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TRANSCRIPT FOR VIDEO #6: HOW TO FIND A CLINICAL TRIAL—WITH DR. WHITFIELD GROWDEN
Interview, Massachusetts General Hospital
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Produced by The GCS Project

(WG—Whitfield Growden, MD; DR—Diane Redington, CRNP)

Slide: **CLINICAL TRIALS**
Patient/Advocate, Diane Redington, and Dr. Whitfield Growden discuss availability, eligibility and decisions regarding clinical trials and the differences in treatment plan options.

DR: Are there any clinical trials for carcinosarcoma and PD-1s?

WG: That's a good question. We do have…again, sometimes carcinosarcomas are generally excluded from a lot of trials. We know that in the phase 1 queue, uterine carcinosarcomas have been allowed in certain trials. ***We're going to be opening a clinical trial that looks at ovarian cancer that specifically does include ovarian carcinosarcoma in its eligibility.*** We've recognized that this is an unmet need. Women with ovarian carcinosarcoma—we've been applying a paradigm that we really have no right to apply because we don't have clinical trials to really back us up on it. But it's the best we have. So that's what we go with.

This is an upfront *immunotherapy trial that's looking at specific checkpoint inhibitors*, and it's actually opening very, very soon here in the Cancer Center [at MGH], and I think it's a national trial run through Pfizer.

DR: Wonderful. We are going to put that on the website. Women need to know, "How do I to decide on what clinical trial to participate in? Where do I go?" It's pretty frustrating for those of us out there.

WG: Well, and it's hard because you can go to clinicaltrials.gov and type in things, and what will you get? It's "drinking from the fire hose." You're getting hit with things that may or may not be relevant to you. And there's so much there; it's almost impossible to sift.

DR: It's pretty tough if you don't have a clinical background.

WG: Or if you don't have a navigator to help you. And a lot of times with clinical trials, our paradigm is that we give what we believe is the standard of care first. And then we think about, if it comes back or if it doesn't respond, then we think about clinical trials. But what you're bringing up is actually really interesting. Maybe immunotherapy trials need to be up front? Maybe they're going to be even better than our conventional therapy? And it takes so many years to become a new first line standard of care because it has to be compared on a large scale to upfront therapy. But what do we know about uterine carcinosarcoma? Is it ever going to see the light of day of an upfront phase 3 large clinical trial?

DR: No, and as a matter of fact…

WG: It may not.

DR: Probably, it'll be a long time.

WG: It would take 10 years.

DR: So, women think that the stage 3 [Phase 3 clinical trial] is kind of the gold standard—the randomized controlled trial is what you want to be in, but it sounds like you really want to be in a Phase 1 or Phase 2 trial.

WG: Well, you know, it's interesting. We have had an explosion in the last 20 years of targeted therapies and immunotherapies. Therapies that are unlikely to work for the whole but will work for a small piece of the whole. And you could imagine that the conventional Phase 3 Trial where you have 1,000 people—500 get one thing, 500 get the other thing. Well, your experimental arm is only going to work in a subset, so you are going to throw it out in any given Phase 3, even though it has the potential to save completely or at least create a durable benefit for a small subset.

So, we've had to rethink our clinical trails. And you are right. *It's been moving toward biomarker trials where you do a test up front for candidacy to get in.* And then if you have the signature [biomarker], you go on a Phase 2, and we look at the response rate. And that's what we've done with less common cancers. And in some settings, we've

been able to get FDA approval for drugs just based on biomarker studies in smaller trials.

It may be that with cytotoxics, like Taxol or carboplatin—well, those work the same in pretty much everybody. And so those are amenable to a big Phase 3 trial like what we did to establish its use. But we maybe need to rethink that in an era where we know things aren't going to work for everybody the same way, and probably we want to pre-select. Because guess what? Ovarian cancer all gets treated the same up front. And what do we know about ovarian cancer? It is probably 7 different diseases on a molecular basis. And uterine cancer is probably the same, but it lags behind ovarian cancer in terms of clinical trials.

DR: Well, one of the issues I see is that a person could be on multiple modalities. They could have original treatment and then it could recur, and then they could have another treatment and then they could have another treatment and that oftentimes eliminates them from participating in a clinical trial. A lot of clinical trials say 2 lines of therapy, two previous lines of therapy.

WG: Right. There have specific limitations on eligibility.

DR: Specific limitations. So…unless you get into the clinical trial tract fairly early then you may be eliminated from even participating in those down the road. Will that change or do women need to consider that as they're seeking treatment?

WG: I think they do need to consider that as they're seeking treatment. And the reason for that isn't so much because they're trying to limit their scope. It's that when you're trying to figure out when to use a medicine, you want to make the group of people you're studying as similar as possible. And unfortunately, that closes the door for some women that have, unbeknownst to them, gone on many therapies they thought in all earnestness were going to help.

I think that it's always good to explore clinical trial options at each stage in therapy. So that before you do a surgery up front, you explore clinical trail and then you weigh the benefit of, do I do something standard or do I do something experimental? And then maybe you chose standard. Maybe your doctor says that it's important that we do something standard because it's probably going to be better than what we have experimentally.

But then, when something comes back, again have the conversation. Is there a trial that I'm eligible for? What's that trial? What's it look like? What's the signature? What's the general signal that that trial was based on? And then, what's the standard of care? And then that goes for each recurrence that may or may not happen. And you always ask the question. Because there's some disease sites—for instance, in the pediatric oncology world, all children go on trial. In the upfront setting. In the recurrent setting.

DR: Really.

WG: Almost all do. Childhood cancers are exceedingly uncommon. Therefore, the only way you learn anything is by essentially always having standard of care versus something new. So, in pediatric oncology, clinical trials are infinitely more common.

In adult oncology, some estimates have been only about 10% of people getting treated for adult cancers go on a clinical trial. That number may have changed

DR: Do you think that will change with the new kind of…?

WG: With the new pipeline of agents? I think it may. *But I also think that clinical trials aren't right for everybody. At the end of the day, a clinical trial is an experiment.* And women—in my case with gynecologic oncology—are donating their experience in order to find out if this could potentially help themselves but also help other women in their shoes in the future. And it's a tremendous kindness that women do, but it's not right for everybody.

DR: Right, they do. One of the things that I have found is there's tremendous variation in how women are treated across treatment sites. And depending on where you go it's going, in many cases, decide whether you're going to make it or not make it, unfortunately, in this.

So, how does a woman who's just got this new diagnosis of this terrible rotten cancer… What do you do? Where do you go? Where do you start?

For example, I went to UPMC—great facility, world class—and I got my diagnosis. And I said, Well, I'm going to go to MD Anderson. I'm going to Sloane Kettering." I went to all the sites. And they [UPMC] said, "Well, they won't tell you anything different than we will." Well, every place I went told me something different. Quite. *Every place I went*. And

they told me **a lot different** from what they told me at UPMC. So…where's a woman…how do you decide?

WG: How to you unpack it?

DR: Right. Exactly. Where to you go? I learned so much along the way. But many women don't have that option, that opportunity, the knowledge, the wherewithal…

WG: Right. The wherewithal to be able to travel and to garner many opinions. So, the way I think about this is—I think that whenever you're dealing with a cancer that we don't have perfect answers for, you're going to see a ***broad range of opinions***. *And whenever you have that broad range of opinions, you really need to be thoughtful about the team that's been put together.*

And I can't speak to other cancer centers, but the style that we think is important, and that I personally think is very important, is that you have people from many disciplines—people that have a little bit of *laboratory experience*, are familiar with *clinical trials*, you have *surgical opinions* that also give *chemotherapy* and you have radiation types of doctors that are familiar with how we use *radiation* in the setting of a uterine cancer.

And they all put together a ***comprehensive opinion***, and ***then they explain why***. They actually try to make it so…at least I try to make it so that people understand, "Why am I offering you this? What's that actually based on?" Because you can go off the rails very quickly by inventing things in a vacuum.

I think the answer to your question is that our sort of National Comprehensive Cancer Center Network (NCCN) Guidelines are very broad in this setting. ***There essentially is no FDA-approved standard.*** Therefore, what they'll do is they'll list active agents. They'll list algorithms that are suggested or recommended or for your consideration.

So, how we follow this, how we treat this, how we even initially diagnose it, what studies we use, can be vastly different based on what environment you're working in. And I think that accounts for the heterogeneity [diversity, differences]. If you had some other type of cancer, where it's very clear what the steps are, you're going to see a little less heterogeneity, I think. Especially at comprehensive cancer centers where they're all going to be following very strict guidelines.

Whereas, with something like this, you're going to see a broad—a broad— set of options. And I think that, you know what it comes down to for me, for my sister or for my family? What I would think would be **the team that you have**. *Do you trust and believe in them? Are you comfortable with them? Is it something where they speak to you and you understand what they're saying and you trust them and you know that they're going to have your best interests and that they're going to answer your phone calls and they're going to support you through.* Because no one has a crystal ball, no one knows what the right move is. But you want to be in a place where you have a full appetizer sampler of options.

For things that are uncommon, that standard of care is not defined, we firmly rely on our friends. Talking, figuring out what's right for you. What types of molecular testing are we going to do? Are we going to profile? Are we not going to profile? Are we going to act on that? Are we going to try to get compassionate use? Are we going to look at clinical trials? What's the clinical trial infrastructure? What are the offerings? Where else are there offerings? These are questions that need to be asked in the setting of carcinosarcoma, for sure. And I would always want people to ask that, and we usually just bring this up.