

GYNECOLOGIC CENTER FOUNDATION

**Moderator: Karen Carlson
October 19, 2007
12:00 pm CT**

Operator: Good morning. My name is (Stephanie) and I will be your conference operator today.

At this time, I would like to welcome everyone to the Gynecology Cancer Foundation Telephone Workshop conference call. All lines have been placed on mute to prevent any background noise. After the speakers' remarks, there will be a question and answer session. If you would like to ask a question during this time, simply press star then the number 1 on your telephone keypad. If you would like to withdraw your question, press the pound key.

At this time, I would like to turn the call over to Dr. Julian Schink. You may begin your conference.

Julian Schink: Good afternoon. I'm Dr. Julian Schink from Northwestern University Feinberg School of Medicine. And I am a member of the Gynecologic Cancer Foundation.

I will be the moderator for today's call. We have a great program planned for you today with two excellent speakers. This is the fifth telephone workshop offered by GCF and we have over 100 people registered for today's call.

The GCF is also sponsoring an ovarian cancer survivor's course tomorrow, October 20...

Woman: Yeah.

Julian Schink: ...at NYU Medical Center in New York. If you are interested in attending the course, please visit our web site, www.thegcf.org for more information.

Woman: (Unintelligible).

Julian Schink: The goal of today's call is to help you understand and learn more about ovarian cancer from the convenience of your home or office. This workshop covers symptoms, screening, and early detection of ovarian cancer along with clinical trials and future treatments.

It is GCF's policy to reveal any known conflicts of interest. Possible conflicts of interest would include financial relationships or other affiliations with businesses or organizations that promote or sell products or services that are the subjects of the health information being discussed in this course.

The GCF's - to the GCF's knowledge, Dr. Coleman discloses that he is a consultant for GlaxoSmithKline, Ortho Biotech, Eli Lilly, Precision Therapeutics, and MorphoTech.

For those of who may not -- I'm sorry. Yeah, for those of you who may not know the GCF, its mission is to ensure public awareness of gynecologic

cancer prevention, early diagnosis, and proper treatment, as well as supporting research and training related to gynecologic cancers.

GCF advances this mission by increasing public and private funds that aid in the development and implementation of programs to meet these goals.

GCF provides a variety of educational materials and courses for ovarian cancer survivors. And you can view these on the GCF web site.

We recently produced a brochure on understanding ovarian cancer, which is available for order through the web site or by calling the GCF at 312-578-1439.

Also if you haven't already done so, check GCF's Women's Cancer Network web site at www.wcn.org, where you will find a wealth of information for cancer survivors, including clinical trials information and a Wall of Hope.

Dr. Barbara Goff is going to begin today's workshop by telling you about current screening and early detection for ovarian cancer. And then Dr. Rob Coleman will follow as he will discuss clinical trials and future treatments in ovarian cancer.

In order to make sure we have enough time for the presentations, we will open the phone lines at about 12:40 for questions and answers. Please note that you will not be able to answer - that we will not be able to answer specific questions regarding your treatment. Those questions are best asks of your managing physician.

I would now like to introduce Dr. Barbara Goff, who is the Director of Gynecologic Oncology at the University of Washington in Seattle.

Barbara?

Barbara Goff: Thank you so much. It's a pleasure to be here today and to get to talk about screening and early diagnosis of ovarian cancer.

And as probably most of the people on the line are aware, ovarian cancer is an ideal disease to screen for. And the reason for that is that when we detect ovarian cancer early, about 90% of women can be cured of the disease. When we discover the disease late, of course, the survival is not nearly as good.

And one of the problems that we face as clinicians is that only about 20% of the ovarian cancers that are detected in this country, in Europe, and elsewhere are actually diagnosed in early stages. But approximately 80% of women present with advanced stage disease when it's much more challenging and much more difficult to cure women.

So there's been a lot of interest in trying to identify methods that we could potentially screen women to try to make the diagnosis early. The two most popular methods that are used currently to try to detect ovarian cancer early are a blood test called CA-125 and then using ultrasound, particularly transvaginal ultrasound as a way to detect abnormalities in the ovaries.

The problem with both of these tests is that they really have not been shown to be effective in either the general population of women who we consider average risk or even in women who have strong family histories, people who we would consider high risk.

And, you know, one of - some of the problems with particularly CA-125 is that it is only elevated in about half of the women with early stage disease. It's elevated in approximately 80% of women with advanced stage disease.

But given our desire to diagnose women in an early stage disease, CA-125 has really not been shown as an isolated test to be very effective in diagnosing women early.

The problem with ultrasound is that while it is quite sensitive, meaning that we often will diagnose ovarian cancer or ovarian masses with ultrasound, the big problem with ultrasound is that it diagnoses so many other benign conditions that end up leading women to undergo surgery that it is not considered a very useful test because so many women undergo so many unnecessary procedures as a result of the transvaginal ultrasound.

And the most recent trials that have looked at using a combination of CA-125 and transvaginal ultrasound together was a very large study called the Prostate, Lung, and Ovarian Cancer trial in which there were about 70,000 participants in this trial, half of whom got screened.

And what they found was that the positive predictive value of using ultrasound and CA-125 together to screen for ovarian cancer was about 1%, which means that approximately 100 women undergo surgery to diagnose one case of ovarian cancer.

And so that really does not appear to be a very effective strategy in terms of trying to diagnose women early because there's so much morbidity associated with that.

So currently the - in - or, sorry, in 2007, the current screening recommendations basically are that we should not offer screening to the general population. That is the American College of Obstetricians and Gynecologists' recommendation.

And the US Preventative (sic) Service Task Force basically gives ovarian cancer screening a grade D, which means there's fair evidence to recommend its exclusion from a period health exam because so many women they feel are harmed by screening rather than helped by screening.

For women who are high risk, basically the current recommendations are that once you have completed childbearing, you should undergo a removal of your fallopian tubes and your ovaries, what we call risk-reducing surgery because screening really has not been shown to be effective even in a high risk population.

So unfortunately in 2007, we don't have a lot to offer women in terms of screening.

There is a lot of exciting research that's being done in proteomics in where researchers are assessing changes in thousands of proteins the blood and looking for specific patterns. There are other tests where people are looking at different immunologic signatures in the blood.

And so there's a lot of exciting research. But at this point in time, we're probably at least ten years off (unintelligible) away or possibly even longer from having an actual screening test that we could offer women in the general population.

And so a lot of my interest in and my research has been since we don't have a screening test, is there anything that we can offer women -- particularly women who are in the average risk population -- to try to make the diagnosis earlier.

And so actually back in 1997, I became very interested in, you know, whether or not there might be symptoms that could help physicians or help women themselves identify that there was a problem that might lead to an earlier diagnosis of ovarian cancer.

And one of the first studies I did I did with Cindy Melancon, who some of you may know was the original editor of Conversations!, the newsletter for women fighting ovarian cancer.

Unfortunately Cindy has passed away from ovarian cancer. But I was very fortunate and able to do several studies with her, which I think have been very influential in terms of identifying the fact that, you know, women with ovarian cancer do have symptoms.

But the first study that we did was a study in which there were 1725 women who had ovarian cancer. And we asked them simple questions about, you know, did you have symptoms, how was your ovarian cancer diagnosed?

And what we found -- which was contrary what - to what was published in all of the textbooks about ovarian cancer -- was that 95% of women with ovarian cancer did in fact have symptoms prior to their diagnosis. The most common were abdominal and GI complaints and the least common were actually pelvic or gynecologic symptoms.

And what was very interesting in this study is that we found that 89% of women with early stage disease -- the disease that has the highest cure rate and in some studies has a 90% chance of cure -- that 89% of those women in fact had symptoms prior to their diagnosis.

When we asked women approximately how long did you have symptoms prior to your diagnosis, most women, about 50%, had had symptoms for less than six months, but some women were waiting more than six months to see a doctor with their symptoms because they just didn't know that these symptoms were serious.

We also asked women, you know, prior to your diagnosis of ovarian cancer, what did your doctor tell you was wrong with you? And here we found that, you know, there was a lot of misdiagnosis that was being done in the United States.

We found that 15% of the women were told that they had irritable bowel. Thirteen percent were told that there was absolutely nothing wrong with them. Twelve percent were told that they were just stressed out and that was the cause of their symptoms. Six percent were told that it was depression that was causing their symptoms.

And so we really felt that this was another area - that there was a problem. Not only did women not know, but clearly physicians didn't really know either that these symptoms could in fact be a sign of ovarian cancer.

Now shortly after our study was published -- and this was - study was published in 2000 -- there was another study that was done from Memorial Sloan-Kettering, which was a case control study in which they took women

with ovarian cancer and they took women who they identified through random digit dialing and they basically surveyed them about symptoms that they had.

And what the study from Memorial Sloan-Kettering found was almost identical to what we had found from our national survey. They found that the majority of women did in fact have symptoms. They also found that 89% of the women with early stage disease had symptoms.

And when they did comparisons in terms of the women without ovarian cancer, they found, you know, very, very significant differences in symptoms such as bloating, abdominal pain, bowel disturbances, urinary disturbances.

And so there really seemed to be a significant difference between the cancer patients and the non-cancer patients. And so this started giving us some clues about, you know, what specifically these differences were.

Now shortly after both of these studies were published, there actually was a fair amount of criticism about these studies. There was concern about, you know, recall bias because these women all know that they had cancer.

There was concern that none of the women actually who - the women who did not have cancer, none of these women were actually going to the doctor. They weren't having problems. They tended to be younger, healthier women.

And so there was concerns that this really wasn't representative of, you know, what is truly going on in terms of women who are coming in to the doctor for complaints.

And so that led us to do another study where again we surveyed 1700 women who were just coming in to the primary care's doctor's office, and then we

surveyed another 160 women who were having surgery for ovarian masses, and again, we asked them, you know, are you - what symptoms do you have, how long have you had symptoms, how frequently are you having symptoms.

And what we found in that study was that in fact women who are coming to the primary care physician's office frequently do have symptoms. But what we found was the big difference between cancer patients and women in the general population was that cancer patients typically had more symptoms such as bloating, abdominal pain, pelvic pain, urinary symptoms.

But also it was that the symptom was new for the patient. It was something that had been present for less than six months. And it was something that occurred with relative frequency, usually every day, every other day. And that seemed to be a huge clue and the difference between the symptoms that, you know, women who don't have cancer have from time to time because we all have bloating, we all have, you know, urinary discomfort periodically, but that what was different about the cancer symptoms was that they really persisted and they occurred with a regular frequency.

And then after we did that study, we really wanted to try to see could we come up with really specific symptoms that were truly predictive of ovarian cancer. And so that led us to do our most recent study that was published in January of this year.

And again, we did another case control study where we did some logistic regression, which is a fancy statistical test to see which symptoms actually predicted whether a woman had ovarian cancer.

And what we did is we identified the most significant symptoms appeared to be bloating, increased abdominal size, abdominal pain, pelvic pain, difficulty eating, feeling full quickly, and urinary symptoms.

And these were significantly - they significantly predicted for ovarian cancer when they occurred more than 12 times a month and they had been present for less than a year.

And so this is really the first time we had been able to say these specific symptoms, if you have them, they may in fact be predictive of ovarian cancer.

And so after these series of studies had been published, which have occurred over the past seven to eight years, the Gynecologic Cancer Foundation, the American Cancer Society, and the Society of Gynecologic Oncologists all got together and we produced a evidence-based consensus - or consensus statement on the symptoms of ovarian cancer basically stating this information and making in a very public way the knowledge that yes, ovarian cancer does have symptoms.

These are the symptoms that women need to pay attention to. These are the symptoms that practitioners need to pay attention to because in fact they may be predictive of ovarian cancer. And we're very excited that that came out in June of this year.

And that information actually ended up on the front page of The New York Times, which was also very exciting. And, you know, it's just another way I think that the Gynecologic Cancer Foundation is really making a difference in the lives of women with gynecologic malignancies.

So that kind of concludes what I have to say about symptoms and early diagnosis.

Julian Schink: I would now like to introduce Dr. Rob Coleman. Rob is Professor of Gynecologic Oncology and Director of Clinical Research at the MD Anderson hospital in Houston.

Rob?

Rob Coleman: Thanks (Skip). It's a great pleasure to be here. And I thank you for including me once again.

Today I'm going to talk a little bit about the clinical trials and the future treatment of ovarian cancer. And I had hoped to maybe introduce a few new concepts and drug - drugs into this - the conversation.

There's so many out there to talk about and so many of them are so early in development, but I think this is a good forum to kind of start a discussion and a dialogue about what's out there and how these new compounds are being addressed.

(Unintelligible) credit one of my patients, who was really the inspiration for doing this talk in this way. When I sat down to present a study to her about the - about a new compound that we were investigating and I went through my usual, you know, introduction into what the endpoints were, the eligibility, and then at the very end of when I thought, you know, everything had been transmitted efficiently and clearly, I had this question come back to me.

And she said well, Dr. Coleman, what exactly is a clinical study? And I started thinking well, wait a minute, maybe we better do a little background

education first because there's so much out there and there's such a - many people know a lot about this, but some people don't know very much at all.

So I thought I'd just spend a little bit of time to go over some of the terms and what exactly is involved in this process.

So a lot of times, you hear the word trial used. And I think to many people, it's a little scary because it kind of sounds very much like trial and error. And, you know, I guess down to the nuts and bolts of things, we don't - we do studies because we don't know exactly how things are going to turn out.

And yet the way that we treat everybody today as a contemporary standard of care management is a result of this process, of finding out and tweaking and improving.

Woman: (Unintelligible).

Rob Coleman: And so I'm not a fan - very much a fan of the word trial. I think we try to use the word study because we're really trying to understand lots of specific aspects. And so it really is under scrutiny that we try to advance the specialty.

So a clinical study is essentially just a research project that involves patients. And its focus could be from any spectrum that that entails. It could be healthcare, delivery, quality, quantity, you name it.

But it's important to know that when you're approached to participate in a clinical study that what they're investigating, even in the earliest stages, the phase 0 studies, which are the newest ones to come on scene, are really the result - are really coming to the clinic after a long process. It's really at the tail end of that process where several years have gone into investigation.

Many people out there know the drug Taxol or paclitaxel. This was a drug that discovered in the 60s. And it (entered) into clinical trial 15 years later and ultimately was approved for ovarian cancer nearly 30 years after it was discovered.

So it's a - it - really it's the tail end of this process that a lot of these investigations are ongoing.

Now a little bit about the anatomy of a clinical study. For those of you out there who have heard this but don't really understand necessarily how this all works, a clinical study is usually headed by one person.

And by the NCI - that one person who's in charge of the oversight of the conduct of the trial is called the principal investigator. There are a number of co-investigators and collaborators that may be involved in specific aspects of the project, but there is somebody, one person, at the lead of the clinical study that is responsible for the conduct and the process of the data as it's accumulated.

There is also a study design and a protocol, which addresses issues like how many people need to be included, what's the eligibility, what - how are the drugs going to be given, when do tests have to happen, and where is this information going to be gathered and stored and how will it be reported.

All of this stuff enters into a document that we call the study protocol. And the - most of the people that the - that patients see in the offices have served this role as either a co-PI or a collaborator or a principal investigator in trials of the (years).

They're the - many of them at large medical centers where you go into a department, a lot of the physicians there have participated or served as - in this role. So they know a lot about how the process happens.

Clinical studies happen in every place that patients are seen. They're - a lot of times they're associated with large cancer centers or large university hospitals, but in fact, many clinical trials and studies are undertaken right in clinicians' offices. And they may have very local or focal objectives. And that's just really study-dependent.

As I mentioned, eligibility is a specific aspect of a clinical study. And unfortunately most trials have some limitations on this eligibility. It varies by the type of study. And I'll discuss that in just a minute. But it - it's done essentially to ensure the safety of the participants.

And this is very frustrating I have to admit for both patients and investigators because we'd like to be able to (include) everybody who walks in the door with a potential study.

But in reality, it - we have to have very careful guidelines in place so that we don't issue an agent that might have potential toxicity. And so these eligibility criteria are clearly spelled out in the study and are thought about extensively before the trial actually goes - is written.

The - all of the protocols that patients are involved in go through a series of oversight by independent organizations. This is done both locally and nationally. Many people will understand this as the institutional review board.

Most of the institutions that even if they're as an outside facility have compliancy programs for which the investigators have to go through a series

of education and have to maintain certificate of. So this is something that I annually renew. And many other investigators have their own local guidelines for what is considered in compliance with the institutional regulations.

But these are again in place to oversee the safety of the participants in these particular research studies.

Many times (unintelligible) a very frustrating part for investigators is that it may take several attempts at modification and revision to take a protocol from a concept stage and its initial draft through an IRB-approved protocol.

But that's to the betterment of everybody and certainly represents the important checks and balances that are in all types of clinical research studies.

So there are a lot of studies - a lot of pluses for participating in a clinical study. Certainly it gives you the access to new drugs and interventions. They have close oversight because obviously toxicity is an important aspect of any treatment-related trial.

It allows patients to take an active role in their healthcare. And if it is something that ultimately turns out to be of benefit, you're the ones that's going to be the most likely to benefit. You're the first to benefit.

On the down side, many of these studies don't have a complete package of side effects, some of them more than others. But in earlier stages of investigation, we may not know exactly what the side effect profile is or in whom these side effects may be more problematic than others.

The new approach might've been a great idea in the lab. I always say we've cured lots and lots of mice. But it may not work in the humans. And there are

important - that's an important translational - what we call a translational aspect that we're trying to overcome with the development of better models.

And a real practical concern is whether or not the health insurances will actually cover all of the costs of the healthcare that's involved. And this can be quite burdensome for some patients.

So just as a primer on what the clinical studies that are out there, I mentioned that the earliest phase is the phase 0s. I won't talk about that because it's a very preliminary look at a new drug.

And there are things - there are studies that are considered phase IV, which are studies which are done outside of the approval process and they're essentially looking for new indications of a - or new delivery of a medicine which is already approved.

But we call the ones in the middle phase, I, II, and III. And they have different goals, size, process, eligibility, and because of that have different numbers of trials that are available for participation in. So let's start with the first.

Phase I studies are studies that are essentially set up to evaluate toxicity of a new compound. These are very small studies. And the process for which patients are - participate in these are generally done in cohorts.

They are - the eligibility is generally open and not restrictive, although it can be. So we may do a phase I trial for instance in endometrial cancer or ovarian cancer, but on the other hand, there may be a phase I study for which ovarian cancer patients can participate, but it's also enrolling patients with colon, lung, breast, and so on.

Because these are (toxicity), these are trials of relatively small size and relatively inexpensive to run from a corporate standpoint for either NCI or - the National Cancer Institute or from industry, we have a fair number of these ongoing at any one time.

Some of the finer details of a phase I study is that these studies are starting - because of the introduction of the biologics, they're starting to undergo some very interesting trial design changes other than the classic where you put three patients on and you look for a toxicity and if there isn't, you go on to a next higher dose level.

The studies may actually may even be randomized. We've used this particular trial design when we've been looking at two infusion types for a specific drug. So if we wanted to look at whether or not a drug administered once a week has a certain toxicity profile and another - and the same drug given once every three weeks has a certain toxicity profile, we may actually write these so that you can enroll into each cohort waiting for the - what we call the washout period, which is the time to see if a toxicity occurs and then enroll in the other one so that there's an efficient way to do this (type of study).

And some phase I studies will go directly into the next phase of investigation where they're actually looking at efficacy.

Now they're - if you go on the web site clinicaltrials.gov, you will see several trials out there. I just have run a few examples of looking at phase I in ovarian cancer. I found 47 trials on this first pass.

Some of these are relevant for ovarian cancer patients. Some of them are not so relevant for ovarian cancer patients. But you'll see these out there. And

they'll - they're easy to go through. They have a number of different categories that you can look at.

But if you were to go through one, you will see that in the front page, it'll tell you who the lead organization is. It'll give you various identifiers so that you can keep track of this protocol. And it will tell you what the rationale and purpose is and the types of diseases that are allowed.

If you click into that protocol a little bit further, you'll see that there'll be some very specific eligibility requirements, whether or not it's gender-specific. You'll see that there will be very - there will be some information about how the cohorts or the patients that are entered, whether it's in a what we call the three-plus-three design where three patients are entered up to six patients per dose level. And you'll see what the projected accrual is.

You'll see information about and terms such as measurable or evaluable disease. And this really reflects as to whether or not they can actually see something on our CT scan or feel it by physical exam or something that can be measured biologically so - such as by an elevated CA-125.

And every study is different. So you almost - if you're interested in these, you have to go through and look at the fine details because it'll tell you whether or not this is relevant for your specific disease and your specific occasion.

Sometimes the - what you've had in a therapy before will be a criteria for whether or not you can participate or not. So for instance, if you have been treated with primary ovarian cancer and the tumor unfortunately recurs within six months, then that may be an eligibility criteria for one trial, but it may be an exclusion criteria for a different trial. So it's important to look at those particular features.

Now the phase II studies are studies that are based primarily on the goal of understanding the activity or the response of the drug in the type of disease that they're interested in studying.

These tend to be a little bit larger studies than the phase Is. They tend to have a staged process, which I mean by that is that generally they'll have a early stopping site where they can evaluate the efficacy, mostly from the standpoint of not enrolling a larger number of patients to an ineffective treatment.

So the eligibility is a little bit more limited than we saw in the phase Is. And there are lots and lots of phase II trials that are out there.

The eligibility - excuse me. The finer details of these particular studies is that they can be looking at a endpoint which is more long term such as like a time to progression or survival rather than just response. And they may actually also be randomized like the phase Is with a different goal.

There are - if you go look at the web site clinicaltrials.gov in ovarian cancer, you'll see that there are more than 160 trials that are open for which response and time to progression are primary endpoints.

These are done with novel drugs, drugs that are standard drugs, that are done alone and in combination. And we are starting to see the emergence of a larger number of these what we call randomized phase II studies where we don't understand necessarily how the - how patients would respond given the amount of previous therapy.

And this has been strategically done so that more patients can potentially participate in a clinical trial or a clinical study because we can evaluate across

a large group of different prior exposures and then compare it between two arms.

Again, the idea here is to look at its efficacy, not to show superiority of one arm over the other, but to see how they - how the new drug may be performing.

One of the hazards we see with phase II studies is without comparator arms is that we can get very different results from different single institutions. And we've seen this in a number of different studies where you see very, very promising response rates, but when they're done in different sites, we see different outcomes.

And what - particularly when they're done in a cooperative group setting, generally the experience has shown that the response rates are not quite as exciting as they initially intended.

Now when the phase II study is applied to the biological treatment, it becomes much more a initial look - an appropriate place to look for activity. Biological therapies may not have specific activity in and of themselves, but they may work particular well in combination with chemotherapy.

So they don't necessarily fall into the line where you escalate a dose to the point of toxicity because they may not have an upper limit. And so what we're - and actually what we're looking for is not necessarily the highest and most amount of drug we can get in, but which dose actually produces a biological effect. And that's in a very exciting new area of understanding these new therapies as they're being developed.

Just some examples that are out there that people have heard about, they have bevacizumab or the drug Avastin has been studied in a phase II study in the gynecologic oncology group.

It produced I think to the amazement of many people response rates that were similar to what we had seen in patients receiving chemotherapy with similar amounts of previous exposure.

We've seen these given also in combination with low dose of chemotherapy drugs, which have again produced responses. And this experience in this particular drug is growing as more and more of these agents become available.

Now the phase III studies are the big daddies. They are the standard of care, the ones that produce - the ones that are done to produce standard of care. These are very large studies. Sometimes they can - depending on the number of arms that are being investigated could be thousands of patients.

They tend to be - fall into the process of randomization as the primary way of evaluation.

The eligibility for these trials does - is somewhat restricted. And because of that, the interpretation of the outcomes is also restricted to the groups that were being studied.

Because these trials are so large and so very expensive, the number of trials that are available is actually relatively small.

(Because) these studies themselves are used frequently to establish a registration pathway for a new drug, so if a drug is trying to have an indication

in let's say ovarian or cervical cancer, it will go up against the current standard of care.

And if it wins or shows at least equivalence in certain settings, then that would be a way for this drug to have a label for which then would be available to women who have the particular disease.

The one aspect about randomization unfortunately some people have issues with is that randomization means you can't pick. Although there may be two or three arms in a trial, the randomization means that you have equal opportunity or probability of getting into any one of those arms.

So even though a drug combination let's say in arm B is something that you're really attracted to, you can't pick that arm for most of those situations. So randomization is really a flip of a coin depending on the number of arms you have in the study.

These are - this is the primary mechanism for which drugs receive their approval. And as you - if you go on the web site clinicaltrials.gov and you search under ovarian cancer, you'll see there's about 15 trials that are ongoing in both the front line and recurrent setting.

But you can also see the conduct of these trials by looking at the number of trials that have been recently closed. There's about 50 there. And this is really the final part of the maturation of new drugs.

Woman: (Unintelligible).

Rob Coleman: Coming down the pipeline that are in this particular phase III of investigation, these are the drugs that are actively looking for a label. And for instance

ovarian cancer, you can see - you'll - if you go on the web site, you'll see drugs such as (yondelis). The drug (unintelligible) is there.

Woman: (Unintelligible).

Rob Coleman: There's - you'll see Abraxane and Xyotax, which are two taxanes. And there are other drugs, which are spindle cell poisons called ixabepilone and (tupelone).

You'll see those drugs there; vaccines such as OvaRex and another one that's also under investigation in that space; there are a number of, you know, biological therapies such as Avastin and other biological signaling and gross factor inhibiting drugs such as...

Woman: (Unintelligible).

Rob Coleman: ...(Sarapin) and Tarceva, which are undergoing this type of investigation. A lot of them are there.

Within the gynecologic oncology group...

Woman: (Unintelligible).

Rob Coleman: ...we're happy to report that we have a number of phase III trials that women can participate in. The largest ongoing front-line trial that we have going that is open right now and eligible for patients with visible disease after surgery and is GOG 218, which is a trial which is randomizing women to (unintelligible) platinum, which is the backbone.

The additional experimental agent in this particular protocol is bevacizumab or Avastin. And it's followed by a secondary phase of maintenance for 15 months.

This is a placebo-controlled phase III trial for which overall survival is the primary endpoint. And there are a number of translational or scientific endpoints, which are being looked at, as well as quality of life.

Another phase III trial within the GOG, which is ongoing that may of you may've heard about is GOG 212, which is looking at a novel taxane called Xyotax. And it's being given to women who are in a complete clinical remission after their first-line therapy.

This particular trial is a no - has a no treatment arm. So although it's not a placebo-controlled trial, there is a arm of the study which would be considered the standard of care. And that would be no treatment.

So this is a three-arm trial looking at paclitaxel for a year, Xyotax for a year, or no treatment.

I had mentioned the drug (yondelis). There was - if you go to the web site, you can see that there was a very large recurrent ovarian cancer study down with the combination (yondelis) and a drug called Doxil.

This was compared to Doxil. It was a study that was ongoing until early this summer. It is now closed and met its accrual goal of 650 patients. And we will hear hopefully more about this in the next year.

There are - there's at least one other clinical trial open looking at the drug (telcida), which has had some difficulty in its previous two investigations in ovarian cancer.

((Crosstalk))

Bob Coleman: ...and there is a - many of you may have heard of the intraperitoneal study, GOG 172. This was a study that received a lot of press in January of 2006 when it was published and was accompanied by a clinical summary statement by the NCI suggesting that this modality of therapy be considered for women who have (unintelligible) reductions.

This was a - again, a result of a phase III investigation and demonstrated both progression-free and overall survival benefit versus what was considered the standard of care in that particular trial

So these have made a significant amount of benefit and enhancements in the quality of life and the survivorship of ovarian cancer, as well as other GYN sites.

I know I've focused quite a bit on ovarian cancer this afternoon, but this process applies across the board to all disease sites. And it's a process for which most drugs are evaluated and brought to the clinic.

Ultimately we would like to be able to have to not do any kind of treatment trials. Prevention would be the ultimate future treatment for ovarian cancer. This is a - an important long-term endpoint that we can't lose site of. This should be where we go. If we can prevent this disease from ever occurring...

Woman: (Unintelligible).

Rob Coleman: ...we would be in the driver's seat for this particular disease.

Woman: (Unintelligible).

Rob Coleman: Customized therapy is coming. We are - hopefully we'll be in a situation where we can take a sample of a tumor, run a series of profiling on it, identify what's the most critical pathways of this, and then deliver therapy and ultimately effect the best opportunity for response.

We're no where near sophisticated enough to do that as of yet. But some of you may have heard there was a recent press release by the American Association of Clinical Cancer Researchers of a small study, seven patients, that was done with this kind of hypothesis which showed that there were targeted pathways available which could essentially affect a cure -- excuse me, affect a response in patients who were otherwise felt to have exhausted all of their options.

So that's a very exciting but very preliminary look at the future treatments for ovarian cancer.

And I'm going to go ahead and stop there.

Julian Schink: So at this point, we would like to open up the phone lines for some questions.

Operator: Thank you.

At this time I would like to remind everyone in order to ask a question, press star then the number 1 on your telephone keypad.

We'll pause for just a moment to compile the Q&A roster.

Your first question is from Andrew of Los Angeles, California.

Julian Schink: Yes, go ahead, Andrew.

Andrew: Yes, thank you very much for your presentation. It's a lot of good information.

I just wanted to ask if there's any clinical trials or new drugs to treat high grade carcinosarcoma?

Julian Schink: Great question. Rob, do you want to tackle that?

Rob Coleman: Sure.

So, you know, the - there are - carcinosarcoma as a specific histology actually affects multiple different organ sites. For the majority of the cases that we're - that is likely being asked has to do with uterine carcinosarcomas because these are where the primary usually is seen.

The - I think there is a lot of investigation underway in high grade ovarian cancer for which carcinosarcomas are included. It - whether or not they're specifically targeted to the carcinosarcoma based on biological pathways, that's not necessarily been the focus.

However, as we understand more about the biology of the carcinosarcoma, which in - we strongly consider these as high grade endometrial type of lesions. So as we understand more about those processes, it's certainly understandable that trials would be focused towards those critical pathways.

At our institution -- I don't know about the others on the call here. But at our place, we were - we have some trials that are looking at patients that are being categorized by that histology. But in terms of the drugs that are specifically targeted to that, we're still trying to understand the pathways to go after.

Andrew: Thank you.

Julian Schink: Other questions?

Operator: Your next question is from Wendy of Berkeley, California.

Woman: (Unintelligible).

Julian Schink: Yes, go ahead.

(Wendy): Yes, yes, hi.

I'm presently receiving intraperitoneals cisplatin and Taxol. And I know that there's a newer study going on where they're studying carboplatin and Taxol.

Man: Mm-hm.

(Wendy): I just wondered if you knew where - how that study was going.

Julian Schink: Rob?

Rob Coleman: So...

(Wendy): For ovarian cancer.

Rob Coleman: Sure, the caller brings out a very good observation. Right now there's a lot of interest in looking at carboplatin as a substitution for (cisplatin) because of the toxicities that we saw primarily in the index study that a lot of people reference, which is the GOG 172 as I mentioned earlier.

The - we have a fair amount of data from our Japanese colleagues that have done intraperitoneal (carboplatin) and it has been really the background for moving this forward in the US as well.

I - we have done phase I trials with (carboplatin), which I have identified what we think is the dose to go forward with. And the process right now, I wish I could tell you I knew exactly what the schema was going to be for the follow-up trial.

(Wendy): (Okay).

Rob Coleman: But it is - but there is a study, which is going to be looking at an IV versus IP type question where right now the leading candidate is to use carboplatin.

So we don't have an open phase III trial yet. We have phase I and II experience and we have a large bank of data from our Japanese friends.

(Wendy): Okay, thank you very much.

Rob Coleman: You bet.

Julian Schink: Thank you.

Operator: Your next question is from Janet of Fremont, California.

Julian Schink: Go ahead, Janet.

Janet: Hello, Doctor. Thank you very much for your time and information.

I'm a ten-year survivor of ovarian cancer, initially stage IA and then graduated to stage IC, treated in Yale, luckily. I did very well with Dr. (Rutherford), who I will thank forever.

My question, though, when I hear when I'm on these calls is more about - because I'm so impressed with I felt that I - one of the reasons I survived besides the drugs is there were more aspects to it and I wondered if that's every considered in your research, such as the mental stress, alternative medicines? I did a holistic approach with his approval. And I do attribute that to my success. But who's to say?

And so my - are these things going to be looked at? Is there any interest in the medical community about the more - looking at the whole picture, not just the drug?

Julian Schink: That's an excellent question. So it's - the question is what is the role of complementary therapies to success in ovarian cancer treatment? And it's certainly being addressed.

Rob, do you want to talk a little bit about what (Aniel Sud) is doing at MD Anderson?

Rob Coleman: Sure.

Julian Schink: Or Barbara, do you have some comments?

Barbara Goff: Well, I think one of the comments I would make is that if you - there have actually - last year there were a couple of interesting studies looking at women with breast cancer and women with colon cancer and they looked - they basically - it was a retrospective study.

But when they looked at women who engaged in fairly moderate exercise following their cancer diagnosis, in both colon cancer and in breast cancer, there was approximately a 30% reduction in death for women who engaged in fairly moderate exercise.

And there was a very interesting editorial that was written in the Journal of Clinical Oncology saying, you know, if there were a pill that someone could take that would reduce the risk of death by 30%, of course, everyone in the world would sign up to do it.

But because this is exercise that requires you to physically go out and do something and make significant lifestyle changes, it's much more difficult to get women to - or anyone, you know, to go out and really make a significant and dedicated lifestyle change.

So I think these are very interesting issues that do need to be studied. The problem -- and this was brought out in the editorial -- is who's going to fund them? They were talking about - they were kind of joking, are we going to get Nike to fund this because you just go out and do it? But a hard part of it is actually funding this research.

Rob Coleman: Yeah, I echo that exactly. I think - and I - it seems like I have this conversation every single time I have a clinic. But I wholeheartedly agree. I think that the question about holistic approach I think means different things to different people.

And I think most people want to have - become active in their own treatment and try to do the best that they can to give them the best opportunity to fight the disease.

I think that there's a lot about holistic medicine we don't know. And it certainly is the purview of good clinical studies to sort this out.

Like (Skip) mentioned, this issue about stress is really interesting. And we've spent a fair amount of time trying to synthesize exactly what it is about stress that causes cancers to be - particularly chronic stress to be particularly unresponsive to.

And it looks as though -- and this needs obviously to be confirmed in real patient trials. But the - our findings were essentially that clinic stress actually leads to an acceleration of the angiogenesis process. And it's mediated specifically through the beta receptor.

And so this is nice because it gives us a nice target to go after because we have a lot of drugs that can impact the activation of the beta receptor. And then many of the people out there who have had surgery have probably already undergone some of this, which is to use some type of medication around the time of surgery.

So we're - it's a lot more to the story, but it's exciting that we're looking beyond just the tumor and drugs.

Julian Schink: Thanks Rob.

I want to thank all of our callers today and our two speakers for the wonderful job they did. I'm sorry that I have to cut this off now, but it's 1 o'clock.

I want you to know that a recording of this call will be available for replay from October 20 until January 19. To access this recording, you can dial 1-800-642-1687. So I'm going to repeat that -- 800-642-1687.

And use the conference ID number, 6974056 for United States and Canada residents. So that ID number again is 6974056. If you need further information about that, please don't hesitate to call the GCF office.

On behalf of GCF, we would certainly like to thank you all for joining us and hope that you found today's workshop useful and informative and have gained a better understanding of ovarian cancer.

GCF's programs are only possible through the generosity of GCF donors. This generosity is vital if we are going to continue to make these programs available.

If you'd like to make a donation, mail your tax-deductible gift to GCF or log on to www.thegcf.org.

Also please know that GCF will be sponsoring our 14th ovarian cancer survivor's course on March 8, 2008 in Tampa Florida. If you would like to attend this course or have any questions, you can email GCF headquarters at info@thegcf.org, or call 312-578-1439.

Thank you, everyone for being with us today.

Operator: This concludes today's conference call. You may now disconnect.

Julian Schink: Thanks everyone.

Rob Coleman: Thanks (Skip).

Julian Schink: You did good.

Rob Coleman: Thanks. I think that went well.

Julian Schink: Yeah, it did.

Rob Coleman: (Unintelligible).

Julian Schink: Catch you later. I have a good talk in New York tomorrow.

Rob Coleman: Are you going to be out there or no?

Julian Schink: No. Hey, we're moving into a new (premise) tomorrow.

Rob Coleman: All right.

Julian Schink: Yeah, yeah, very exciting.

Rob Coleman: (Unintelligible) so exciting.

Julian Schink: You're not going to believe this place.

Rob Coleman: No, I can't wait to see it. I'm going to be on that first tour to go visit the place next week.

Julian Schink: Okay.

Rob Coleman: Or in November.

Julian Schink: Yeah. Well, I'm going to set up some tours when everyone's in town that - on November 1, so.

Rob Coleman: That's awesome.

Julian Schink: All right.

Rob Coleman: All right, buddy. I'll see you soon.

Julian Schink: Take care. Bye.

Rob Coleman: Bye-bye.

END