

Scott Redding: Welcome to the 3Ps of Cancer Podcast, where we'll discuss prevention, preparedness, and progress in cancer treatments and research, brought to you by the University of Michigan Rogel Cancer Center. I'm Scott Redding. We're here with Dr. Anne Schott to talk about clinical trials, in particular around understanding early stage and investigator initiated trials. Let's meet Dr. Schott. She's a medical oncologist in the breast oncology program, and the Rogel Cancer Center's Associate Director of Clinical Research. Her clinical trial expertise includes being the Deputy Chair of SWOG, a national clinical trial organization funded by the National Cancer Institute, and her research is focused on the development of new breast cancer treatments through clinical trials. Welcome, Anne. People hear about clinical trials, but don't always know what exactly that is. Could you give us a little background on clinical trials?

Anne Schott: Sure. Clinical trials are basically research studies that involve people. In a trial, an intervention is made to affect a medical outcome. That intervention could be something like administering a drug, or doing some sort of medical procedure, or it could be something like providing a means to support a person to lose weight or feel less anxious. The main thing is that there's a question being posed, and the trial is designed to answer that question.

Scott Redding: What kind of questions might those be asking?

Anne Schott: Well, in the case of an individual with cancer, you might be asking the question of what is the chance that this new drug will cause the tumor to shrink? That would be sort of a classic oncology question. Or, in patients who have early stage cancer, you might look at some combination of treatments, surgery, radiation, drugs, and ask not about the tumor shrinking, but about whether or not it reduces the number of people who relapse. Or, in the case of someone who's a survivor of cancer, and is having side effects from their cancer treatment, you might ask about means to reduce those side effects and improve their quality of life.

Scott Redding: It sounds like there's a lot of reasons why a clinical trial's important, but why would I, if I'm a cancer patient, why would I want to consider a clinical trial?

Anne Schott: Well, a clinical trial treatment might provide you with access to a new treatment that's not available to people outside of the trial, and it might have direct benefit for your condition. But, you would need to realize that the new treatment may not be better than, or even as good as, the standard treatment. In some cases, a trial may not benefit you directly, but could provide information that would improve treatment for future patients. That would be the case in the type of trial that gives half the patients the usual treatment and the other half the new treatment, for example. You could be assigned to the usual treatment. You might want to join a trial either to get access to a new treatment, or to contribute to knowledge that could improve the health of other patients with a similar condition to yours. People in clinical trials who chose to enroll are followed very closely, and I would dare say their situation is

examined more closely than patients getting standard of care. Just this close observation and attention to detail may improve the care of patients on clinical trials compared to standard treatment.

Scott Redding: So can I get the same kind of clinical trial at another cancer institute as I would at University of Michigan, or where do I seek these different trials?

Anne Schott: Sometimes the answer is yes, you can get the same trial at a different institution, and sometimes no, because some trials are run at multiple centers at the same time. For example, the clinical trials group that I vice chair, SWOG, it's a national clinical trials organization, and it's trials are open at thousands of sites across the US and Canada. But some trials are only opened at a few, or even sometimes only one center at a time. University of Michigan as a comprehensive cancer center prides itself on developing and testing new cancer treatments for patients, and in the earliest trial phases, the U of M Rogel Cancer Center may be the only place that the trial is open. So really, it depends, and you need to ask the investigator that question, if you're being approached to participate.

Scott Redding: You just mentioned that it kind of depends on early phase, and if it's started here, that this might be the only place. Can you maybe explain a little bit more about what you mean by early phase trials, and are there different phases?

Anne Schott: Yes, so trials have classic definitions of phases. Phase I trials sometimes are the trials where it's the first time a drug has been used in a human, for example, but there are other Phase I trials where maybe the two drugs have existed, but they've never been used in combination. In the Phase I trial, you're really looking at safety and dose as two of the main questions that are being answered. That's not to say you're not also looking at effectiveness, but the trials are really designed to answer that dose and safety question.

These early phases of trials are where we learn the most about what is the appropriate dose, and where we start to get information about which conditions that treatment might be most effective for. But it's rare for an early phase trial, such a Phase I trial, to change the standard of care, because the FDA requires larger confirmatory studies before approving the drug or the drug combination for widespread use. But I will say, in the cases of really rare diseases or a brand new drug that has an extraordinary response, we have seen a few instances where a Phase I trial led to accelerated drug approval.

Scott Redding: Is it common for places to be offering these Phase I trials? Does every cancer center offer Phase I trials, or can it only be found at certain kind of cancer centers?

Anne Schott: Phase I trials take a certain level of expertise that is usually only available at large cancer centers, or sometimes specialized groups that really focus just on doing Phase I trials. Many Phase I trials are actually coming from industry, so it's

really the industry that's sponsoring the trial, and you may be joining in. We do those here, because we are very interested in bringing the newest treatments to our patients, but we're even more excited about the Phase I trials that aren't industry sponsored, but they're actually homegrown research here at our institution, maybe with a brand new drug, or maybe actually using an older drug in a new way that nobody ever thought of before, based on the laboratory research that we've done here.

Scott Redding: I think I've seen things about that recently, where there's sometimes some of these heart medicines have been able to be effective treatments in certain cancers as well.

Anne Schott: Yeah, and that's a real win in many ways. First of all, the drug's safety is well known. The expense is much less, especially if it's an older drug and you can repurpose it for a cancer indication. That's a real win if you can find something like that that works in a new indication.

Scott Redding: We talked about some of the early Phase I trials here and in other places. How are these early trials changing treatment options?

Anne Schott: Well, I think that some early phase trials aren't able to change, at that stage, the available treatments across the US, because they need further confirmatory studies in order to move it forward to a regular indication. For example, if we have a brand new drug developed here at Michigan and we're in a Phase I trial trying to work out the best dose and the best schedule, at the end of that Phase I, we'll know a lot about safety, side effects, dose, and schedule, but we then need to take it to a larger study, and just in certain kinds of cancer, to understand, well, is this a drug or a combination that works in breast cancer and what kind, or is it better for colon cancer? It's really that second and third phases of trials, the Phase II and Phase III trials, where you collect enough information on the effectiveness of that drug and how it compares to standard treatments, and that's what really changes practice.

Scott Redding: If a trial starts off as a Phase I, does it typically, if things seem to be moving in the right direction, that it typically moves to a Phase II? Does it stay here? Does it move to maybe another cancer center or area? How does that work, either here or at other cancer centers, the movement of phases as treatments go?

Anne Schott: Well, along with the phase, there's actually an increase in the size of the trial, in order to develop all of the evidence you need to prove that something is better than standard of care. Typically, a Phase I trial will be pretty small, maybe 30 patients or so. But Phase II trials may be two or three times that size, and Phase III trials may be 10 times that size. When you get to a Phase III, it's almost always a multi-center, and sometimes multi-national, effort to get the number of participants in that study, in order to actually change the standard of care.

- Scott Redding: How long does it take from start of a clinical trial in a Phase I to FDA approval as change to standard of care? What is that look like from a timeline standpoint?
- Anne Schott: Unfortunately, it's still years, although it depends on the situation. Usually, you can get the evidence you need from Phase I trials within a year. But those confirmatory trials, those Phase IIs and Phase IIIs, they can take a year or two to get started, and then another couple years to finish. I think a fast timeline is on the order of four to five years, and slower timelines longer than that. Although, I think things are changing, as we're seeing bigger affects you can prove that the drug or the treatment works with smaller numbers of patients.
- Scott Redding: At what stage in my treatment or diagnosis should I consider a clinical trial? Should it be, I've been diagnosed and I've got an early stage cancer, or do I need to wait until I'm more of an advanced stage cancer patient?
- Anne Schott: I think any of those particular phases could be appropriate to looking for a trial. There may not be as many trials available for a patient with a highly curable early stage cancer, because in many respects, the questions have been asked and answered, although there're different questions to ask in that group of patients. For example, we have a trial in breast cancer that's looking at, are there patients who don't need radiation? You could participate in a study where you actually don't get a treatment. I think in every phase, you should look at it. Certainly, with recurrence of disease, I think that's an important time to understand what all of your options are. We strive here to have appropriate clinical trials asking appropriate questions for every stage and condition that a person with cancer may come in with.
- Scott Redding: Great. I really appreciate the time today. If there was any kind of last minute thoughts or ideas for anyone that might be considering a clinical trial, what they should look for, or what are some key things as takeaways?
- Anne Schott: I think it's really important to talk with your physician about the availability of clinical trials at the center. I firmly believe that participation of physician and physician groups in clinical trials is an indicator of their quality. These are people who are thoughtful, who are looking to go the extra mile for their patients, and it's something that if your physician is a person who suggests that you participate in a clinical trial, I would feel that that physician is really doing the best thing by you.
- Scott Redding: So if you ask your physician, and maybe they don't know, are there places that people could look for, if they think that a trial that might be appropriate looking for, and then they could take that back, maybe, to the physician, are there areas where they could look for that?
- Anne Schott: Yeah, so the National Cancer Institute requires that any group that accepts federal money, which is essentially all the major cancer centers in the United States, that you actually publish, or list, your clinical trial on a site called

clinicaltrials.gov. It's a reasonable site, it's fairly searchable. It can be pretty hard for a patient to wade through the findings, but the information is there. Probably a better way to look for the trial also is to go to a renowned center that does clinical trials, and just understand what the offerings are there. You have to remember that you need to receive your treatment at the place that has the clinical trial, so even if they have a clinical trial halfway across the country, it just might not be practical for you to go there, so you want to take advantage of the local resources.

Scott Redding: Well again, thank you for taking the time today, and I really appreciate it. Thank you.

Anne Schott: No problem.

Scott Redding: Thank you for listening, and tell us what you think of this podcast by rating and reviewing us. If you have suggestions for additional topics, you can send them to cancercenter@med.umich.edu, or message us on Twitter @UMRogelCancer. You can continue to explore the 3Ps of Cancer by visiting rogelcancercenter.org.