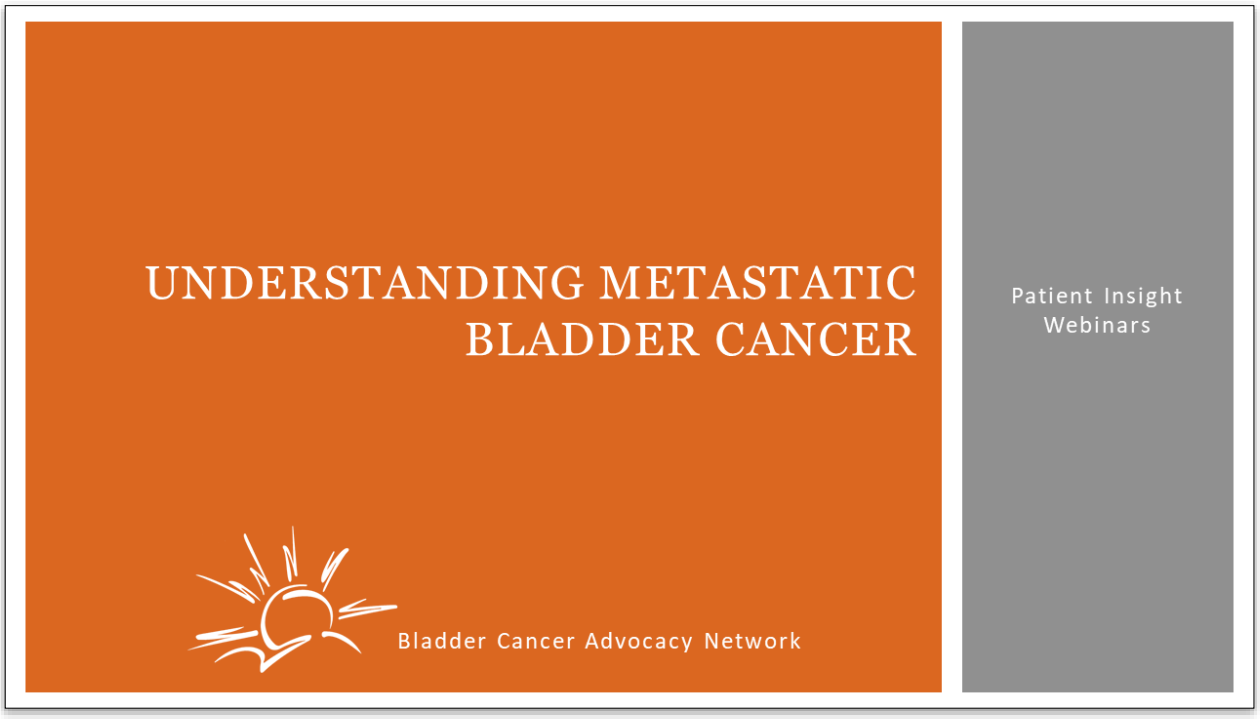


Stephanie Chisolm:

We're really delighted to have our speaker today, Dr. Alicia Morgans who is here as the director of the survivorship program at the Dana-Farber Cancer Institute. She's here to talk to us about metastatic and advanced disease. And we know that a bladder cancer diagnosis can be terrifying to a patient and their families. And we really want to help you understand what you need to know about this advanced or metastatic diagnosis and what are your treatment options?

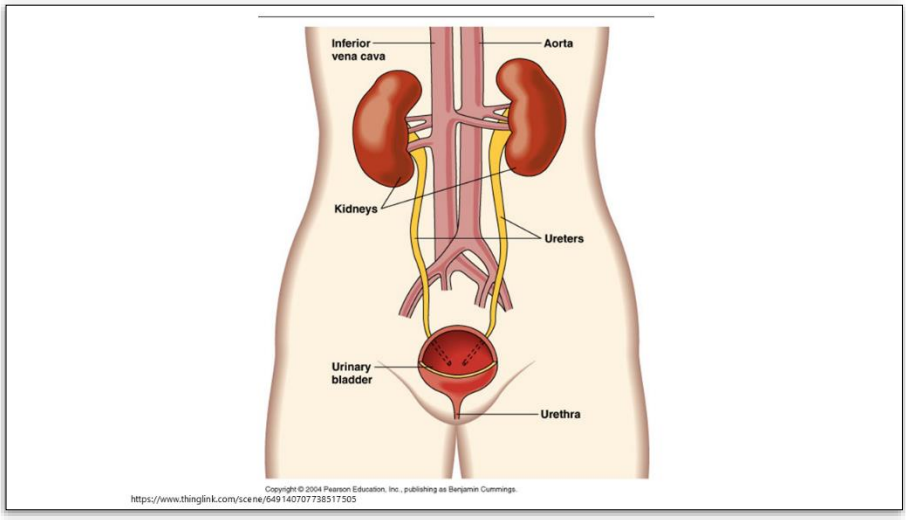
Dr. Morgans is a clinical investigator. She does actual patient care, but she's also a very prolific researcher, and she has a lot of experience in clinical trials, particularly focused on patient reported outcome measures and is very involved in an incorporating what patients really want and what they really need into the care of her patients. And I think that she's going to give you some really wonderful information today. So Dr. Morgans, it's a pleasure to have you here.

Dr. Morgans:

Thank you so much, Stephanie. And I really appreciate everyone for being here today. As you heard, I am a GU [genitourinary] medical oncologist. So I take care of people with bladder cancer and I partner with them as they move through the treatment over time and help them to try to make the best

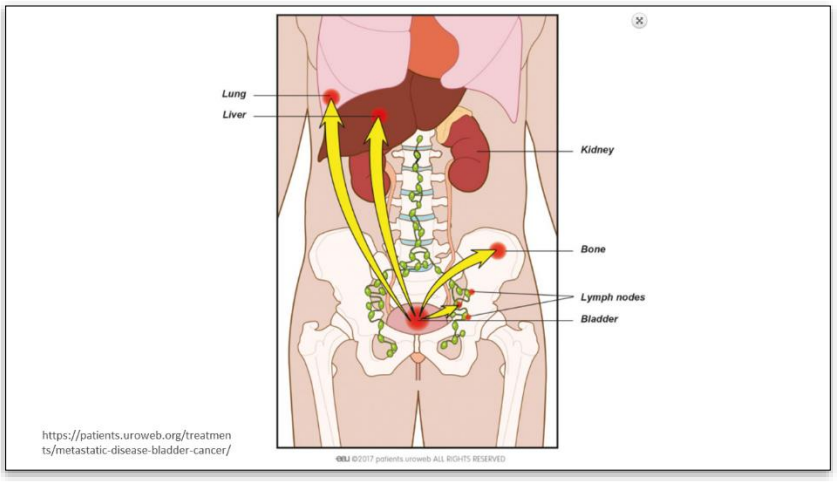
decisions for them, because these are very personalized decisions and, of course, impact every day of a person's life if he or she is suffering from bladder cancer. And I'm also the medical director of the survivorship program at Dana-Farber, where I'm trying to work with the team to really elevate the needs of bladder cancer survivors and ensure that we are really asking patients what they need as they go through this process. So I appreciate the opportunity to speak with you today and certainly appreciate all the feedback that you have as you're listening and as you have questions throughout this conversation.

As we focus on metastatic bladder cancer, I am going to just give a little bit of background and then talk about how we approach treatment for metastatic disease. And there are a few key approaches, including chemotherapy, immunotherapy and targeted therapies, which, of course, also include antibody drug conjugates, which are our newest treatments. And then we'll summarize at the end and really ask questions of you to understand how you need things to be answered or what questions you might have that I can help with.

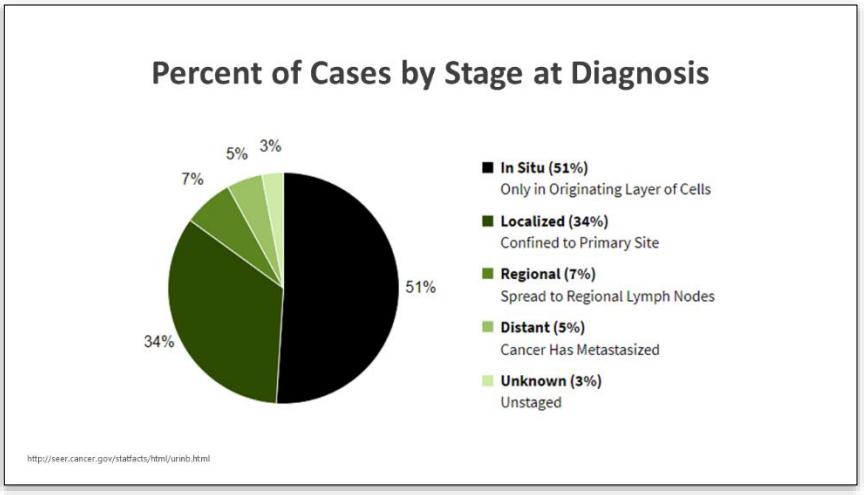


So urothelial cancer is broader than just bladder cancer. We always say bladder cancer, but we actually mean cancer that extends up those yellow ureters that you can see between the bladder, which is the red thing at the bottom and the kidneys, which are the two kidney bean shaped things up towards the top of the screen. So urothelial cancer, a bladder type cancer can extend from the bladder all the way up those ureters. And these types of cancers are very similar, because they come from the same origin cell type in the body and we treat them very, very similarly as we move forward. I will say bladder cancer in most contacts as I talk going forward, but know that if you have an upper track urothelial carcinoma or an upper track cancer, that means that you still have the same type of cancer, it's just up through the ureters and sometimes up into the kidneys almost. And all of these are really treated very similarly, because again, they come from the same parent cell.

Dr. Morgans:

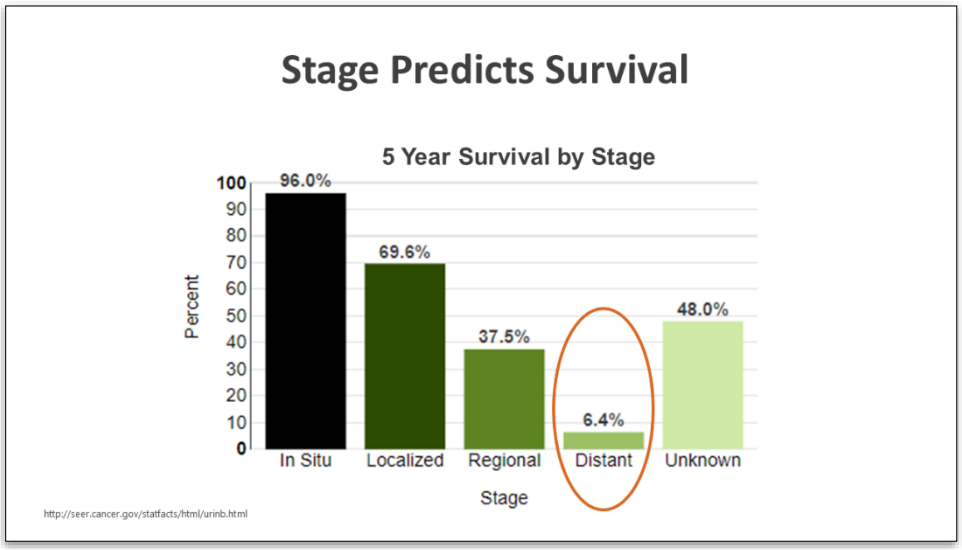


When we think about metastatic urothelial carcinoma or metastatic bladder cancer, I think we also need to define that. So metastatic just means spread from its origin. So in this case, it would have spread from the bladder or spread from those upper urothelial cells, those ureters, or even the area very close to the kidneys into other places. And commonly, in this type of cancer that can be in lymph nodes, in bone, in lung or in liver. And it can go in other places, sometimes unfortunately to the brain or in other places in other organs, but those are the most common places. So lymph nodes, bone, liver, lungs, those are the most common places.



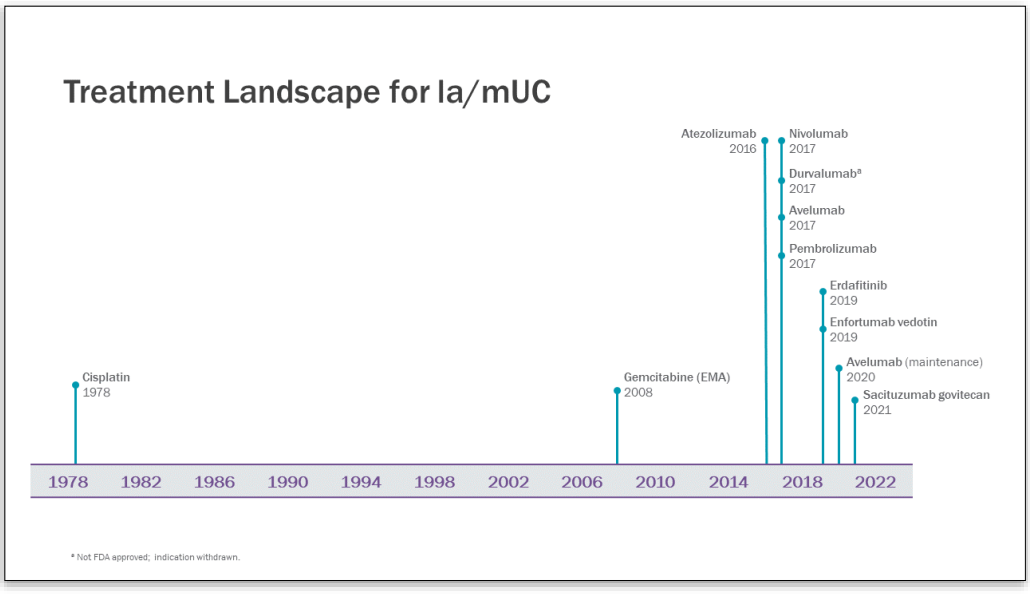
So we also know that in this type of cancer, there are different stages like in any kind of cancer. And for most people, they are diagnosed with in-situ bladder cancer, which really means bladder cancer that's not even digging really into the wall of the bladder. But for this talk, we're going to focus on the smaller percentage of patients who actually have metastatic bladder cancer spread outside of the bladder into other areas. And these patients have a different expected outcome. Their history is going to be different and they are actually a group of people where we don't currently have a cure for metastatic bladder cancer. For patients who have bladder cancer, that's all still in the bladder, we do have curative treatment approaches. We do have ways that we hope to cure the cancer, but once it has spread outside of the bladder, that's a much harder thing to do. And we try, and there are patients who have these miraculous responses, but we don't really, at this point, have a clear way to cure cancer of the bladder that has spread far outside the bladder.

Dr. Morgans:



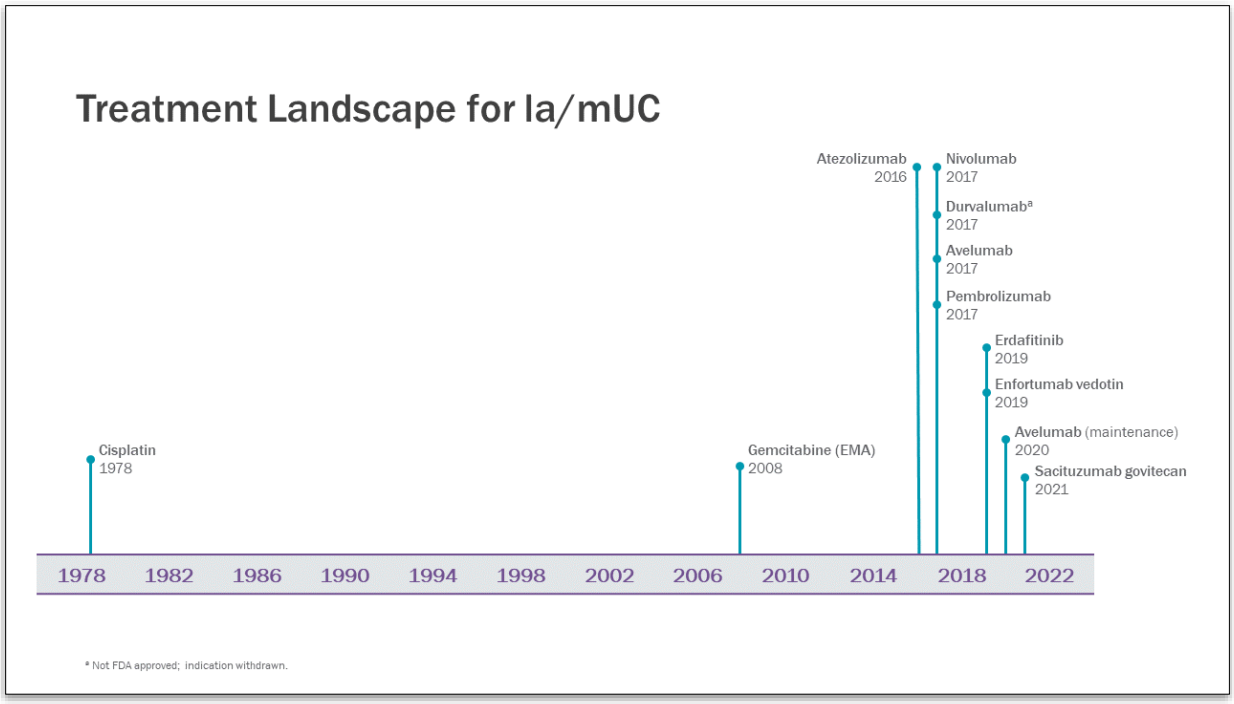
And that is really reflected in the survival information that we have. So when the disease is all still in the bladder and not even really digging into the bladder wall, the five year predicted survival is almost 100%. It's 96%. When it becomes distant, and that's another word for metastatic bladder cancer, into more distant lymph nodes and into things like bone or liver or lung, that survival at five years is all the way down to 6.4%. And this is the most updated information that we have from SEER, which is our cancer registry here in the United States. And I would say that this is something that I do think will change over time.

And I'm hopeful and I think all of our researchers and clinicians are hopeful, because we are making great strides. And in the next five years, I hope that this particular graph among all the others is something that we are able to shift. So that, that group of people who have distant disease will see higher rates of survival at five years. That is one of the goals that we have, of course, as a community that cares for people with bladder cancer. So let's dig a tiny bit into treatment and there are lots of options for treatment, but these are options that actually have come about and been described pretty recently.



If we look at this timeline, I think it's pretty striking. We can see that back in the 1970s back when many of the people on this call may be have been very, very young or not even born potentially, back all the way in the 1970s, we only had a drug called cisplatin. This is a chemotherapy agent, and importantly, it's actually still the backbone of our chemotherapy drug armamentarium, but it was the only thing we had all the way back in 1978. And at that time, there were clinical trials that demonstrated that it could do really important work in urothelial or bladder cancer.

If we fast forward into the 2000s when I imagine everyone on this call was around, we can see that we finally got an indication for gemcitabine, which is another chemotherapy in 2008. So up into the 2000s,



even to 2010, we're really dealing with chemotherapies for urothelial or bladder cancer. And chemotherapies we know are agents that we call cytotoxic treatments. These are treatments that go into the system, into a body and they go into lots of different cells and they destroy those cells. And that's a really positive thing when they're destroying cancer cells, but they're not targeted treatments. And so they do cause destruction and symptoms in cells that are normal cells. And that's what leads to our side effects of things like chemotherapy.

Dr. Morgans:

So when you go into hair follicle cells, you has hair loss. And when you go into cells in the GI tract, so anything between the mouth and the anus, you're going to have things like mouth sores or nausea, stomach upset or sometimes diarrhea. So these kinds of things happen with chemotherapy and they happen relatively often. And these are very important drugs in our treatment of urothelial carcinoma or bladder cancer, but it was a pretty sparse landscape for us for a long, long time.

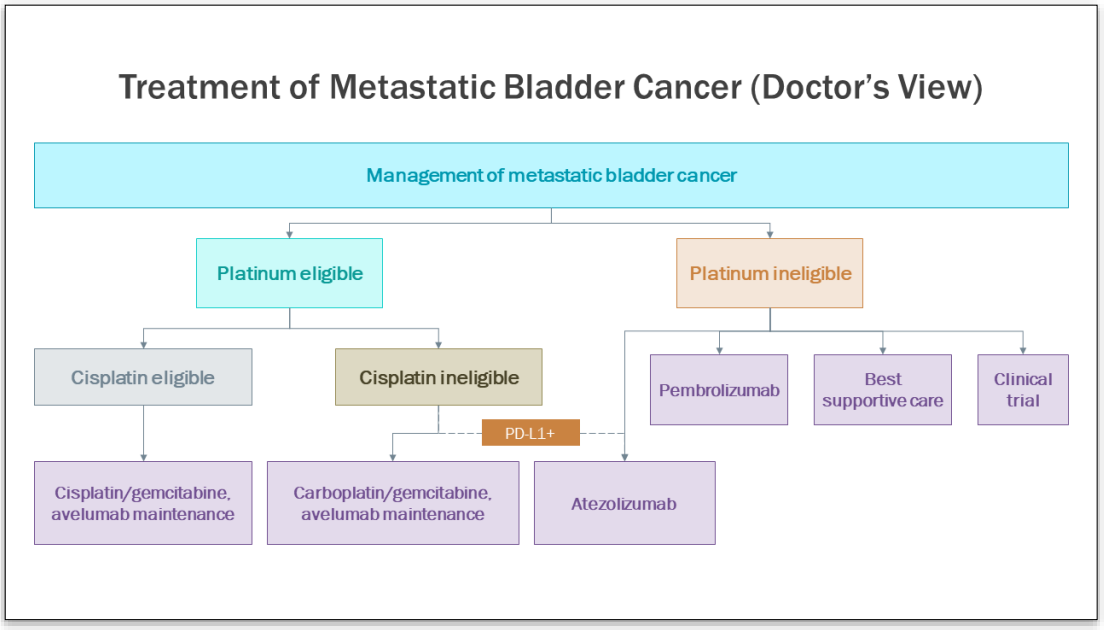
And then we hit around 2015, 2016, and we started having clinical trials. And finally got our first approval in 2016 for atezolizumab, which is a PD-L1 targeted agent that really was transformative, the first in a slew of approvals of immunotherapies. Treatments that harness the immune system to attack the cancer cells and cause fewer side effects in most people, they certainly can cause really destructive side effects in a few people. So smaller group of people, but for most people, gentle treatments that simply train the immune system to attack the cancer cells and help people feel better and live longer.

Atezolizumab was followed closely by nivolumab, durvalumab, avelumab and pembrolizumab. Four approvals in one year. All of them being these immunotherapies, this was incredible. We in the bladder cancer world were rejoicing, because as I showed you, there's nothing in decades. So really exciting times. And this was followed relatively closely by additional approvals in 2019 of erdafitinib is a targeted treatment for particular mutations in FGFR. And then enfortumab vedotin, avelumab in a different space, a different patient population, and sacituzumab govitecan. So lots of complex names, but really exciting stuff. And all of last things that I mentioned except avelumab, which I already told you as an immunotherapy, these are all targeted type treatments, erdafitinib targeting specific mutations and

enfortumab vedotin and sacituzumab govitecan being antibody drug conjugates, and I'll explain those in just a second, targeting certain proteins on the cells of cancer to deliver really potent chemos right on the cancer so that we hopefully don't have as many side effects and symptoms associated with the non - discriminant or general effects of chemo that can happen on cells that are not cancer. And that's what causes all the side effects.

So it's extremely exciting in bladder cancer and urothelial cancer. And really, I'm grateful that we are all here to live in a time when we have these treatments and others in the pipeline going forward.

Dr. Morgans:



When doctors are thinking about how do we treat metastatic bladder cancer or urothelial cancer, we have a lot of things to think about. And this is a schematic of a way that we try to categorize patients to understand how we can use the treatments that we have most effectively. And as doctors, we have to use the treatments that we have for certain patients with certain types of bladder cancer at certain points of the disease. And we really have to match the right treatment that's all based on the right trial for the patient in front of us. And so this is just one of the ways that we think about this. This is the schematic for how I think about the first treatment that we use in metastatic bladder cancer.

So first, doctors are often thinking about patients, are they going to be chemo eligible or not? And that's what this word platinum eligible or two words platinum eligible or platinum ineligible means, because the chemos that we have are platinum type chemos, these type chemos are pretty effective, really effective we think in bladder cancer. Cisplatin, like I mentioned, is the first one that was approved. This was in the 1970s. We have not changed since then. So, are you eligible for a chemo in that family, the cisplatin family or not? And if you're eligible, then we think about whether you can get that really potent cisplatin, very effective chemotherapy or not. And if you can get cisplatin, then can give you an immunotherapy on the back of that to try to be even more effective. And we'll go through how we get to that and what the data is.

And if you can't get Cisplatin, what chemo can we give you? Can we give you some immunotherapy on the back end? Can we try to make things better that way? And if you can't do that, can we do immunotherapies? And that gets us back into the people who really can't get chemo, because there are people like that, there are a lot of people in my clinic that can't get chemo. What immunotherapies can we use? What clinical trials can we think about? What other treatments can we use to try to make the days that a person has feel better, because we can do those kinds of things, those supportive care

things. Whether you're getting chemo, whether you're getting immunotherapy, whether you're getting a targeted therapy, we always need to be thinking about those things that make the day to day life better.

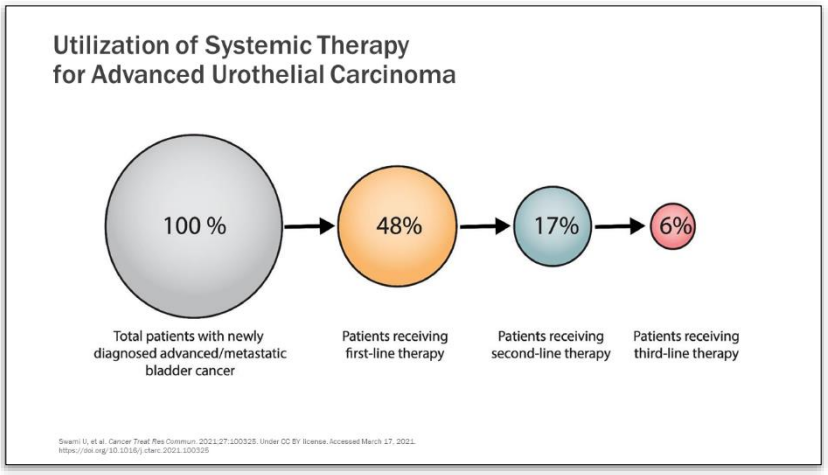
Dr. Morgans:

And so I encourage everyone in the audience to think about that as you're going into see your doctor, what else can I do to make my day to day better? What can I do to improve my pain? What can I do to improve my mood? What can I do to improve my appetite? And just keep asking those questions, because there might be things that can be added. On top of the treatment that's really focused at your bladder cancer or your urothelial cancer, there are things that we can add, there's counseling we can use, there are nutritionist, there are exercise folks, there are physical therapists who can help make the day to day better even if they're not directly attacking the cancer themselves, because you have to have a strong mind and a strong body to go through all the things that we go through. And that's actually true for patients, but it's true also for caregivers. So remembering to get support for the people around the patient, the loved ones, the family members, because they need to recharge too and need to think about how to keep themselves mind and body healthy as well.

So this is how we as a doctor community think about that first treatment for bladder cancer or urothelial cancer. And this is just step one, and it gets pretty complex as we move through the line. And one thing I want to be really clear about too is that systemic therapy, that includes chemo therapy, immunotherapy and all the other treatments that we'll talk about, is something that as we go through treatment after treatment for a given person, a given patient, the likelihood that, that person is going to get the next treatment goes down each step of the way. And that can be for a host of reasons. That can be because the person has become too ill or if the person has decided not to do more treatment or the person has passed away.

But if we aren't able to keep a person strong, mind and body, each step of the way, we're going to lose people over time. And if we don't treat them, then we won't be able to make a difference in their cancer. That's not to say that people don't need to make those choices to focus on quality of life or to not move forward with further cancer directed treatment. But we as a community who treat patients with bladder cancer, recognize that we need to do better in supporting people from one line of therapy to the next so that we can try to get each patient as many opportunities to get each life prolonging and quality of life improving treatment along the way as we possibly can.

And what this figure demonstrates is that if we go from all people, 100% of people at the beginning, with each line of treatment that we go after that, after each treatment fails that patient, about half of the population, about half of the patients drop off and don't get the next treatment opportunity. And so we need to think as a community, how do we help support people, get them the treatments that they need, and of course, help improve their quality of life, whether they're getting treatment or not. So that's just something that we think about.



BCAN would like to thank our sponsors

for their support