



Diane Z. Quale: Welcome to Conversations About Bladder Cancer. I'm Diane Zipursky Quale, the co-founder of BCAN. Today, are going to talk about a very important but complicated and complex issue, bladder cancer clinical trials. We're going to unravel the mysteries of clinical trials with our expert guests, who are going to give us direct and simple advice to help us better understand clinical trials. So joining me today is Dr. Jonathan Rosenberg, who is the Chief of GU Medical Oncology at Memorial Sloan Kettering Cancer Center in New York City. Jonathan's a world-renowned expert in bladder cancer with extensive experience in both designing and conducting clinical trials. Also with me today is Blaine Brower, a nurse practitioner at the UNC Bladder Cancer Center of Excellence at the Lineberger Cancer Center in Chapel Hill, North Carolina. Blaine manages the care of patients receiving treatment on bladder cancer clinical trials and she's involved in all aspects of clinical trials research, including study design and monitoring patients' responses.

Diane Z. Quale: So thank you both so much for being here today. And I thought we'd get started just with the basics and talk about what is a clinical trial. Is there a simple definition for a clinical trial?

Dr. Rosenberg: So when we think about clinical trials, they're testing generally new treatments or new ways to use existing treatments, they're focused first and foremost on the safety of the treatment, then on the efficacy and how well it works. And then eventually comparing to the standard treatments to ensure that the new treatment is actually better. They are designed to learn something from and hopefully patients will benefit from new and interesting treatments.

Diane Z. Quale: So, in simple words, we need clinical trials to get new treatments for bladder cancer?

Dr. Rosenberg: Absolutely.

Diane Z. Quale: And to do a clinical trial, we need patients who will enroll in this study. Is that right?

Blaine Brower: I think that's fair to say.

Diane Z. Quale: Okay. So I think many patients have the perception that clinical trials are really only for people who have no other treatment options. Is that true?

Blaine Brower: The simple answer is no. Clinical trials, as Jonathan was stating, are designed to test safety and efficacy and that can be done in many aspects of care. Treatment regimens can be administered in the upfront setting or as in first line treatment.

Diane Z. Quale: And when you say upfront or first line, you mean that's my first round of treatment?

Blaine Brower: Yes, that's correct. That's the first treatment that you have ever seen. They can also be given in an adjuvant setting or after your first round of setting or your after surgery treatment. They can also be given in areas where we're looking at maintenance therapies where no other treatments are available at this time.

Diane Z. Quale: Okay. And Jonathan, are there different kinds and types of clinical trials?

Dr. Rosenberg: There are several phases of clinical trials, each of which is aimed at testing something slightly different. Phase one trials are for testing the safety, primarily, of the new treatments. Phase two trials are for testing the efficacy, how well something might work. And phase three trials are used to compare, generally, an existing treatment with a new treatment. And then there are things called phase four trials, which are so-called post-marketing trials after a new treatment is standard, to evaluate whether or not there are any safety issues that might not have come out in the first three phases of clinical trials.

Diane Z. Quale: So, do most new drugs then go through each phase of a clinical trial?

Dr. Rosenberg: Almost every new drug. There are some drugs that are so astoundingly effective in phase one that the FDA in the United States, the Food and Drug Administration, has approved them, but almost everything goes through phase one, phase two and phase three, and if a phase three trial looks positive, as in good, and the patients are having better results, that may end up leading to a new drug or a new treatment approval.

Diane Z. Quale: Okay. So, at all these different phases and types of clinical trials, are there safeguards for the patient's health and safety?

- Blaine Brower: Yes, there are several safeguards in place for patients' health and safety. Patients have to meet eligibility criteria, which means that they have to be physically fit and able to withstand these treatments. There's also treatment parameters in place where we monitor these patients very closely to make sure that they're not experiencing what we claim to be adverse side effects. So in every phase of treatment, there are several stops in place to make sure that the patients' health is first.
- Dr. Rosenberg: In addition, there are often independent committees that are reviewing safety on clinical trials, whose main goal is to stop a clinical trial or modify the treatment in the trial if there are patient safety issues that are unexpected or more severe than expected.
- Diane Z. Quale: Okay, great. So, as a patient, why should I consider participating in a clinical trial? What's in it for me?
- Dr. Rosenberg: One of the most important things to remember, unfortunately, with bladder cancer is that we're not curing as many patients as we'd like and so our treatments are not the best they possibly could be. They are the best we have today. And the way to get to the best treatments of tomorrow is through patients who are willing to enroll on clinical trials. In general, we're testing treatments that we think are going to be better. We don't know they always going to be better because otherwise we wouldn't be doing the clinical trial. The hope is that we'll be getting to the place where we're ultimately having patients with better outcomes and higher chances of cure.
- Diane Z. Quale: So, I'd participate in a clinical trial to help advance science, but is there a specific personal benefit to me as a patient in terms of my prognosis, to participate in a clinical trial?
- Blaine Brower: Well, in thinking of what clinical trials are designed to bring new treatments to the forefront, yes, I think there's a benefit because you should be getting what is considered to be the latest and greatest treatment option to treat bladder cancer.
- Dr. Rosenberg: And I also think there's additional attention paid to the frequency of visits and the focus on safety, and that side effects may be caught earlier in patients who are on clinical trials. There's increased monitoring for side effects for patients who are on clinical trials because of the requirements of the trial. You might be getting the next best treatment, we hope, but you're also getting hopefully very attentive care that is sometimes beyond what standard treatments entail.
- Diane Z. Quale: So I will always, on a clinical trial, be getting the standard of care?

Dr. Rosenberg: Yes, in general, you should be. Because if you're not getting the standard of care, you're not on the right trial. Even in trials where we don't give treatment in certain patients, it's because the standard of care is not to give treatment to those patients. For example, for patients who've had certain types of procedures, we don't know if treatment afterwards makes sense or not and the standard is to watch. And so in those patients, there may be a situation where they're not getting treatment.

Diane Z. Quale: Okay. So the standard of care might be just watchful waiting?

Dr. Rosenberg: Correct.

Diane Z. Quale: And a clinical trial could be either watchful waiting or a new treatment. But in every case, I'm still getting the standard of care.

Blaine Brower: Correct.

Diane Z. Quale: But if there's a trial where the standard of care is watchful waiting and the other part of the trial is a new treatment and I decide to enroll in this trial, do I get to choose? Can I be sure that I'm going to get this new treatment?

Dr. Rosenberg: So those kinds of trials are often randomized trials where a patient agrees to participate in the trial but they may not know which treatment they're getting and sometimes there's a placebo involved. A placebo is no treatment essentially but it's done in a way so that nobody, the doctor nor the patient know which one you get.

Diane Z. Quale: So I'm getting a pill or a treatment of some kind?

Dr. Rosenberg: Or an IV of a treatment that's actually salt water or sugar water. And in those situations, you know that the trial has that. You should ask your doctor about that or your healthcare provider. You should always know if the trial has a possibility of a placebo, but a placebo is never a surprise, or it should never be a surprise. You should know that it's a possibility and the decision you make is the decision to participate or not. You and your doctor may not know what kind of treatment you're getting, if it's a placebo, or if it's a treatment.

There are other trials, where we call open label trials, where they are randomized to a treatment and a different treatment, or a treatment and no treatment. If no treatment is the standard and in those situations, you would know what you're getting. You don't get to pick which one you get if you enroll in the trial, you're randomized, which is usually done by a computer or some other formula, to go to one treatment or another, you then get to learn which one you're on and you can make decisions from there. In general, the no treatment arm is the standard option in those situations.

Diane Z. Quale: So, typically I would know which treatment I'm getting?

Dr. Rosenberg: You would know whether there's a possibility of a placebo, and if there isn't a possibility of a placebo, in general you will be notified of which treatment you're getting.

Diane Z. Quale: Okay. So I'd want to know because of the impact of the different treatments, it's part of what we call an informed consent as to whether or not I'd want to do that. Okay. So, if I decide to enroll in a clinical trial and for whatever reason, I feel like stopping before it's completed, can I get out of it?

Blaine Brower: Absolutely. Eligibility, once met, you sign consents that says you'll participate in the clinical trial. However, if at any given time, the clinical trial becomes a burden to you or you're experiencing side effects that are undesirable, you can always stop clinical trial treatment. You may have a few follow-up visits to ensure safety in thinking of the treatment that you've received on trial but you can stop participation at any time.

Diane Z. Quale: Okay. And is there any average amount of time that a trial goes for? So if I'm signing up for a clinical trial, am I on the trial for six months, 12 months, two years or is it completely dependent on the trial?

Dr. Rosenberg: It's completely dependent on the trial. There isn't a particular standard ... it depends on the type of treatment you're receiving. It depends on what kind of follow-up is required after treatment is done, and so people are enrolled in trials that can vary in the length of follow-up, ranging from very short-term treatments to much longer term treatments.

Diane Z. Quale: And Jonathan, in your experience, what's been the longest term for a trial?

Dr. Rosenberg: So there are people who we have on clinical trials of the first immune checkpoint inhibitors who are still receiving therapy four years later. They are on treatment and some of them are doing exceedingly well.

Diane Z. Quale: And those are even though the checkpoint inhibitors have now been approved for bladder cancer?

Dr. Rosenberg: Correct. So there is a lot of intense interest on how well they work in the long term and we don't know yet how well they work in the long term, except for following the patients on the first trials over a long time.

Diane Z. Quale: So they are still considered to be on trial even though the drug has been approved?

Dr. Rosenberg: Correct.

- Diane Z. Quale: Okay. So an important question, will my insurance cover participation in a clinical trial, recognizing that insurance itself, medical insurance is a very complicated issue, but does insurance cover clinical trials?
- Blaine Brower: So commercial insurance does cover clinical trial costs. There are standard of care tests, procedures that have to be run through your insurance the way you would if you were on standard of care. I encourage all patients to call their insurance to verify what their co-pay is in relation to office visits and trial visits, as well as what the deductible is for their annual year as far as thinking of what's going to be covered.
- Dr. Rosenberg: And many clinical trials have experimental therapies or things that are done specifically for research, and the patient is not expected to pay for the experimental medicine. The patient is not expected to pay for tests that are only for research purposes but tests that are part of the normal care, as Blaine said, that you would get anyway if you were getting standard treatment, are generally covered by insurance. And most insurances will cover clinical trials but there are some exceptions and you should talk with your insurance company about that.
- Diane Z. Quale: Okay. Now, I know from my own experience, as well as hearing from others that once you make the decision to enroll in a clinical trial, it can take a long time before the trial actually gets started. Why is that? Why does it take so long?
- Dr. Rosenberg: Well, there's a period of time that starts from the date someone signs consent in order to confirm that it's safe for them to go on the trial and that they meet the criteria of the trial, and that includes re-assessing their cancer often. It includes special blood tests, biopsies, it might include tests on the tumor material from biopsies or prior surgeries, to determine whether the patient and the trial match up properly so that we can then proceed. And that can take several weeks, even up to a month at times.
- Blaine Brower: Yes, all these pieces are very difficult to coordinate at times and so it does take several weeks to get patients enrolled and started on treatment.
- Dr. Rosenberg: It's obviously anxiety provoking for patients who have to wait.
- Diane Z. Quale: Very much so.
- Dr. Rosenberg: And we recognize that and try to make things run as smoothly as we can, but unfortunately, it's a human process and so in general, it goes very well but not always.

- Blaine Brower: And patients should recognize that all of these tests and procedures that are being done upfront are our new baseline, our benchmark to monitor their progress while moving through treatment or on trial.
- Diane Z. Quale: Okay. I know you do a lot of clinical trials at Memorial Sloan Kettering, I know there are a lot of trials at UNC. Why aren't clinical trials available everywhere?
- Blaine Brower: That's a good question. Clinical trials takes a lot of manpower and it takes a large infrastructure. There are several healthcare providers involved in the process, clinical coordinators, pharmacists, regulatory individuals, and a lot of small institutions don't have the resources and infrastructure in place to be able to offer clinical trials.
- Dr. Rosenberg: In order to do clinical trials, you need these resources in place to ensure patients' safety and make sure that federal regulations and state regulations are followed appropriately so that you are conducting the research ethically and a lot of small practices, medical practices in the community may not always have access to clinical trials because they don't have that infrastructure. There are mechanisms where some practices do actually access clinical trials quite effectively through the National Clinical Trials Network, the NCTN, or through other organizations that particularly cater to small practices but much of the time, these trials are found at larger academic medical centers.
- Diane Z. Quale: So how do I, as a patient, find out about clinical trials? Who do I talk to?
- Blaine Brower: I encourage you to talk to your healthcare provider, your healthcare team, whether that be your physician's staff, your nurse practitioner staff, your nursing individuals and personnel. They have available resources just as BCAN does. You can go to the BCAN dashboard and search out bladder trial clinicals. You can also go to clinicaltrials.gov and there's also information on there.
- Dr. Rosenberg: Right. So both of those are outstanding resources online the patients can search directly but sometimes it's hard to figure out if you're eligible for a trial. Often that requires a visit to the place that has the trial open in order to see whether or not it's truly an option because there's a lot of medical terminology on these websites that make it difficult to figure out on your own if you're actually a candidate for the trial.
- Diane Z. Quale: So if I've spoken to my doctor and she hasn't given me any suggestions for a clinical trial and I go on the BCAN website, go to the clinical trials dashboard, I find a few that I know I can at least travel to, is there a number I call? How do I find out whether or not I can even go for that first appointment?
- Dr. Rosenberg: Often there is a phone number that's available and associated with the trial that you can call and get information and sometimes that may be a nurse who's

doing intake, sometimes it might be patient access type of staff and they'll work with the medical team to determine whether or not it makes sense to come in, hopefully, and that's the best case scenario.

Diane Z. Quale: Yes, so we know that people will, in many cases, have to travel for a clinical trial, hopefully, not too far. So for some of these clinical trials that you are both involved in, your institution is involved in, is the clinical trial available more than just at Memorial Sloan Kettering?

Dr. Rosenberg: So there are multiple trials that are open at multiple places. Some hospitals have regional affiliates nearby so people can get care closer to home in their communities but still be part of the same institutional network. And then there are what are called multi-center trials, which are open widely, depending on the type of trial and where it might be offered. That could be offered at multiple places in the country and so the same trial might be going on in San Francisco, Washington, DC, New York, and North Carolina with different doctors at the different sites responsible, along with their nurse and nurse practitioner staff, to conduct the trial at those sites, but it's the same clinical trial at multiple places.

Blaine Brower: Correct. And clinical trial treatment I would like to point out and to echo, although available at various institutions, you cannot take the clinical trial agent at one of your smaller facilities.

Diane Z. Quale: That's what I was going to ask. So, if my local doctor in Washington, DC, tells me there's a clinical trial at Memorial Sloan Kettering in New York City that I'm eligible for, I go up, they say I'm eligible. I can't have that medicine sent down to my doctor in Washington, DC, to be part of the trial down here. Is that right?

Dr. Rosenberg: Correct.

Diane Z. Quale: Okay. Well, thank you so very much for joining me today to help us unravel this very complicated but very important issue because as we said in the beginning, we need clinical trials to discover new and better treatments for bladder cancer and to do that, we need patients willing to engage in clinical trials. Thank you so much for joining us today. If you need more information, you want more information about clinical trials, please go to the BCAN website, we have a whole section on it, providing additional content as well as our clinical trials dashboard, where you can go and find trials that you might be eligible for.

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