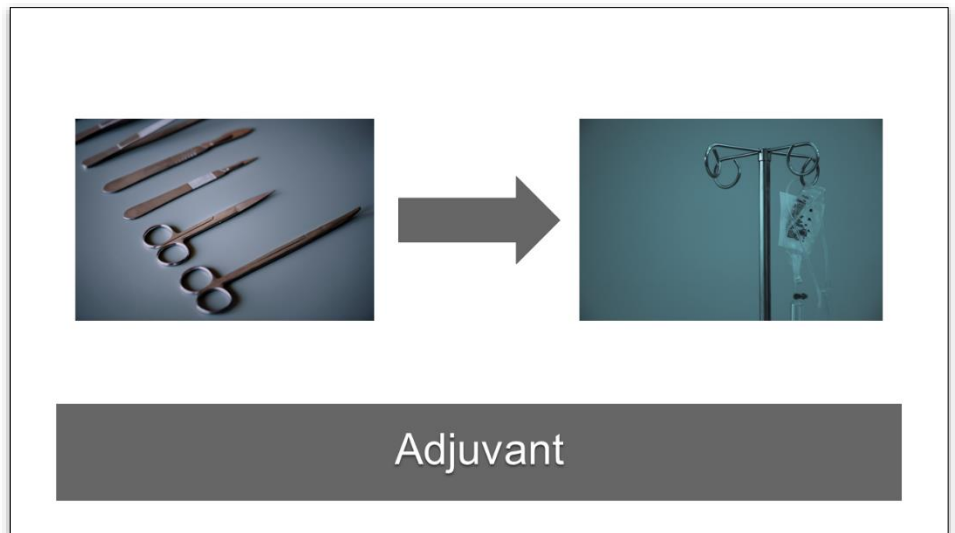
We only get partial information from the biopsy, the TRBT that's performed as the diagnostic procedure because most of the time that can only tell us that there's been invasion into the muscle layer of the bladder. But of course, when a urologist performs that procedure, they can't keep digging deeper and deeper to really see the depth of invasion through the wall of the bladder.

Because if they keep resecting, ultimately, they'll resect through the wall of the bladder and create a hole in the bladder. So, most of the time, we feel pretty confident prior to surgery that calling bladder cancer muscle invasive because we can determine that based on the pathology.

But understanding the nuances of stage beyond that are somewhat more difficult. And so, what that means is that our ability to prognosticate, our ability to understand who's at higher likelihood for having microscopic spread of cancer versus who's not is more limited than once the bladder is removed.

And we can really assess the depth of invasion into the wall of the bladder very accurately, and we can assess whether or not there are regional lymph nodes involved with cancer under the microscope because those lymph nodes are resected as well.

So, the use of chemotherapy prior to surgery in the neoadjuvant setting is really employed in individuals with muscle invasive bladder cancer while we're a little bit more refined in the criteria to use chemotherapy after surgery. So, that's the adjuvant setting.



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