Triple-Negative Breast Cancer (TNBC)
Audio Conference

April 22, 2011

MS. OLIVIA FRITZ: Thank you for joining. As a reminder, this educational activity is designed to allow oncologists and other healthcare professionals who treat patients with TNBC an opportunity to discuss clinical management strategies to improve patient care. Unfortunately, this clinical discussion is not intended for patients. If you are a patient, we apologize for any inconvenience and invite you to access educational handouts that we have developed specifically for patients with TNBC. To request these materials, please e-mail info@med-IQ.com. Welcome to the Triple-Negative Breast Cancer Community of Practice audio conference with expert faculty Dr. Lisa Carey and Dr. Eric Winer. I'm Olivia Fritz, your moderator for today's discussion. This audio conference is being recorded. However, resale of the content is prohibited. During today's call, Dr. Carey and Dr. Winer will discuss the latest in the assessment and management of triple-negative breast cancer. You will have an opportunity to ask questions related to the clinical care of your patients with TNBC and receive insight from faculty. This activity has been developed as part of the educational initiative Triple-Negative Breast Cancer: Evaluating Current Practice Patterns, for which Dr. Carey and Dr. Winer serve as faculty.

As part of this initiative, you can access a complimentary certified CME research and findings paper, which includes a report of current evidence, national survey findings in practice research related to disparities in care, and available therapies and treatment options in development for TNBC. Patient educational materials are also available as part of this series. All materials can be accessed online at www.med-IQ.com/A519.

I am pleased to introduce Dr. Carey and Dr. Winer. Dr. Carey serves as Medical Director of the UNC Breast Center at the University of North Carolina Lineberger Comprehensive Cancer Center in Chapel Hill. Dr. Winer serves as Director of the Breast Oncology Center and as the Thompson Senior Investigator in Breast Cancer Research at Dana-Farber Cancer Institute in Boston.

DR. LISA CAREY: Good afternoon everyone. The goal for today's program is to discuss how we medical oncologists care for women with triple-negative breast cancer, what we currently understand about the biology, and what we anticipate to be the advances in detection and treatment in the future. On behalf of Dr. Winer and myself, we'd like to welcome you and invite you to join in our discussion.

DR. ERIC WINER: Thanks. There has been a great deal of attention around this disease in recent years, and there are many challenges remaining in treating patients who have triple-negative breast cancer, both because we're still in search of targeted agents for this subtype of breast cancer and because we know that women who have triple-negative breast cancer have a higher recurrence rate, particularly in the first few years after diagnosis, than some other patients with breast cancer. Many of the questions we received in advance of today's conference are focused on the biologic basis of triple-negative breast cancer and various treatment regimens, so we'll begin with a discussion of a few of the pre-submitted questions.

MS. FRITZ: We will begin the question and answer session.Med-IQ received several questions in advance of this teleconference. Dr. JaNeen Dancy will share one of these questions at this time. DR. JANEEN DANCY: Dr. Carey, this question is for you. Is there a specific tumor type in triple-negative breast cancer, and are there any clinical pathological features to define the different prognostic subtypes of triple negative instead of genetic testing?

DR. CAREY: I think that if you ask about a specific tumor type in triple negative, I assume the questioner was asking about the molecular subtypes within triple negative. No, there isn't a particular one that defines triple negative, although the majority of triple-negative breast cancer is made up by what we call the basal-like subtype of breast cancer, which has some unique biologic features, although the therapeutic implications of that still are not clear. From the standpoint of pathology, most triple-negative breast cancers tend to be higher grade, not always, but there's certainly an enrichment there. There are some features that are more likely to be ductal or mixed, at the very least mixed ductal and lobular, but there aren't necessarily particular features outside of some of the things that go along with, for example, BRCA-associated

breast cancer, which is usually triple negative and can have some features like medullary features or pushing margins, some of those kind of interesting histopathological finding, but they're not at all pathognomonic in that sense. They're more associated. Eric, do you have anything to add to that?

DR. WINER: No, I think that's pretty comprehensive.

MS. FRITZ: Thank you.

DR. DANCY: I will continue with the pre-submitted questions, this one is for you Dr. Winer. Should all patients have BRCA or BRCA1/2 testing?

DR. WINER: This question arises from the fact that triple-negative breast cancer is particularly common in the setting of patients who have BRCA1 mutations. In the setting of BRCA2 mutations, in truth, most of the cancers are estrogen receptor-positive. There are some that are triple negative, but probably not many more that are triple negative than in the general breast cancer patient population. So, should a woman with triple-negative breast cancer automatically be tested for BRCA1 or I suppose for both? The answer is “probably not,” but one's threshold for looking for a BRCA1 mutation should be lower in a patient with triple-negative breast cancer than in other patients. Overall, if you take the entire population of patients with triple-negative breast cancer, probably somewhere in the range of about 10% have a BRCA1 mutation. Not surprisingly, that's associated with having breast cancer at an early age, a positive family history, being of Ashkenazi Jewish background, which increases the chance of finding a BRCA mutation. So, this is a question that does always go through my mind any time I see a patient with triple-negative breast cancer. But, for example, if I'm seeing a 75-year-old woman with no family history whose not of Ashkenazi Jewish background, has a large family in whom none of the members of the family have breast cancer, I'm typically not very worried about a mutation. At least at the moment, our treatment approaches don't differ according to whether someone has a gene mutation or not. If in fact they ultimately do differ, that would be more of a reason to test everyone.

DR. DANCEY: Dr. Carey, this next question is for you. The participant writes the following. I am interested in your

thoughts about the estrogen receptor-negative, progesterone receptor weakly positive phenotype. In your opinion, does this phenotype resemble the triple-negative breast cancer tumor, or is it different?

DR. CAREY: That's a hard one. The reality of clinical testing for ER, PR, or Her-2 is that we have to acknowledge that there is a certain play in these things. We have ER and PR strongly positive tumors, and then we have ER and PR weakly positive tumors. While they are all categorized as hormone receptor-positive, we worry about the ones that are at the lower end and whether they truly are hormonally sensitive. That said, our own pathology colleagues have reviewed these data and the ASCO/CAP combined assessment of where you can define a threshold for hormonal sensitivity, which is really what we're all interested in here. They cannot find a threshold anywhere more than 1%, which is why they said that any staining for ER or PR should be considered a hormone receptor-positive breast cancer, with the obvious implications being that you should at least consider endocrine therapy for such a patient. I think we all suspect that for a tumor like one that is ER negative and PR only weakly positive, it wouldn't surprise us to find that there are more in whom they truly were not hormonally sensitive, but we simply don't have a gauge to say that they are actually triple negative. We can't say that at 5% or 10% of PR we can now change these guidelines and call them triple negative, but we can say there is probably a higher likelihood of those to be essentially a false negative in terms of functional signaling through the receptor. That's why, for many of the triple-negative trials, hormone receptors up to 10% are permitted to participate in the trial, but I think the flip side is you do not offer endocrine therapy. I have to say that, in my own practice, if it's staining at all I follow the ASCO/CAP guidelines, and I offer endocrine therapy.

MS. FRITZ: Thank you. Doctors, we do have a live question in cue, and this question comes from a doctor with the University of Pittsburgh.

FEMALE VOICE: Hi, my name is - - . I am one of the fellows here at the University of Pittsburgh. I have a question about management. After the trial, Expand the Access Protocol - - Metastatic Triple-Negative Breast Cancer - - second-line therapy, does bevacizumab (Avastin) still play a role in

triple-negative breast cancer? Is docetaxel/bevacizumab (Taxol/Avastin) a reasonable option for these patients?

DR. WINER: At least for the moment and over the next few months, bevacizumab is still an approved drug for the treatment of breast cancer in the United States. It's a drug that appears to work at least as well in triple-negative breast cancer as in ER-positive breast cancer. It is not an agent when added to chemotherapy that improves survival as best we know, but it is an agent that, to a modest degree, improves progression-free survival. I think that if you want to use it in a second-line setting, I don't think that's unreasonable. I wouldn't be very enthusiastic about using it much beyond a second-line setting given the data that were initially published by Cathy Miller looking at patients who had had multiple prior regimens and randomizing them to capecitabine with or without bevacizumab. I realize that's a different chemotherapy backbone than you're talking about, but it's just hard for me to get too enthusiastic about bevacizumab in patients who have been heavily pre-treated. Does that help?

FEMALE VOICE: Thank you. Yes, that helps. Thank you very much.

MS. FRITZ: Thank you for your question, and, again as a reminder, you may press "0" "1" to ask a question. We now return to Dr. Dancy for another pre-submitted question.

DR. DANCY: I'm going to continue with this next question that is asking about the role of platinum agents in triple negative.

DR. WINER: There is the suggestion that platinum solves and specifically carboplatin and cisplatin may have more activity in the setting of triple-negative breast cancer, although having said that there hasn't been a terribly comprehensive look at platinum - - in other subtypes of breast cancer, specifically ER-positive and HER-2-negative breast cancer in the modern era. In the setting of triple-negative breast cancer, there have been at least two pre-operative trials that have been done using single-agent cisplatin that have led to pathologic complete response in the breast with four cycles of single-agent cisplatin of about 20%. Whether that's better than any other agent in that setting, any other single agent, we can't say, but there is some activity. In the metastatic setting, there will be data presented at ASCO this year by Steve Isaacof

[phonetic] from a trial that Dr. Carey and I were both involved in in the Translational Breast Cancer Research Consortium, where both carboplatin and cisplatin were looked at in patients with triple-negative breast cancer. And while I don't want to give away too much from that presentation, both drugs clearly had a modest degree of activity. So, I think these are agents that can be used in patients who have triple-negative advanced breast cancer. In the setting of advanced disease, you have the advantage of knowing whether a drug is working or whether it isn't working within a few cycles. If it is working, so much the better. If it isn't, you can always stop. I do want to say, however, that in the setting of early-stage disease, so in the adjuvant setting, in my mind there is not a role outside of a clinical trial for the use of either carboplatin or cisplatin as part of an adjuvant regimen. Adjuvant therapy isn't something that we should be making up on the fly. It's treatment that we should be taking from well-done prospective trials, and there simply have not been such trials in the adjuvant setting in triple-negative breast cancer.

DR. DANCY: Thank you, Dr. Winer. Dr. Carey, should we treat women with triple-negative breast cancer with adjuvant therapy at an earlier stage than for women with non-triple-negative breast cancer?

DR. CAREY: Yes and no. I think the question relates to when do we use chemotherapy specifically in the adjuvant setting, and, I think when you model the risk, decisions about adding chemotherapy to adjuvant treatment start with what is the baseline risk for the patient in terms of her risk of relapse and death. So, if you use, for example, adjuvant online modeling to try and estimate the risk to this patient of her cancer recurring and causing death, then triple-negative breast cancer, almost by definition, to get to the same reduced risk of relapse, you need to use chemotherapy at a lower stage simply because a hormone receptor-positive breast cancer patient has the benefit of endocrine therapy, which makes that first dent. I don't think the decision-making for triple-negative is any different from HER-2, and, in fact, I think the independent data regarding risk of relapse in the untreated setting is actually stronger for HER-2 breast cancer having a poorer prognosis than it is for triple negative. But here is the cautionary tale. I think there is a tendency to use the

relapse estimates in Adjuvant! Online as being distant metastatic risk, and it simply isn't. The way Adjuvant! Online was set up includes, particularly at those lower stages, a lot of local disease, including contralateral disease. So I think for triple negative, if you're using Adjuvant! Online, you should probably look at the mortality estimates. The 10-year mortality estimates are pretty mature for this particular group, because the risk of relapse tends to be earlier. You can use that to guide when the absolute benefit of chemotherapy is appropriate. My own tendency is to not use it in T1N0 tumors, for example, and then anything above that becomes a balanced discussion with the patient. Eric, do you have anything to add to that?

DR. WINER: I agree completely, and I think that in recent years there have been a number of people who have pushed for treatment, even in patients with the tiniest sub-wall tumors, 2- and 3-millimeter cancers in the setting of negative lymph nodes. While triple-negative cancers are biologically more aggressive, size still matters a lot. Those patients, as best I know, still have a fairly favorable prognosis, and you have to be very careful about adding therapy.

DR. DANCY: Dr. Winer, how does breast cancer stage affect the choice of chemotherapy regimen? We've sort of touched on that just a little bit.

DR. WINER: My threshold for giving what I would call a third-generation regimen, meaning an anthracycline- and taxane-containing regimen, is somewhat lower for patients who have triple-negative disease than for patients with ER-positive and HER-2-negative disease, where I'm generally less inclined to use chemotherapy at all in some patients and where I might be less willing to go with one of those third-generation regimens. In my mind, there are essentially two choices in terms of adjuvant therapy. You either give what I would call one of the simpler regimens—either A/C, T/C, or CMF—or you give an anthracycline-taxane-containing combination. For a patient with stage 1 triple-negative breast cancer, I'm quite comfortable giving one of the earlier-generation regimens: A/C, T/C, or CMF. For patients who have anything more than that, I tend to give an anthracycline/taxane combination. I know that there are people who would also give an anthracycline/taxane combination to a woman who has a 1.3-centimeter, node-

negative cancer. I can't argue with them, but I also think that one can think about doing a little less in that situation too.

DR. WINER: Lisa, thoughts?

DR. CAREY: No, I think that's appropriate. What I usually end up saying to the patient who is on the - - dilemma, they oftentimes have a very strong opinion themselves, and I usually say, listen, here is the range of reasonable for some of these things. A third-generation regimen can give them the absolute benefits, which is oftentimes on the order of just a percent or two and tell them what that entails. Then they can make that choice.

DR. WINER: Finally, if you're doing a sequential anthracycline/taxane-containing regimen, you can start with the anthracycline and you can see how the patient does and how she feels after getting four cycles of therapy and then make a decision.

MS. FRITZ: Thank you. Doctors, we do have another live question in cue. This question comes from a doctor with the Anchorage Oncology Center.

FEMALE VOICE: Hello, this is - - , and I actually was going to ask about the adjuvant therapy following Dr. Winer's comment on not to use platinum outside of clinical trials. I think you answered that just now so my question is for people with recurrent disease or metastatic disease when we do not have access to PARP inhibitors. What do you recommend outside of a clinical trial?

DR. CAREY: I have to say, and I'll let Eric speak to his own practice, but, outside of a clinical trial, I tend to use the same regimens across all the subtypes of cancer when I'm choosing chemotherapy. In an asymptomatic patient, I will tend to use sequential single agents. In a patient who is symptomatic or has rapid progression of visceral disease, I'll use combinations, either doublet chemotherapy or a bevacizumab-based combination. Otherwise, I don't know that I change the nature of the drugs that much. I may use a platinum drug, not first line, but I might move it up the food chain a little bit, but not a significant change over the general approach, which is very variable in terms of the patient. If they have pre-existing neuropathy, that's going to change the choices you have compared to a patient

who doesn't. Or, if she doesn't want to lose her hair, it becomes oftentimes a patient-specific choice, but the triple-negative part, if I'm going to chemotherapy, doesn't make a big difference to me.

DR. WINER: I agree entirely. We don't know that any one agent is better than another in triple-negative disease. Again, with the possible suggestion that maybe there is a little more activity of the platinum salts and I also wouldn't give carbo or cis as a first-line regimen outside of a trial. I would think about using it at some point in time. The other unfortunate thing about triple-negative metastatic breast cancer is one doesn't have an endless number of opportunities usually to give different regimens. If I remember right, in our own look at our data here at Dana-Farber, the median number of regimens that patients received was about three. Very few patients received a great many more than that. This is not a situation where we're running out of drugs that work in breast cancer. Unfortunately, we just don't have very effective drugs, particularly once you get beyond the first- or second-line setting.

DR. CAREY: The only thing I'm going to add is just to remind people that the platinum question is actually being addressed in a randomized trial in the neoadjuvant setting. If you are wanting to participate in this and you see a patient with at least a neoadjuvant appropriate tumor, in CALGB40603 patients receiving taxane with or without platinum, and it's also asking a bevacizumab question and then they move on to their anthracycline. Do keep that in mind. It's available through the CTSU.

DR. WINER: In terms of the PARP inhibitors, we don't have any that are commercially available. But the other issue is, at least at the moment, other than in patients who have BRCA1 or BRCA2 mutations, we don't know that these agents will add in sporadic triple-negative disease. I think it's still an open question, and I think it's one that will continue to be pursued.

FEMALE VOICE: Thank you.

DR. DANCY: Dr. Winer, continuing with the discussion about what one can do when treatments fail them, what new information is available regarding non-pharmacologic treatment or therapy for women with triple-negative breast cancer? Can

you speak about lifestyle changes, diet, body mass index, exercise, or stress reduction? Are these things that you counsel your patients on?

DR. WINER: In the adjuvant setting, I could imagine that lifestyle change, specifically weight loss and exercise, might, and I emphasize might, play a role in reducing the risk of recurrence. In the CALGB, we are in the process of developing a study not specifically for patients with triple-negative breast cancer, but triple-negative breast cancer patients will be included looking at a lifestyle intervention. In the metastatic setting, it is very hard for me to imagine that a lifestyle intervention is going to have a dramatic impact on the natural history of the disease, with the exception that I think anything someone can do to make themselves feel better—to be psychologically in better shape, to feel that much better adjusted, that much more at peace—may allow them to do a little bit better with their treatment.

DR. CAREY: I'm going to add something because I think Eric has hit it exactly on the head. The caution here is that we really don't know what the impacts are of lifestyle changes. They can make people feel better, and I think a healthy lifestyle is appropriate all the time. But I also think we put women in a difficult position if we suggest that whether their cancer progresses or not or recurs or not is their responsibility. To do so really would be doing so in the absence of evidence that that is an okay thing to do. To be honest, I don't think it's fair to tell a woman or to imply that whether a cancer recurs or not is based on whether she ate birthday cake with her child. I'm always a little bit troubled by the implication that the responsibility for cancer behavior is on the woman herself.

DR. WINER: I agree.

DR. DANCY: Thank you. Dr. Carey, I have another question for you. Can you please comment on the relationship between Ki67 and prognosis?

DR. CAREY: Ki67 is a biomarker of proliferation, and it's a good one. It's not a perfect one, but it's pretty good. It co-varies. In truth, the question about any biomarker is does it tell you something you don't already know? I don't necessarily think Ki67 is a particularly helpful marker in triple-negative cancers, simply because these are typically

high-grade lesions and they generally have a high-proliferative index no matter what way you use to measure it. I'm unaware of any data that suggest that, within this subtype, Ki67 adds independent data regarding prognosis or chemotherapy sensitivity, which is another way that people have suggested using it. So, I don't use it as a particularly valuable thing. We note it when it comes as part of the pathology report, but it doesn't change the tumor's behavior in a way that I'm aware of.

DR. DANCY: Thank you. Dr. Winer, if I could ask you to share your thoughts about the MUC1 vaccine therapy for triple-negative breast cancer?

DR. WINER: I There are many vaccines that have been tested in very early-phase trials. Is there a phase 3 trial of this going on?

DR. CAREY: There are MUC1 vaccines that have been developed and actually have been tested in some later-phase studies, and I think the current findings are encouraging but not definitive within any kind of subtype of breast cancer, with MUC1 being a commonly encountered lipoprotein on breast cancer and an obvious target. In truth, the vaccine, sort of the immunologic approaches to breast cancer treatment, are very promising, but they are technically quite challenging. These strategies haven't been as successful as I think people thought a few years ago, not because they won't work but because they're harder to do than people appreciated. Your immune system is pretty good at what it does, and the issue of tolerance is a very real one.

I think if there's a trial available, I've personally put patients on vaccine trials when they're available and appropriate, but certainly it's not something that I would do off of a trial even if it was offered. I'm not aware of any being offered off trials, but that's the state as I know it.

DR. WINER: The role of immune-based therapies is still being explored. I think there's more enthusiasm for them now than 5 or 10 years ago, but I think it's going to take very different approaches than we've taken in the past to have a real impact.

DR. DANCY: Let's see how you feel about this question. I will

direct it to Dr. Carey. Is more radical versus less radical surgery a benefit in managing triple-negative breast cancer?

DR. CAREY: Not that we're aware of. I have to say, in general, I'm not aware of any data that suggest that the risk of local recurrence and the risk of distant recurrence diverge to a significant degree, meaning if a tumor type has a higher risk of distant, it also tends to have a higher risk of local. However, much of that is regional-type relapses and doesn't really have implications in terms of management of the primary tumor and surgical decisions. The one caveat to that is in patients who have triple-negative breast cancer in the setting of a BRCA1 mutation. In those patients it is not necessarily more or less radical, but certainly it is appropriate to discuss with the patient whether she wants to take a preventive approach because they are at higher risk for developing a second cancer. But, in terms of lumpectomy versus mastectomy, I'm not aware of any reason to make different choices from the standpoint of that decision. About the recent ACOSOG Z0011 data regarding the omission of axillary dissection in patients with lumpectomy and a limited number of sentinel nodes, I don't think subtype necessarily plays a big role there either.

DR. DANCY: Dr. Winer, this question asks for you to comment on the role of triple-negative breast cancer follow-up of brain metastasis after radiotherapy treatment.

DR. WINER: I think this requires a little bit of background. It has turned out, and I don't think this is something that any of us appreciated 10 or 15 years ago, that brain metastasis in the setting of metastatic breast cancer predominantly, not exclusively, arises in two settings: in patients with HER-2-positive disease and in patients with triple-negative disease. Again, not that it never happens and that brain metastases never occur in patients with ER-positive, HER-2-negative disease, but they don't with any real frequency. In the setting of HER-2-positive disease, brain metastases for some patients become a dominant clinical problem, largely because the patients are generally doing well for an extended period of time with their systemic disease and they unfortunately develop progression after their cranial radiotherapy. In the setting of triple-negative breast cancer, unfortunately,

this is less of a problem because oftentimes women succumb to their distant disease, distant non-CNS disease, before their CNS disease progresses after radiotherapy. There are a limited number of patients who will receive a course of radiotherapy, either stereotactic radiosurgery or whole-brain radiotherapy, who will develop progression after that treatment and who are otherwise still doing reasonably well. Typically, that is progression that would arise when other disease is also changing.

Dr. Carey's group has a study that is ongoing that is being led by Carrie Anders [phonetic] and being done at both the University of North Carolina at Chapel Hill and in the Translational Breast Cancer Research Consortium. It is looking at iniparib in combination with CPT-11, if I remember correctly, for patients who have progression of their CNS disease after radiotherapy. There are patients who have been enrolled in that trial, actually quite a number of patients, so we will begin to get some sense as to the activity of this regimen in that setting. In terms of the specific question, which is what is the appropriate follow-up, clearly in somebody who has progressive CNS symptoms, it makes sense to re-image the brain. Outside of symptoms, I think the follow-up is a bit up in the air. There are some who would recommend repeating some type of CNS imaging several months after initial radiation, and there are others who would again favor waiting until there's any kind of symptomatic change. I think it's really got to be based on the patient and what is going on with her systemic disease and what you feel like the options would be in terms of treatment approaches. Lisa?

DR. CAREY: I agree. I think once a patient has had brain mets, some sort of serial imaging is probably a reasonable thing to do simply because reversal of symptoms sometimes can be a little bit trickier, and sometimes there are options, either surgically or radiosurgically, that are local and can be employed outside of systemic. I do think, you know, we're excited about the iniparib/irinotecan trial, which is broadly open around the country. It is a reasonable thing to consider for patients that someone would like to refer.

DR. WINER: The whole follow-up issue is one that you really have to tailor to the patient, and it's going to be very different in that patient who otherwise is doing well, where you're concerned about developing symptoms, versus

the patient who has a very heavy burden of disease outside of the CNS and who is struggling with that.

DR. CAREY: Yes, absolutely.

MS. FRITZ: Thank you, doctors. We again go to Anchorage Oncology Center for an additional live question.

FEMALE VOICE: Thank you. Could I just follow up on what was mentioned just now? Did I understand, and maybe I'm wrong, are you recommending PCI for patients with triple-negative or HER-2-positive tumors if they are doing well otherwise?

DR. WINER: No, not PCI.

FEMALE VOICE: Okay.

DR. WINER: PCI, for anyone who isn't familiar with the term, prophylactic cranial irradiation, and I don't think either of us would recommend that for any patient for multiple reasons, including the fact that we don't know how effective it would be, and it's clearly an approach with some amount of toxicity. I think in the patient who has had brain metastases, most of the time in the setting of triple-negative breast cancer and HER-2-positive disease, it's often multiple brain metastases and many of these patients get whole-brain radiotherapy for that.

FEMALE VOICE: Thank you. I was actually going to ask on the pathology, once the pathologist diagnoses triple-negative, what kind of molecular markers do you recommend for somebody in the community if the patient is not on a clinical trial?

DR. CAREY: I'm not aware of any that necessarily will help you make decisions. We don't obtain anything else.

DR. WINER: We don't either, although Lisa's colleague Chuck Peru and others have written and talked about this claudin-low versus more classical basal-like phenotype or genotype and phenotype potentially outside of a clinical trial or some research study. I don't know of any value in terms of pursuing that further. I think that will change because I think we all believe that triple-negative breast cancer isn't one disease entity. It's probably several, but we just don't know how to apply it in practice.

DR. CAREY: What's out there now are an increasing number of trials broadly across breast cancer patients, where they

are looking to enrich using particular molecular markers, PI3 kinase mutations, and EGFR amplification. There's a number of these sorts of things. We'll be seeing more and more of them, and getting your patients screened for some of these kinds of novel targeted treatments I think is going to be the way of the future, and you should be open to that. One of the translational breast cancer research consortium studies that's open right now in ER-negative breast cancer actually screens for the androgen receptor as a potential therapeutic target. I think we're very hopeful that these will be the way of the future.

FEMALE VOICE: Thank you.

MS. FRITZ: Thank you. Our next question comes from a doctor with Island Oncology/Hematology.

FEMALE VOICE: I'm just curious to know, for example, in HER-2-positive disease we say that doxorubicin (adriamycin) seems to work better. Is there a chemotherapeutic agent that we should prefer in triple negative as first-line or can we choose whatever we want.

DR. WINER: I think you can choose whatever you want. I don't think that there is a preferred agent. There are data that would say that taxanes work better and data that would say that they don't work as well. You can say that about almost every agent. For a while a few years ago, there was a relatively low level of enthusiasm for capecitabine in the setting of triple-negative breast cancer because of a number of studies where there was the suggestion, and I emphasize suggestion, that it might be less effective in that setting, but then more recently there have been some papers indicating clear activity. I think that you really don't need to make different decisions about chemotherapy choice for a patient with triple-negative disease versus another patient with breast cancer.

FEMALE VOICE: Also, one more thing, TC, docetaxel cyclophosphamide, versus AC, they say it's almost the same in early-stage breast cancer, not talking about triple negative in specific. Does that hold the same rule for this type also?

DR. WINER: There were a relatively limited number of patients with triple-negative breast cancer in the TC versus AC study. The study was small. It has never been replicated,

and I am perhaps in the minority but I am not convinced that we know that TC is absolutely as good as any other regimen. It's a regimen that does have a moderate amount of toxicity. I think if you want to use it, it's probably fine, but I would not say that it's a preferred regimen. I know that there are others who disagree and point to that US oncology study that compared the two regimens where TC actually looked like it was a little bit better, and they're quick to say this is the preferred regimen. I don't agree with that.

FEMALE VOICE: Well, if the patient has cardiac toxicity, then--

DR. WINER: [interposing] Absolutely, and I think that if for whatever reasons you feel strongly about wanting to use TC, you're unlikely to do a patient harm. I just don't know that it's any better than anything else.

DR. CAREY: I think it's a very reasonable regimen. I frequently use it, particularly in patients with cardiac toxicity, but realize that the NSABP study—including four cycles of TAC, which essentially is just TC with adria added, the doses are essentially the same—did not suggest that it was even as good as a sequential ACT regimen. We have to be cautious in assigning its line. I think it's a good regimen. I don't personally think it's likely to be as good as a really modern third-generation regimen.

DR. WINER: The one warning is don't make the extrapolation, which some people are making at the moment, that anthracyclines only have a role for HER-2-positive disease, that they don't have a role for triple-negative disease, and that therefore four cycles or even six cycles of TC is are the preferred regimen for triple-negative disease. I think for a patient other than somebody with very early-stage triple-negative disease, the preferred regimen is one of the anthracycline/taxane-containing combinations and probably preferably a sequential regimen, since those appear to be a little bit more active—an anthracycline-containing regimen like AC or FEC followed by a taxane.

MS. FRITZ: Our final question comes from a nurse case manager with Blue Cross/Blue Shield.

FEMALE VOICE: I wanted to see if there are any clinical trials out there for someone who has a residual tumor after chemo and surgery with triple-negative breast cancer.

DR. WINER: Lisa, you want to talk about ABCD?

DR. CAREY: I'll let you do it. You're giving the status update.

DR. WINER: All right, this is my dream question because you allow me to advertise a clinical trial.

FEMALE VOICE: I know your clinical trial. Is there anything else besides that, not that I don't like it. I just wanted to know because I'm from Massachusetts, so I obviously know the Massachusetts one. I was just wondering if there's anything else out there.

DR. WINER: I don't think there's much else out there. So the clinical trial to which you're referring, just so that other people are familiar with it, is a trial for patients who have received preoperative chemotherapy and in the setting of triple-negative breast cancer have residual disease at the time of surgery. It randomizes patients in two ways. It randomizes them to low-dose chemotherapy with a metronomic regimen of cyclophosphamide (Cytoxan) and methotrexate with bevacizumab or no therapy. Then there's a second randomization to a lifestyle intervention, which is both diet and exercise versus no lifestyle intervention. I'm not aware of other randomized studies in the post-neoadjuvant setting, and there aren't many other studies in general in that setting.

FEMALE VOICE: Thank you very much.

DR. WINER: Lisa, do you know of other studies?

DR. CAREY: I don't. The NSABP was working on a concept, but they've had some struggles with figuring out what drug to be testing in this setting. It's a thorny one. It's a great clinical scenario and one where we would like to test things but it's not so easy to do.

DR. WINER: It's possible that Cathy Miller in Indiana actually has a small study of Veliparib, which is one of the PARP inhibitors; ABT-888 is [phonetic] the other name for the drug, possibly in combination with something else in this setting, but it's a small trial.

FEMALE VOICE: Okay.

DR. WINER: But certainly one that would, if a patient lived in that general region, be appropriate.

FEMALE VOICE: Thank you.

MS. FRITZ: Thank you for your questions and thank you doctors. This concludes today's Triple-Negative Breast Cancer Audio Conference, which has been sponsored by Med-IQ and supported by an educational grant from sanofi-aventis U.S. Access additional complimentary materials as part of this series, including a CME research and findings paper and patient educational handouts, at www.med-IQ.com/A519. Thank you all for your time and commitment to improving TNBC patient care.