BCAN Patient WEBINAR SERIES

Clinical Trials: Advanced or Metastatic Bladder Cancer

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Part I: The Basics

Presented by

***Andrea Apolo, MD** is a Lasker Clinical Research Scholar and tenure-track investigator and Chief of the Bladder Cancer Section of the Genitourinary Malignancies Branch of the National Cancer Institute. She received her MD from Albert Einstein College of Medicine in New York, and completed an internal medicine residency at New York-Presbyterian/Weill Cornell Medical Center. She followed up by a medical oncology fellowship at Memorial Sloan Kettering Cancer Center, and then joined the medical oncology branch at the NCI, with the charge of developing a bladder cancer translational program. She holds board certifications for internal and medical oncology.*

Dr. Apolo served in international committees, including the genitourinary tract of the Education Program Committee and a member of the Scientific Program Committee of the American Society for Clinical Oncology, otherwise known as ASCO. She's a member of the Bladder Cancer Program Committee of the Society of Urologic Oncology and shared the Bladder Cancer Advocacy Network's Think Tank Steering Committee.

***Betsy Plimack, MD, MS** is an Associate Professor of Medical Oncology and the Director of the Genitourinary Clinical Research at Fox Chase Cancer Center in Pennsylvania. She's an expert on the treatment of genitourinary malignancies with a focus on bladder cancer. Her research is directed towards the discovery of novel therapeutic approaches and predictive markers for patients with advanced bladder cancer. Dr. Plimack has extensive clinical experience with immunotherapies, and novel combination therapies. She serves on the National Comprehensive Cancer Network Guidelines Panel for Bladder Cancer, the ASCO GU Program Committee, and the Bladder Cancer Advocacy Network's Think Tank Steering Committee. She's also on the American Joint Committee on Cancer, Kidney/Urinary Tract Expert Panel.*

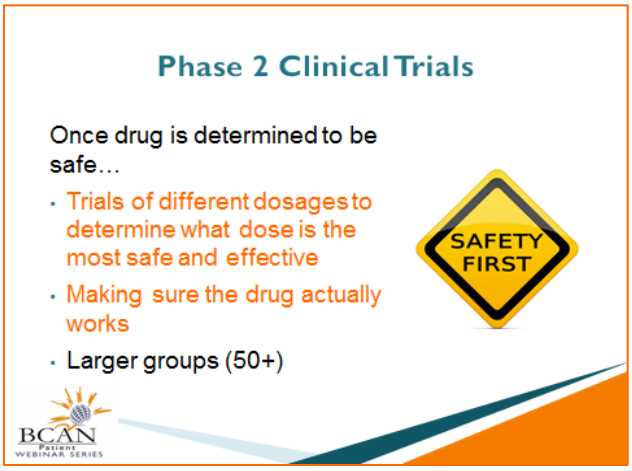
Betsy received her undergraduate degree from Yale University, and completed her MD degree and residency in internal medicine at New York University School of Medicine. She went on to a medical oncology fellowship at MD Anderson Cancer Center, and received a master's in patient-based biologic research from the University of Texas, Graduate School of Biomedical Science.

Dr. Andrea Apolo: I'm going to start off really generally talking about clinical trials, and what is a clinical trial. These are studies involving patients and there are a lot of different types of studies. They don't all have to be testing a new drug. We're going to focus today mostly on therapeutic clinical trials for patients, where we are testing new treatments. That can be alone, in combination, but there are other clinical trials too that are testing new interventions like surgery, radiation, or that are looking at biomarkers for predicting response in some patients. Also there are imaging trials where we can be looking, for example, at a new CT scanner or a new PET scan trace search to see if we can detect disease sooner versus the standard of care.

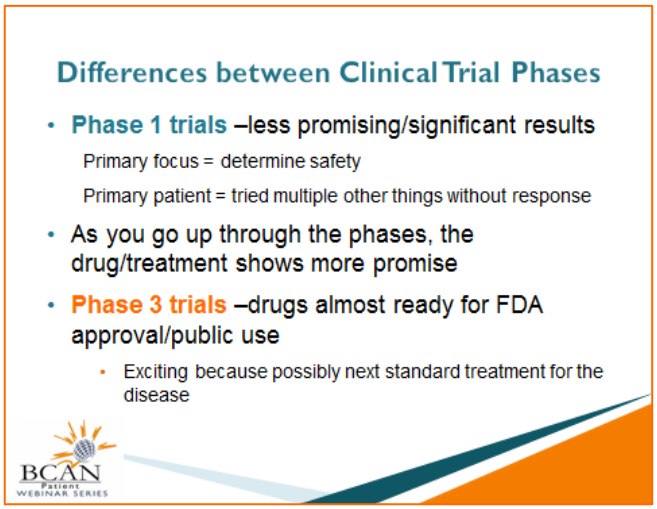
There's a lot of different phases of clinical trial. Phase 1 clinical trials are where we are looking for the safety of a new drug. A lot of these, so there's different types of Phase 1 clinical trials, but many of them are first in human. That means that the drugs have never been tested in a human before. They've been tested in either certain types of animal models, but this is the first time. We usually start off with a small dose and then escalate up, just for safety, to make sure that the drug is tolerable in terms of side effects. The goals of the trial are not always to see how efficacious it is, we usually go onto other phases of trials where we test that.

These trials are generally smaller. They tend to be about 15 to 25 patients. There are types of Phase 1 trials where drugs have been used in thousands of patients, but it's a new combination of two drugs that are commonly used, and that we're testing. We're asking the question, "What is the toxicity when you combine these two well-known drugs together in this population of patients?"

Then there's Phase 2 trials, where we are looking actually to see if we can find some early efficacy, which means does this work in this patient population? These trials are a little bit larger. They tend to be about 40 to 50 patients and everybody gets the drug at the same dose, which is different than the Phase 1 dose where everybody is getting a different dosage of the drug.

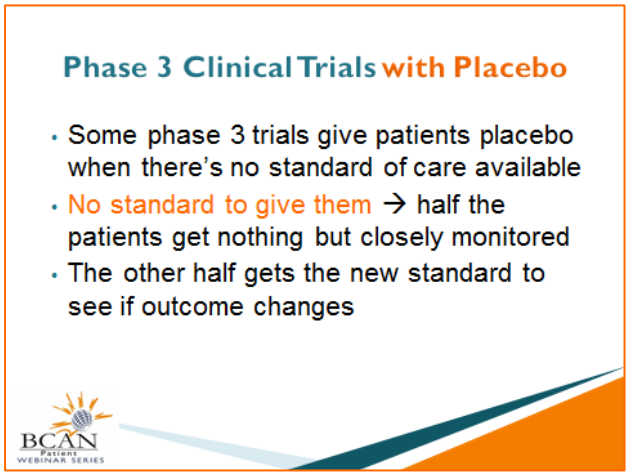


Then there's Phase 3 clinical trials. These are much larger clinical trials, usually about 500 patients or an average ranging from three to even 1,000 patients. Testing really how well this works, this new treatment modality, compared to standard of care.



In terms of efficacy, Phase 1 trials have a little bit less efficacy than other trials because I think a lot of it is it's never been tested in this either patient population or at the right dose, so we're dose-escalating up. It could be a good drug that works in this population, but you're just really slowly going up on the dose. Phase 3 trials at that point, you know that the drug is active; you know it works in this population. Can this become a new standard of care? It's often tested comparing to the standard of care. These trials are sought after because we know that they're efficacious.

Although some Phase 3 trials you can't test against an arm, so it's two arms, but then I think that's the next slide, where it talks about the two arms. Fifty percent of the patients will get one treatment, the other will get the other. There are some Phase 3 trials where certain patients will get a placebo, especially when there's no standard of care. There's nothing that we standardly give these patients. Half the patients will get nothing, because that's often what we do. We follow the patients clinically, and then the other patients will get this new standard to see if it changes outcome.



Sometimes in both arms we test the standard of care plus something else. For example in the neoadjuvant studies, both arms underwent removal of the bladder, or cystectomy, but in one arm patients got removal of the bladder plus chemotherapy. Patients are getting standard of care, often in some trials plus a new therapy.

Dr. Betsy Plimack: Andrea just went over the different types of clinical trials that there are, but ultimately for each patient in their conversation with their doctor, they'll be offered usually a specific trial, or maybe two different trial options in addition to a standard treatment. That's generally the way we discuss clinical trials is as an option for patients. There are a certain set of questions that are important for everyone considering a clinical trial to think about and ask. In asking those questions, which we'll get to in the next few slides, there's some clear pros and cons in general of participating in clinical trials that are important to be aware of.

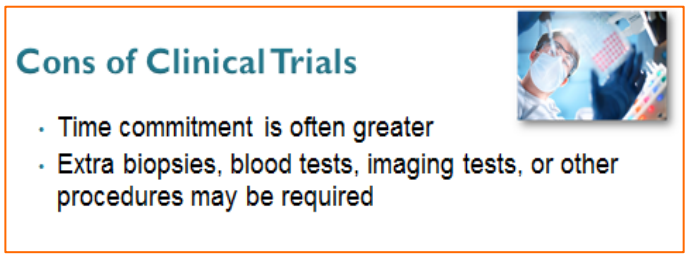
The pros of participating in clinical trials are that the clinical trial option typically adds another option to the list of treatments available to each patient. Typically, standard treatment can be given after the clinical trial therapy where the reverse is less often true. For instance, if you're considering a standard treatment and a clinical trial treatment, if the clinical trial treatment doesn't work, there are fewer stipulations on the use of the standard treatment, and so often your doctor can then use that as a second option. There are eligibilities for clinical trials that sometimes they not always limit the number of prior treatments one can have, and so that's an important thing to keep in mind.

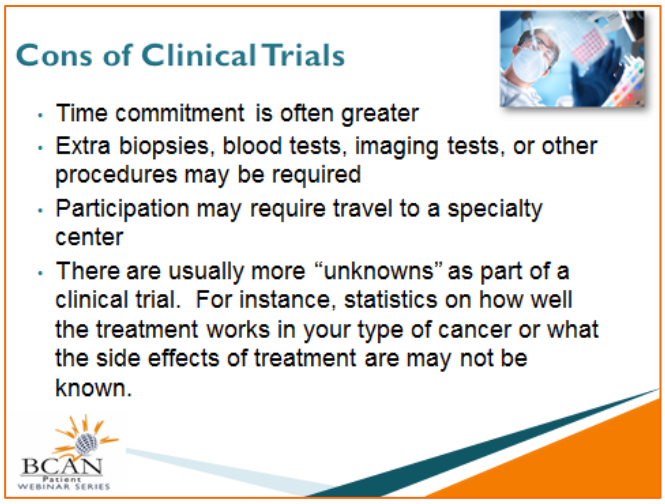
What Andrea and I always tell our patients, is that the clinical trials offer the opportunity to try something that we hope will be better than standard options. I think those of us that are active in clinical research truly believe we can and we must do better for our patients. We are generally not satisfied with the standard, especially for patients with metastatic or incurable disease. We're always looking to find something that will work better than what we have available. While it's certainly not a guarantee, it's an opportunity to try something that we hope will be better.

Usually there's a reason why we hope it will be better. Either that drugs or combination worked before in other cancers, but they've worked in the lab or other scientific rationale that supports the trial. All new approved treatments were once trials. All of the new treatments that we have now for bladder cancer were tested as clinical trials by patients coming for decades before any of us, and some more recently. Participation in a clinical trial not only helps move the field forward, but more importantly, offers each individual patient a chance to get a breakthrough treatment earlier, or first. When we look back at the patients at our Center who have been on some of these trials when the drugs first came out, they were able to achieve that benefit from the treatment earlier because of a clinical trial.

Then another pro of participating in a clinical trial is that generally care is better monitored, or more closely monitored as part of the trial. It's not that you won't get good care outside of the trial, but because we collect the data from patients on clinical trials so rigorously, there's that extra oversight and that extra set of eyes. Scheduling is usually more, there's more oversight to that because it's something we have to get right as part of a clinical trial. That's a minor benefit of participating in a trial.

There are of course drawbacks to participating in clinical trials as well, and they're equally important to consider. Generally the time commitment for participating in a clinical trial is greater in a number of ways. Often extra visits to the doctor so that we can keep a close eye on our patients who are on trial. There may be extra biopsies or imaging tests or other procedures required.

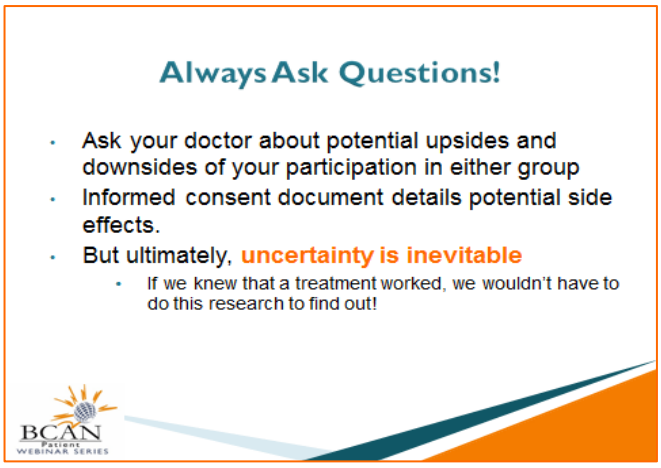




For a lot of our patients, the clinical trials aren't available at their local cancer center, and so travel is a built-in part of study participation for a lot of our patients. Another drawback to clinical trials is there's obviously, by definition, more unknown. There will be some piece of the clinical trial that your doctor will say, "We don't know the answer to this, this is why we're doing the trial." For instance, where I can put statistics on how well certain approved treatments work for an individual patient, we may not have those statistics to describe how well a clinical trial therapy works. The same is true in some cases for the potential side effects of treatment.

Some clinical trials are testing a drug that's very well-known from its use in other cancers, in bladder cancer for instance. In that case we know a lot about the side effects. Other drugs are newer or specifically for bladder cancer, where we may not have as much data, and there [inaudible 13:41] unknown issue in terms of participating in clinical trials.

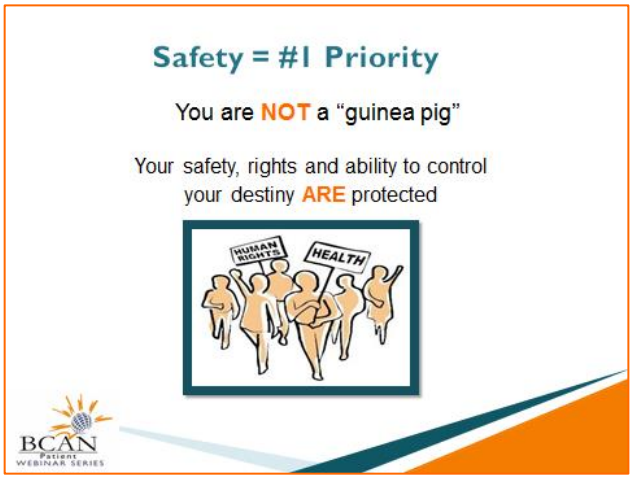
In considering the pros and cons of trial participation, there are some questions that you'll certainly have. We give them a lot of information when we present a clinical trial. As part of a clinical trial you get a document called an Informed Consent, which describes everything your doctor's reviewed with you in probably even more detail, in terms of the scheduled potential side effects. What's known and what's not known. Important to know is that signing a consent form does not promise that you will take part in the trial, it doesn't promise that you will stay in the trial. That decision is completely up to the patient and they are allowed to withdraw at any time. We just ask that you let us know so we can help you do it safely.

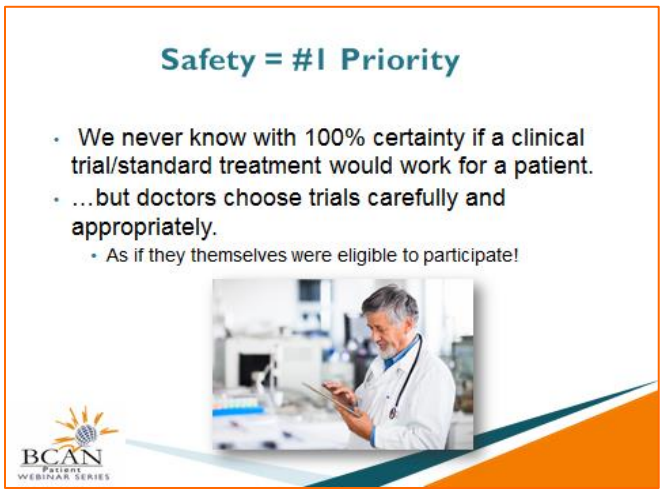


Then each individual trial will generate a certain number of questions from patients. Please feel free to ask your doctor any of the questions on your mind about clinical trials. Ultimately as the slide says, uncertainty is inevitable. If we knew the treatment worked, then we wouldn't have to do the research to find out. There will always be an element of uncertainty in terms of trial participation. At the end of the day, your safety and your comfort is really the most important thing. Taking a risk by participating in a clinical trial can be a calculated risk, weighing the pros and cons.

What we always tell our patients is that they have to feel like the right decision for you to participate, and if it doesn't, there is nothing wrong with going with the standard of care that your doctor has recommended.

What Andrea and I would really want to emphasize as part of this, is that you are not a guinea pig. We do not do these trials to test new agents. We do them to develop new agents that help our patients. I think neither of us would do what we do if we didn't feel that that care for many of our patients has come from a clinical trial. Again, we wish we knew 100% if a trial treatment or standard treatment would work for a patient. We don't know that, but we choose the trials that we open at our Center extremely carefully. We only open trials that we think are appropriate, and we feel good about presenting to our patients.





I would even go so far as to say we only open trials that we ourselves, if we were in the situation, would feel comfortable enrolling in. That's the one that's set for you. In general, your safety and your rights are paramount and priority. Again, as part of a clinical trial, that I think we've just talked about, there are always extra monitoring. Again, for safety, we need to be drawing extra blood tests, scheduling extra checkups. Your study coordinator may be calling you. The flip side to that is we think this is really important that we have an agreement with our patients that if we worry about you, you come in to see us if we need to evaluate you. A lot of the things that we are on the lookout for as part of a clinical trial may not be obvious to your local physician.

Should you participate in a clinical trial? Ultimately, it's a very personal decision. I think the key is to ask all your questions. If you don't have all the questions on the tip of your tongue at that first visit, go home, read the Informed Consent and make a list. You can always call your doctor or the coordinator to ask the questions. They key things that you should know when you're considering a clinical trial, for this main purpose of the study, is the study randomized and is there any blinding to treatment? Difference is that the placebo used for, is there a subject that you'll be getting where you don't know if you're getting a study drug or a placebo.

You would also want to know if any of the drugs in the clinical trial are currently already approved, and if so, in what setting and how they're being used. You will want to know if the treatment works and how long you can stay on the study. That varies depending on the setting and the trial. You are welcome to ask your treatment team about the credentials and research experience of the study staff. Again, always know that your medical care will continue. Whether or not you participate in the study, your doctor will still take care of you.