Program Title: Clinical Trials and Ovarian Cancer
Presented by: Support Connection, Inc.
Originally Recorded on: September 15, 2016, 8 pm – 9 pm (EST)

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Topics:

- Myths and realities: What clinical trials are, and what they aren't
- When to consider clinical trials
- How to find clinical trials you're eligible for
- How to approach your doctor about participating in a clinical trial regardless of where the trial is being conducted
- Targeted therapies
- The role of genetics
- What's on the horizon

Stephanie Blank: I am really happy to be here tonight. I was excited to be asked to speak about one of my favorite subjects, which is of clinical trials and ovarian cancer. I'm going to go through a lot of things and will have a lot of time for questions afterwards, if you have any, and I hope this discussion meets your needs.

So, basically, an outline of what I'll speak abought tonight, this is probably what you saw when you found out about this webinar. But I'll speak about clinical trials and ovarian cancer; what exactly are clinical trials; myths and realities of clinical trials; when to consider clinical trials; how to approach your doctor about participating in a trial; and how to find a trial; targeted therapies and the role of genetics; what's on the horizon; and questions and answers.

So, we hear about clinical trials all the time, but the really basic **definition of what a clinical trial is**, is it's any investigation of a new drug or combination of drugs, clinical intervention or treatment. And this includes looking at new, unapproved drugs, or FDA-approved drugs that are being used in different situations for different reasons, and also new combinations of drugs. And the reason why you have to study two drugs together is because they might interact with each other. So you can't just necessarily assume that if one is good and another is good, both together are better.

Importantly, all clinical trials involving human subjects are required to have Institutional Review Board approval, or that's also known as an IRB, and you've probably heard of that before. And basically what an IRB is is a group that is formally put together to review and monitor research involving human subjects or patients. And basically, the whole purpose of these IRBs is to protect the rights and welfare of human subjects. So, it is important for you to know that safety is really a primary concern in these trials.

And just to take a step back, clinical trials are just one part of what has to happen for a drug to go from the laboratory to, you know, the market. So, basically, in this picture on the right, it's a little bit of an old diagram at this point, but it basically shows the timeline and how many ideas or compounds start at the beginning and end up at the end. So, first something is developed in the laboratory and then a small proportion of those go on to be studied in the preclinical setting, and that is usually being studied in animals, sometimes in cancer cells or -- it's usually animals. And then you go to clinical trials. And after clinical trials, things can get approved by the FDA. But you can see here that, first of all, let's just say we start at thousands of compounds; one will make it all the way to the market. And it takes a good 12 years from something to start in the laboratory to actually end up on the other side, where you can see an ad for it during the Super Bowl or whatever.

So, when you talk about clinical trials, you hear about the phases of clinical trials. And I'm sure a lot of you have heard this before, but you can't skip phases -- I'm sorry, a drug, not a person. If there is a drug in existence, it has to go through Phase 1, then through Phase 2, then through Phase 3. It can't really skip. There are some new types of trial design that we won't necessarily get into. But, in general, Phase 1 trials are looking at safety, dosing and side effects; Phase 2 are looking at how effective the drug is, and it's usually just measuring response rate, like does something shrink; Phase 3 is taking something that has passed through Phase 2 and comparing it to standard treatment. So, actually, importantly, a lot of drugs will not pass Phase 1, or will not pass Phase 2 to get to Phase 3.

And just in a little bit more detail, after preclinical, Phase 1 trials, where you have toxicity as the endpoint, the advantage to these kind of trials as a patient is that they usually have the widest entry criteria, and I'll speak a little bit about that later. But it's not one of those trials where you say can't have had any chemo before, or can't have had all these different kinds of chemo, because most of the time they cast a broader net. But the con is that you are getting a drug that we don't know that much about. So, there is limited data and there is limited toxicity information.

Now, in this day and age, most of the time when people are doing Phase 1 trials, they are also interested in, to some degree, how effective the drug is. But in the purest sense of what a Phase 1 trial is, it's really looking at toxicities, and you might -- these are the trials where people have to go get their blood drawn to see how the levels, about how their body is clearing the drug, and that type of thing.

In Phase 2 trials, again, we're looking at response, and the positive there is that usually there is some preliminary data to suggest you're getting a good drug, and you might get access to new drugs or treatments before they're approved. And cons, this is where you begin to have much more strict criteria for entering. For example, in some ovarian cancers you have to -- you know, a pretty kind of common now entry criteria would be somebody who has had at least three but not more than four prior lines of therapy. So, it's a very small window for a lot of these drugs, and it starts getting even narrower as you get higher up the phases.

Phase 3, your endpoint is comparison to a current standard of care. And the pro, of course, is that you may get better treatment. The con is you may not get the experimental arm. Usually, if somebody is going in a trial, they're going in not because they want to get standard of care, but they want something different. You could get standard of care treatment here, and the new treatment might be more difficult. Sometimes the standard, as defined by a trial, doesn't move as quickly as a standard as defined in the community. For example, way back before carboplatin was standard by studies, everybody was using carboplatin for women with ovarian cancer, because it's an easier to tolerate drug that cisplatin, but the standard treatment in a lot of the trials was still cisplatin. So, if you went on a trial and got the standard arm, you would get a cisplatin-based therapy, whereas, if you were just going to your doctor and getting standard therapy, it would be carboplatin. So, sometimes you could end up getting a standard arm that's not even exactly the standard arm that you might have wanted, but in general you are getting a standard treatment.

There are a lot of **myths about clinical trials**, and it's been very interesting to talk with a lot of women about their feelings about clinical trials. So, I'm just going to go through the myths. As you can tell from the top of the slide, if it's on here I think it's not true, so I'll try to refrain from just saying it's not true after I say to these things. But one myth, of course, is that clinical trials are not safe, and they certainly are safe. Every single factor is monitored probably even more closely than it is when a woman is not on a trial.

This is a big one. Being offered a clinical trial means I'm out of options, and that is absolutely not the case. There are trials that are offered at the very beginning, there are trials offered at all points in time. And, again, if you view a trial, as I'm going to try to convince you to, as an opportunity to get potentially something new, and before you get it otherwise, that you can see that it is not for that purpose.

My insurance won't pay for a clinical trial. I have a slide on that, actually, to follow this, and generally that is not the case. If I'm on a clinical trial I'll be treated like a guinea pig. I don't know exactly what that means, but later on, I mean, people do get excellent care on clinical trials.

If I'm on a clinical trial I'll have no input into decision-making regarding my care. That is absolutely not true. You are always the boss of your care. At any point in a clinical trial you can say I don't want to be on this trial anymore and you can stop. And I wouldn't necessarily count on getting either better or worse care if you're on a clinical trial. It's more regimented, and I'll speak about that in a little bit.

Who pays for clinical trials? Clinical trials are really expensive. Sometimes private foundations, sometimes it's the government, and these are usually through grants that can be individual grants, cooperative groups, and the big one that now ovarian cancer trials are through is called the NRG, and it is a combination of the three groups that are listed there to the right. And these are -- you know, in ovarian cancer we find cooperative groups to be especially a great venue for accomplishing clinical trials, because you need a lot of women to get any answers in clinical trials. And, also, you end up getting people from all across the country, so that any results that you get are more applicable to all people that exist. So, it's not like you only have people in Palm Beach, Florida on your trial, and then you don't know if it's something that everyone eats there or what it is that's making things better. So, basically, you want to have a wide net, and that helps you. SPORE grants are another kind of government-funded grants that fund these trials. A lot of trials are funded by industry, and these are usually, you have to remember always with these trials that their goal is to get their drug to market, and this is basically they're looking for new drug approvals and new indications.

Some clinical trial realities to counter the mix. Clinical trials are why women with ovarian cancer live longer and better today than ever before. That's a really important statement. Participation in clinical trials contributes to the advancement of science. Participation in clinical trials can get me access to treatment I would not otherwise be able to get. And also true, there may be less flexibility in my treatment if I enroll on a trial.

Why participate in a clinical trial? I mean, the main reason, it is a benefit to society, as I just mentioned. Clinical trials have gotten us to where we are now, but actually the vast majority of people do not participate in clinical trials. In terms of being a benefit to an individual, trials are done with significant oversight, and you can get a promising new drug way before you otherwise would. Lots of times the drugs are tested and paid for in clinical trials.

This is just sort of an out-of-date graphic representation of what I was saying about ovarian cancer. Women are living longer and longer, and each of these dots is when we saw the results of a certain clinical trial that just basically moved us that much further along this curve. So, people are living longer and longer and longer, and there are -- the next dot is up higher on the curve, so we should probably get a 2015 bar for the next time we do this.

Clinical trial benefits. Again, you have access to new drugs and interventions. You do get very close monitoring. You play an active role in your healthcare. You are among the first to benefit, and lots of planned Phase 3 trials are positive, so you're getting something good.

In terms of the risks, the logistics can be burdensome. There is really less flexibility in treatment, and the reason -- this is what I was talking about before. If you're getting a regular treatment off trial in your doctor's office and you want to go on vacation and delay your chemotherapy by two weeks, you can do that. But if you're on a trial and you do that, you may be taken off the trial, so you really do have to go with the schedule that the trial is dictating.

Additionally, the trials oftentimes will tell you when the scans are supposed to be. Obviously, if you need a scan sooner, you would get it, but trials generally scan more frequently than somebody necessarily would be scanned otherwise because they want to get a lot of information about how you are responding. There may be side effects that are not known about. There is an element of we don't know everything about this drug, that's why we're trying it. And, again, not everybody is in trial; we'd like to change that.

So, when do you consider clinical trials? The best point to consider -- sorry. Clinical trials are available all along the ovarian cancer treatment continuum. So, there have been trials for women at increased genetic risk for ovarian cancer who don't even have cancer yet. There are trials that involve even surgical techniques or making decisions about surgery at the very beginning. Frontline chemotherapy when disease comes back. Sometimes there are trials when you don't even have something that's on a scan just to see if it's sort of a maintenance type therapy. There can be all different types of times at which one can go on a clinical trial.

The main time to consider a clinical trial is when you're at a decision-making point, when you're making a change in treatment. If you do not have disease and it's not necessarily likely that you would enroll in a medication clinical trial unless there was some reason. Now, if you finished treatment and you have nothing going on, there are sometimes some trials that you can go on to take a medication just to see if you can keep everything away. But if you're getting a treatment that is working that's not on trial, I wouldn't recommend necessarily leaving that treatment to go on a trial. But if you get to a point where you're making a change, that's the best time to consider a trial. And at every treatment point you want to consider how that choice may affect your future trial options. So, what I said before was that there are a lot of trials that eligibility would say maybe you have to have three but no more than four prior treatments. So, if you're on one of those, that's a good time to look at your options, because you might not have those options if you don't take them now.

When I'm talking with people about whether they're going to go on trial or not, I will always say that if you start with this, you can go to trial after, or if you do not go on the trial now you may miss that opportunity. Additionally, some trials have very few spots and they can be hard to get, so that is something else. If you have a spot on a trial that you're interested in and you're trying to decide if you want it or not, and that might likely not be there later, that may help you make your decision.

How to approach your doctor about participating in the clinical trial. As I said before, anytime you're changing course you should ask. So, ask when you're changing treatment, ask when you're finishing treatment. Even if your doctor does not have a trial for you, another institution may, and it's not unreasonable to go to another institution if there is a trial you want. It does not mean that you're disrespecting your doctor; it means that you're looking for clinical trials, which is being proactive in your care.

It is a good idea to do some research of your own as well, and I'll speak very soon about that, because it's actually tricky to do that research. But your doctor may only know of the trials at his or her institution, and you would certainly want to look more broadly. The other thing is, if you're looking for trials and only

looking for trials, you want to know what your -- you're not just going to start cold-calling doctors and finding out what trials they have. You should go to a doctor who has a trial that you might be interested in.

How do you decide whether to participate in a clinical trial? There are a lot of different questions here: whether we have other options? What's being investigated? What are the risks? What are the costs? Logistics? What's in it for you? And what's in it for future generations?

So, if you've decided to consider a clinical trial, there are a couple of details that anyone explaining the clinical trial will go through with you. And these are all really important. First of all would be eligibility, which I was speaking about before. Exactly what the treatment entails, whether or not there is randomization, whether or not there is blinding, and I'll speak to you about both, of what these things are. What's the goal of the trial is one of the endpoints, and getting off the clinical trial.

So, **eligibility** is criteria for entry into a trial, and it usually includes the type of cancer and prior treatment. And in some situations it could even include, you know, that your tumor has a certain protein on it, or there are different types of -- I'm trying to think of another type of entry criteria. It can be that you had a certain amount of time that you had a certain type of therapy. It may be that if you're on another medication, you're not a good candidate to go on this trial. And that usually, if there is exclusion criteria, they're usually there for safety reasons. So, entry criteria ensures that the people in the trial are as similar as possible disease-wise as a result of any treatment being studied to be attributed to the drug and not to some other factor. So, it is frustrating to find a trial that you really want and not be eligible for it, but the trial design at the beginning has to be very laid out in order to have a trial that is valid.

You want to know what the treatment entails. Very importantly the schedule. There are some trials that are going to require you to come more times than you would otherwise have to, get more blood drawn, more testing done, and you would want to certainly know that, and that goes into your decision-making. There may be extra testing. I had patients on a trial where even after the treatment worked and they had nothing else going on, the trial was dictating for CT scans every, I believe it was every nine weeks, and that was just not acceptable follow-up for some of my patients. And they decided to go off for that reason, because they didn't want to have CAT scans every three months and they weren't on treatment. So, that was sort of excessive assessments for where these people were. You want to know about the length of treatment. Sometimes it's a very set amount and sometimes it's not. And you want to know about the follow up.

So, randomization only -- it used to be that only Phase 3 trials would have randomization, but now there are some randomized Phase 2 trials as well. But what randomization is, it's literally flipping a coin. It's a method of assigning patients to treatment groups. And, again, this is another thing that avoids bias on the part of the investigator or patient, and the goal is to create groups that are similar so you really can compare whether the drug is working better. Not that all the people that had, you know, less disease left on their surgery or in one group, or all the [triathletes] are in one group. Or if the doctor was running a trial and they wanted something to work, they might skew things. This makes the groups as similar as possible.

Now, blinding is basically either the participant doesn't know what treatment they are receiving, or double blind is when neither the doctor nor the patient knows what is being received. And these also add to the validity in terms of things like side effects that you might -- if you have more side effects if you're on a study drug, or something like that. So, this is also sort of one of the gold standards for trials. Lots of times you can tell, if you're on a trial, which arm you're on based on your side effects, and that is something that people do all the time, but in principle and theory, they should be blinded.

So, endpoints are determined when designing the study, and this is a whole other hour of talking, so I won't go into the whole thing. But there is a lot of debate among the ovarian cancer community about

what the best endpoint is for ovarian cancer trials. And part of the reason why the endpoint is so important is because trials and endpoints are how we get more drugs approved for ovarian cancer. And that is ultimately what we want. We want to have more options, more good options for women with ovarian cancer.

In general, people think of overall survival as the best endpoint, which is basically how long you would live from diagnosis. In ovarian cancer, thankfully, women live a long time, and women end up having many, many lines of therapy. And for that reason a lot of women, even if they didn't have that drug on a trial, will get it at some point in time. So, it makes it hard, because you can't tell -- there is just too much crossover; there is not necessarily people that won't have that drug.

Progression-free survival is how long you go before your disease gets worse. And this is before something grows on your scan, and this is an endpoint that has a lot of bias. For example, if you never check a scan again you're never going to have progression, but this is something that has been used more in ovarian cancer trials. The big advantage here is that this is to be a shorter trial. If we're talking overall survival for women and women are living years and years, then the trials need to go years and years, and it's going to take that much longer for us to realize if the drug we're looking at is good or not.

Quality of life is a really important and hopefully increasingly used endpoint meaning, are women living better? That's the best question, and I think ultimately we're hoping to end up with some sort of composite endpoints, which would mean taking into account both how women are doing and how long they're living. Are they living well? Another common endpoint is just response rate, which would be is something shrinking on a scan?

Getting off of a clinical trial, you can come off a trial for any point for any reason. You can just say I'm tired of this; I don't want it. You may have to go on that trip, whatever it is. You're not bound by signing a consent for a trial. Now, you may be taken off the trial. When a trial is designed there are rules for patients coming off the trial, and generally these would be if your disease grows. If you have a toxicity associated with the treatment, like, say your liver doesn't do well with it or something like that, or if you're not able to comply with the protocol, meaning you're not keeping your visits, or that type of thing.

So, **how to find clinical trials**. I think this might be hopefully the most helpful part if you're interested in clinical trials. The main way to find clinical trials, of course, as I mentioned before, is to ask your doctor. I think you do need to go a little bit wider than that generally, so support organizations such as Support Connection, can be very helpful with that. Websites, and then there is also -- in some situations there are individuals that are clinical trial navigators, and that seems to me to be a great idea, because it's a really complicated process to find clinical trials.

So, I put a couple of screenshots up here just to show you, because everyone really is going to go to the Internet to find the trials. This is the government's, it's clinicaltrials.gov, and this is sort of where people will off the cuff tell you to go look for trials, because this lists all the trials. But this is the most unuser-friendly website you will ever meet in your life. So, I see people that, you know, they've gone through it, the kids have gone into it; everyone comes in frustrated. So, this is sort of the one that everyone will tell you to use, but it's not very user-friendly. So, I'm going to show you some other ones.

The Ovarian Cancer National Alliance that now is emerged and it even has more initials on it. Anyway, if you look this up, they have a clinical trial navigator. You would type in ovarian cancer and you'll go forward and they would list for you what you would want. Another couple of good ones, both T.E.A.L. and SHARE, which I'll speak about momentarily, not only have a website where you can similarly type in specific criteria, but they also have clinical trial navigators, which would mean you can call up and somebody will help you find the clinical trial. And these are people that frankly are very devoted to this, and I think this is a great service that more people should use. I would say if I were looking for a clinical

trial, I would try these navigators and the website things, which I'll show you in a minute. So, this is the T.E.A.L. website, and this is SHARE, and you can also get that in Spanish, so that is certainly good.

Now, I found -- this is an organization that I think does a really good job with their website for finding clinical trials, so I just wanted to walk you through how this one works. Basically, this called the Coalition of Cancer Cooperative Groups, and it is an org, so I guess it's a nonprofit. So, you would go to the website, you click on I'm a patient with cancer, and then the place where people frequently have trouble working these, I'll show you. So, there are certainly easy things to put in here, you know, gender, ethnic, these are all optional. You don't have to put these things in necessarily. When you get to what kind of cancer you have, you type in ovarian. If you had tubal cancer or primary peritoneal cancer, you would also type in ovarian cancer. That's actually important to know and people get confused about that.

This is a question that really trips people up: What kind of ovarian cancer do you have? Most people who are on this call, probably, or most people who had their first line treatment with Taxol-Carbo, most of those people would have epithelial ovarian cancer. So, I think that is just one thing that people get to and they just say what am I doing? I can't do this. So, epithelial ovarian cancer is the most common. Here they have fallopian tube and peritoneal cancer as well.

In terms of subclassifications, the main thing that these website usually want to know is, are you -- the terminology is platinum-sensitive or platinum-resistant. If you have recurrent disease, has it been more than six months since you had platinum?

In terms of other things, these are some other criteria. If you're being treated for current disease, your primary stage doesn't matter at all, so just go to recurrent; don't worry about this. And using that, you can get a list of trials. Now, I'm going to go back a page just so we don't have to look at this for a minute until we're ready.

Women sometimes travel for trials, and I think that is something that if you're very committed to a trial and you find one, it may be something that you decide to do. You do not have to do that, but I would not necessarily rule it out. In some trials, in many trials, actually, travel may be paid for, so that's something that you could certainly look into. I wouldn't necessarily rule out a trial because it wasn't right in your hometown.

So, I'm going to move on a little bit and speak about **targeted therapy**, because a lot of the trials that we're doing now are related to targeted therapy. And to explain targeted therapy, the way I try to explain it is like this. Chemotherapy basically works by killing cells that are growing faster than other cells in the body. But cancer cells have -- and cancer cells grow more quickly than other cells in the body. But in addition to growing quickly, the reason why they grow quickly is because they have inner workings that are different from normal cells. They basically don't obey the stop rules that other cells do, and in targeted therapy we exploit those differences. So, we may turn off chemical signals that tell the cancer cells to grow and divide. We may change proteins in the cells so the cells die; we may stop making blood vessels, trigger the immune system, or carry toxins to kill the cancer cells.

The role of genetics -- you know, all women -- this is really important, actually. All women with a diagnosis of ovarian cancer should undergo genetic counseling and be offered genetic testing, because we used to think that only 10% of women with ovarian cancer had a genetic predisposition, but now we're learning that actually up to 30% of women with ovarian cancer will have a genetic predisposition to the disease. And this can have a profound impact of prognosis and treatment, and also on trial options.

So, another way that we can -- and this is all going to come together, I promise. Anyway, another way that we can look at your tumor to see if you would be a candidate for certain targeted therapies would be through molecular profiling. And what this is is basically taking the tumor itself and testing it to get its molecular characteristics. And then this can be used to identify and prioritize drugs that are more likely to

be effective for -- this is what so-called personalized medicine is, is using molecular profiling to select drugs.

Now, in terms of genetic molecular profiling, we've learned that a lot of either women or tumors with BRCA mutations have different responses to cancer treatment. So, the BRCA mutation can influence how cancer responds to treatment. And in patients -- there's a typo here, I'm sorry. In patients with BRCA mutation, cells have trouble repairing themselves when the DNA is damaged. And there are specific drugs called PARP inhibitors which make it even more difficult for cells to repair damaged DNA. And so these drugs are especially effective in drugs that have this mutation. And this drug, a PARP inhibitor, olaparib was approved, I guess it was December 2014, for ovarian cancer, and that was a new approval which we hadn't gotten for a long time aside from some other ones.

So, homologous recombination, this is a pictorial representation of it. I did steal this from another website, I'm sorry to say that. Anyway, I thought it was very good, though, so basically DNA is found in all cells in the body and its common for one strand or both strands to break. And when that happens the DNA has to be repaired, and damaged DNA can be repaired by two proteins -- either PARP or BRCA. So, in patients that have a BRCA mutation, only PARP can do this job, and if you inhibit the PARP, then they're not going to repair and then the cells are not going to live. I thought that was kind of a better explanation of that than I've seen before.

In terms of **future direction** for ovarian cancer clinical trials, the diagram on the right is from the recent Ovarian Cancer Report that was put out by the National Academy of Medicine. And it basically shows how we think about the different points in time of how long to continue on ovarian cancer care. So, some of the new directions include more PARP inhibition, which is what I just spoke about. Angiogenesis, and what angiogenesis is is basically cutting off the blood supply to tumors, and that's been working very well. Immunotherapy is extremely hot right now. It's basically using the immune system to help fight the tumors, so it's a different approach as well. Survivorship, looking at better ways for people to live, minimizing side effects of treatment. And, of course, prevention.

So, new directions. We're going to pre-select patients more carefully for trials probably through molecular profiling. We will look -- we'll be able to determine sooner if things are working or not by using even things like saliva or breath or something like that.

Drug development in clinical trial facts. New medicines are responsible for a 40% gain in life expectancy over the last 25 years. This is overall, not just ovarian cancer. And it takes 10 years-plus for a new drug to begin testing in humans. One in 50 ever make it from the laboratory to humans. And the cost of a drug is $500 million to $800 million. Less than one-third of drugs that begin in clinical testing are evaluated in Phase 3 trials, and less than 5% of cancer patients participate in clinical trials. And it's challenging even to get a clinical trial running, and this is reflected in the fact that investigators are dropping, unfortunately.

Clinical trials are critically important for the future of ovarian cancer care, advancing cancer care to dual effort from researcher and patients alike. Patient empowerment and involvement; this is really a way for people to help move this forward and make things better for other women with ovarian cancer. Without clinical trials the goal of improving patient results and quality of life is impossible.

What can you do? You can help raise awareness. You can join an advocacy group. You could be politically active, encourage Congress to fix the drug shortages. We're not too bad right now, but this has been an issue. And most importantly, lobby for increased research funding for ovarian cancer. Participate in clinical trials when you can, and support foundations that support women's cancer research. Remember, research cures cancer. Any questions?

Robin Perlmutter: Thank you, Dr. Blank. This is great information.

Caller #1: I have one, which is I've been treated with -- I've had two recurrences that were treated with carbo and a taxane, and on my third recurrence I was treated with radiation. And I wondered if that counted like into the -- how you add up on whether you're eligible?

Stephanie Blank: That's a great question. So, I would say radiation usually wouldn't be considered a line of chemotherapy or a line of treatment, so that probably wouldn't -- you'd still get the three. There are some treatments, though, that -- there are some trials that if you've had radiation that might make you ineligible for it, or the dosing might need to be different if you had radiation. So, it's something that your doctor would need to take into account, but hopefully it wouldn't add to your number of lines of therapy.

Caller # 1: Thank you.

Stephanie Blank: Sure.

Caller #2: Dr. Blank, are you aware of any immunology clinical trials that are going on right now?

Stephanie Blank: Yes. Hello. I recognize that voice. Yeah, there are a number of immunotherapy trials. They're usually at certain centers. I think the NRG had a trial that is actually I think on hold right now, looking at some of the immunotherapy agents, specifically -- it was a big one, so I just wanted to make sure -- nivolumab with or without ipi. So, these are like the two big drugs that are used in melanoma, and that was for persistent or recurrent epithelial, ovarian -- you know, persistent, recurrent cancers. And this was offered at a number of different sites. There are a lot of Phase 1s available. Most of the trials now are using these types of agents. The name is escaping me right now, which way of immunotherapy they are, the checkpoint inhibitors. And these are available on a lot of different sites. But these trials, a lot of them are Phase 1, and the spots go very quickly.

Caller#2: Thank you.

Caller #1: I have another question, which is, I have clear cell, and so many of the descriptions always seem to specify serous.

Stephanie Blank: That's a -- you know, clear cell is thought to be a little bit different molecularly, and actually there are some specific trials that are being designed for clear cell specifically. So, I think clear cell is one type, and the other type that is sort of breaking off into its own trials are mucinous tumors. Serous are more common and more of the BRCA mutations are in the serous tumors, but clear cell may have its own type. It's pretty -- there are some -- I can definitely think of some trials where it has to be serous, but not all. If you needed something I would certainly look specifically at some clear cells trials, though.

Caller #1: I was told in one other setting that there weren't a lot of clear cell trials.

Stephanie Blank: No, there are not a lot, because it's a fairly new concept. I mean, it's considered in the rare -- now the GOG considers it in the rare tumor group, so they have special effort looking specifically at drugs for clear cell. There is a Phase 2 that -- let me just see if it's open. Cabozantinib, which is a specific angiogenesis drug that is actually temporarily closed, which means that they are looking at the data that will probably open up again. And that was a multicenter trial. But there is not a ton, you're absolutely right about that.

Caller#3: -- say that I'm actually in a trial --

Stephanie Blank: Yay.

Caller #3: -- for an immunotherapy vaccine at Roswell Park in Buffalo.

Stephanie Blank: Fantastic.

Caller #3: And I do know that there are spots, because it's -- they're targeting a specific protein. So, I guess it's kind of hard to find women who have this protein, because it only shows up in 25% of the tumor tissue, but I just did want to put it out there that it exists. I've had four out of the five vaccines. It's a Phase 2b. I had my first recurrence in April and I went right from surgery basically into the trial.

Stephanie Blank: Fantastic. Is that the ESO one?

Caller #3: Yes.

Stephanie Blank: Yes, that's fantastic. And do you live in Buffalo, do you mind me asking?

Caller #3: No, I'm on Long Island.

Stephanie Blank: Right, so you travel.

Caller #3: I'm traveling, yes. I'm fortunate, my husband is mostly retired and I work part-time, so we can take the trips. I have to go up there every four weeks. And when I first started the trial, at first I had to go up there to see if I qualified, then I had to go back two weeks later when insurance and everything cleared. And then I had to go back two weeks after that, because they had to pharmaceutically test the drug in my bloodstream.

Stephanie Blank: Right. You're giving much more information than I could possibly give, so thank you, because that's -- but it's something you've decided to do and you've committed to it, right?

Caller#3: Right, right. Like I said, I've had four out of the five vaccine treatments. I go back next week. I also -- it's also a two cohorts, so there was cohort 1, which was just the vaccine -- or cohort 2, which was the vaccine, which is Phase 2b, and then Phase 1, an oral medication that I call the Pac-Man drug for lack of any other way to describe it, and I got that one. So, it's five times for the vaccine and seven months on the oral medication.

Stephanie Blank: Fantastic. Well, good luck to you. That's really great. And that's a good point, too. Like, if you want immunotherapy trials, you want to look at some of the best centers, one of which is Roswell Park. Another one -- there are other ones that are really good. Roswell Park is one of the leaders. So, if you want one of those, you're going to have the best odds of getting one, if you go to a place that has a lot of active trials. There aren't that many Phase 2 -- I can't think of another ovarian cancer immunotherapy trial that is that far along in terms of phases of testing.

Caller #3: There is a doctor who is running the trial, he's very optimistic and he's a lovely man, and he seems to feel that this will, in the not too far future, replace chemo as the means of treatment.

Stephanie Blank: Fantastic. Well, thank you.

Caller #3: You're welcome. And thank you.

Caller #4: My question is, what factors should be taken into consideration to balance missing a clinical trial opportunity if I'm in current treatment?

Stephanie Blank: So, are you saying, like, fear of missing out?

Caller #4: Yeah. You mentioned something earlier about there was a balance, or missing a clinical trial opportunity if you're in current treatment. What kinds of things should I take into consideration?

Stephanie Blank: Yeah. I mean, I think if you're being treated for recurrent disease and something is working, even if it's not on trial, I wouldn't recommend abandoning something that is working for a trial. And I guess one thing that I didn't want to -- I shouldn't make it sound like that, because the reality is that there will be new trials down the road, that even if you miss this opportunity, there may be another opportunity. That is a good thing about these trials. I think it's more if you're at a time when you need to switch that you would want to consider what you're talking about. Did I answer your question?

Caller#4: Yes, you did. Thank you.

Stephanie Blank: Okay, sure.

Robin Perlmutter: We have one woman that commented in the chat, Dr. Blank.

Stephanie Blank: Thank you, Tanya, for mentioning Clearity. The Clearity Foundation does molecular profiling. It helps women get this. It's a fantastic foundation and they do have a great clinical trial search engine and probably a lot of people that can explain a lot. So, thank you, actually, for that comment. I do not mean to intimate that the sites that I had up there were exhaustive, because there are a lot of good ones and I hardly know all of them. But the Clearity one is especially good, so thank you for that.

Caller#1: I have another question. I was just kind of -- I'm curious as to what ideas attract doctors to explore?

Stephanie Blank: You mean to encourage patients to go in trials?

Caller #1: No, well, to design a trial.

Stephanie Blank: You know, I think people that want to design trials really believe -- you know, it's a real belief that this will work and make things better for people. I think people get very excited about certain drugs and really want to see if they're going to work. So, I think partly it is just a desire to move the field forward. In designing a trial there is a lot of statistics that goes into it. Designing these trials in these cooperative groups, it's like a lot of people arguing and all this kind of stuff, because all these people have these ideas about what should be done. I think it's sort of -- it's very rewarding in some ways to come up with a way to test something that you think is valid. I think people enjoy the challenge.

Caller#5: Hi. I came in late. Can I just make a comment?

Stephanie Blank: Please.

Caller#5: Yeah. I'm entering into a clinical trial next week, I hope, I believe.

Stephanie Blank: Great.

Caller#5: And it's using a chemo drug but also looking at an inhibitor drug. They're calling it a Wee1 inhibitor. Are you familiar with that?

Stephanie Blank: Uh-huh.

Caller#5: And I want to just put in another plug, I guess, for Clearity, because we're looking at my tumor analysis and that's pp53 protein that apparently a lot of people with ovarian have. So, this trial is hopefully going to try to target that. And it is near my home, so it is certainly working out well, but I also appreciate the comments about traveling if need be. But those kinds of inhibitor drugs are not part of the immunologic therapy; is that correct?

Stephanie Blank: Right. And there are interesting -- I mean, immunology is getting a lot of, kind of play, but there are some very interesting other sort of pathway-specific drugs that are out there, and that is one of them. I've heard a lot of excitement about the Wee-1 inhibitors, and there are some antibody conjugate delivery type systems that are very interesting as well. A lot of them will require, as the woman who went to Roswell Park was saying, that you get your -- you know, you need to see not only something that Clearity would have, but specific testing that they might do to see if your tumor has a specific protein.

Caller#5: Oh, yeah, I'm getting a couple of biopsies, one before and one after, and the one after I get started with the drug. So, yeah, some trepidation, and there is a lot of preparation for this, but I do think you're followed very carefully, so that makes me feel better, too.

Stephanie Blank: Yeah, absolutely. Well, good luck.

Caller#5: Thank you.

Stephanie Blank: *[Dr. Blank reads a question that was typed into chat.]* There is a question here that says does multiple surgeries eliminate you from trials? The answer to that is no. Sometimes you need to have measurable disease to go on a trial, and what that means is that there is something that can be seen on a scan that can be measured and needs to be a certain size. So, if you have recurrent disease and you have a surgery, you would no longer have measurable disease. But that is not how I would make a decision about surgery or not, basically.

[Dr. Blank reads a question that was typed into chat.] What will help research get fast-tracked so that new findings get into clinical practice faster? I think increasing funding to increase trials. And basically the FDA last year around this time had a forum looking at endpoints in clinical trials. I think we're working to design trials that will get us answers more quickly, looking at sort of novel trial designs to do that.

And I couldn't agree with you more. [*Dr. Blank reads a question that was typed into chat.]* You wrote that the NIH randomized controlled trial process seems to have so many restrictions that it takes forever to translate outcomes to practice. The traditional kind of path that we've done has taken a long time, and I think there's a lot of lobbying that's going on with the FDA to try to change that. I'm very much hoping that these composite endpoints can be very helpful that way, because that would give you just more information. Overall survival is the longest. Thankfully, we have long overall survival for ovarian cancer, but it takes the longest to get those answers, so you want things better, to be able to find quicker but then also have validity. So, it's a little bit tricky.

Robin Perlmutter: Okay. So, I just want to thank Dr. Blank for your time, your expertise, your passion, dedication and commitment to the ovarian cancer community. And to all of you tonight who have participated, came out on this very important topic, we look forward to seeing you again on future webinars. And I just want to wish you all a goodnight. Thank you.

Stephanie Blank: Thank you.