

# Triple-Negative Breast Cancer: Current Approaches and New Frontiers **CME**

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## Target Audience

This activity is intended for medical, surgical, and radiation oncologists, nurses, ob/gyns, and other healthcare professionals who care for patients with breast cancer.

## Goal

The goal of this activity is to educate clinicians about the classification, incidence, special challenges, current standard treatment, and potential emerging therapies for patients with triple-negative breast cancer.

## Learning Objectives

Upon completion of this activity, participants will be able to:

1. Distinguish between basal-like breast cancer and triple-negative breast cancer, using both laboratory and clinical definitions
2. Describe current standard best practices for treatment of patients with triple-negative breast cancer, as well as novel approaches under investigation

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Eric P. Winer, MD; Lisa A. Carey, MD; George W. Sledge, Jr, MD; Elizabeth S. Frank, EDM  
Available As: [Slides/Video](#) | [Slides/Transcript](#)

### Triple-Negative Breast Cancer: Current Approaches & New Frontiers (Slides With Video)

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**Triple-Negative Breast Cancer: Current Approaches & New Frontiers (Slides With Transcript)**

<p><b>Triple-Negative Breast Cancer: Current Approaches and New Frontiers</b></p> 	<p><b>Eric P. Winer, MD-moderator</b> Chief Scientific Advisor Susan G. Komen for the Cure Professor of Medicine Harvard Medical School Director, Breast Oncology Center Dana-Farber Cancer Institute Boston, Massachusetts</p>
	<p><b>Lisa A. Carey, MD</b> Associate Professor University of North Carolina, Chapel Hill Medical Director UNC Breast Center, University of North Carolina School of Medicine Chapel Hill, North Carolina</p>
	<p><b>George Sledge, Jr, MD</b> Scientific Advisor Susan G. Komen for the Cure Ballé-Lantero Professor of Oncology, Indiana University School of Medicine Indianapolis, Indiana</p>
	<p><b>Elizabeth Frank</b> Patient Advocate Susan G. Komen for the Cure Dana-Farber Harvard Cancer Center Boston, Massachusetts</p>

**Slide 1.**

**Eric P. Winer, MD:** Hello. I am Dr. Eric Winer, Chief Scientific Advisor to Susan G. Komen for the Cure, Professor of Medicine at Harvard Medical School in Boston, and Chief of the Division of Women's Cancers at the Dana Farber Cancer Institute. I am pleased to be joined by a number of colleagues today. First is Dr. Lisa Carey, Associate Professor of Hematology/Oncology and Medical Director of the Breast Program at the University of North Carolina in Chapel Hill. Dr. George Sledge is Ballé-Lantero Professor of Oncology at Indiana University School of Medicine in Indianapolis. And finally, Liz Frank, Patient Advocate at Dana Farber Harvard Cancer Center in Boston, Massachusetts, and I might also add that Liz is a breast cancer survivor and has a *BRCA1* mutation. I'd like to welcome you all to this Spotlight panel discussion entitled, "Triple-Negative Breast Cancer, Current Approaches and New Frontiers."

## Educational Goals

- To review the biology of triple-negative breast cancer, with particular focus on molecular characteristics that may be exploited as therapeutic targets
- To discuss current and emerging treatment options

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### Slide 2.

The educational goals of today's program are to review the biology of triple-negative breast cancer with particular focus on molecular characteristics that may be exploited as therapeutic targets and to discuss current and emerging diagnostic and treatment options. We're going to have a very free-flowing discussion touching on a whole range of different topics.

## What Is Triple-Negative Breast Cancer?

### Triple-Negative Breast Cancer: *Introduction*

- Triple-negative: 15% of all cases of breast cancer
- Hormone-positive
  - Endocrine therapies (tamoxifen, aromatase inhibitors)
- HER-2-positive
  - Trastuzumab; lapatinib; others
- Triple-negative
  - Surgery
  - Radiation
  - Systemic chemotherapy
  - Targeted therapies??

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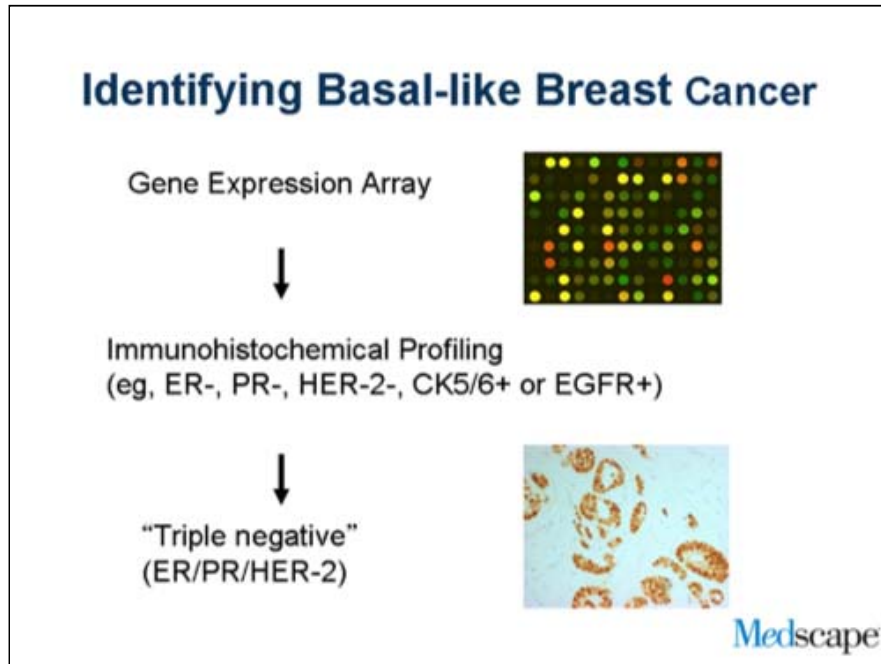
### Slide 3.

Although triple-negative breast cancer represents only about 15% of all cases of breast cancer in the United States, and this may differ in other parts of the world, it's responsible for a disproportionate number of breast cancer deaths and is also responsible for a disproportionate number of cases in young women with breast cancer. The use of endocrine therapies for women who have hormone-receptor- positive breast cancer plays a major role and makes a major difference in decreasing recurrences and controlling breast cancer in those women who have advanced breast cancer. In women who have HER-2 positive breast cancer, we have

trastuzumab and, more recently, lapatinib and potentially a whole range of other agents that will be available in the years ahead to help control the disease, and for many women, to help cure the disease.

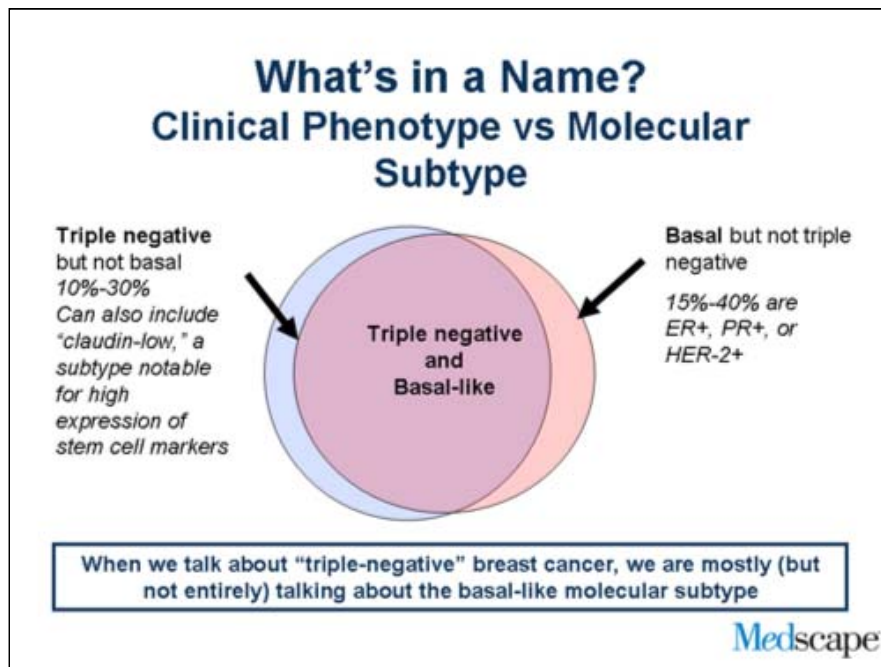
For those women with triple-negative breast cancer, we have surgery, radiation therapy, and chemotherapy, but we are still in search of optimal targeted therapies, and those are therapies we need in short order.

So why don't we start with some basic definitions because there is often a lot of confusion about definitions. I am going to start with Lisa and ask if you can talk a little bit about the difference between what is called triple-negative breast cancer and what is often called basal-like breast cancer. These terms are frequently used interchangeably. Even when people give lectures they go back and forth between these 2 terms. Is there a difference? How much overlap is there? What is the term we should be using?



**Slide 4.**

**Lisa Carey, MD:** The term depends on the circumstance. So we'll start with the basal-like breast cancer subtype, which is one of the molecularly defined subtypes. The ability to look across the entire genetic component of a tumor has allowed us to see that there are several different subtypes of breast cancer. One of them is this basal-like subtype, which has very unique biologic characteristics. That definition depends on being able to do a gene expression assay, so scientifically it's a pretty rigorously defined entity but it isn't something you have in the clinic. The basal-like subtype on a molecular level is characterized by low expression of hormone receptor-related genes, so that would be ER [estrogen receptor] and PR [progesterone receptor], as well as all the other genes that go along with them. Low expression of HER-2-related genes, and that's where the triple-negative part comes from because typically these tumors are, on clinical assays, ER-negative, PR-negative, and HER-2-negative. There are a whole bunch of other genetic characteristics that we don't have any assays for in the clinic but because of that tendency for these tumors to be ER-, PR-, and HER-2-negative, there is a big overlap with triple-negative breast cancer.



**Slide 5.**

In truth, if you look at triple-negative breast cancer and you are able to do arrays on them, about 80% of them will be basal-like, and by the same token if you look at basal-like, about 80% of them will be triple-negative.

**Dr. Winer:** So there is a lot of overlap.

**Dr. Carey:** There is a lot of overlap but it's not a perfect overlap, so whenever we use triple-negative breast cancer when we're trying to get to the biology of basal-like breast cancer, we're by definition introducing some inaccuracy and some misclassification that we really have to acknowledge as we do our trials.

**Dr. Winer:** Although clinically at the moment, we don't know that there is necessarily a big difference.

**Dr. Carey:** We don't. We actually don't know that and that's a very good point. We suspect there are differences but they may be subtle and they may only be important once you get to some of the more targeted therapies and things that are investigational.

## Who Gets Triple-Negative Breast Cancer?

**Dr. Winer:** Right. And George, who gets triple-negative breast cancer?

## Incidence of Triple-Negative Breast Cancer: United States

- Triple-negative breast cancer is more common in
  - Young women
  - Women who are carriers of *BRCA1* mutations
  - African-American women

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### Slide 6.

**George Sledge, Jr., MD:** Triple-negative breast cancer is more common in younger women. It's more common in women who have tumors that are *BRCA1* mutations. We know that the younger African-American women have a significantly increased likelihood of having triple-negative breast cancer, and that has been a source of great fascination among researchers. Is this a genetic something that dates back millennia or longer? Or is this something that is epidemiologic and related to the environment in which these women grow up?

**Dr. Winer:** And I guess although some studies have suggested that it's young African-American women, there are also studies that have suggested that African Americans in the United States across the board have higher rates of triple-negative breast cancer. Is that your understanding Lisa, as well?

## High Risk for Triple-Negative Breast Cancer: United States

- Young, premenopausal women
- African American women

**Highest Risk = Young AND African American**

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### Slide 7.


**Dr. Carey:** Yes. In some of the early studies, clearly it was the premenopausal African-American women who had the highest risk.

When those studies, including one that came from North Carolina, were expanded and they had a bigger sample size, it became clear that the risk is being young and being African American, which means that the highest risk is being young and African American.

**Dr. Winer:** And I want to get to patient perceptions of triple-negative breast cancer in a minute, but before we do just a quick question about the rest of the world. So we've been talking about the United States, we've been talking about young women, we've been talking about African-American women, but there is this suggestion that in other parts of the world there is triple-negative breast cancer that arises perhaps more commonly than we see in the United States, although I think we all have to recognize that there are problems with the way records are kept elsewhere. So what is the best thinking about that? George, Lisa, either of you?

## Triple-Negative Breast Cancer: Worldwide

- > 50% of African women with breast cancer have triple-negative disease
  - Data collection?
  - Longevity?
  - Comorbidities?
  - Screening?
  - Therapy?



**Slide 8.**

**Dr. Carey:** I think it is really important for people to remember that anybody can get any subtype of breast cancer. There isn't a group of patients that exclusively get one kind or the other, including *BRCA1* mutation. It occurs in that setting and most but certainly not all will get this basal-like subtype. The best characterized group outside of the United States for triple-negative breast cancer of course is the African studies that suggest that more than half of women in Africa who get breast cancer have this triple-negative subtype. The problem is the one you were alluding to, which is if you have imperfect collection of data and you have places where people's longevity is different and their tendency to get other diseases or die at earlier ages and there is not much screening and therapy -- you know then you start introducing a whole lot of things that can affect the proportion of people who have a particular disease where it isn't necessarily reflecting a population-based estimate the way it is in the US studies.

## Race vs Environment?

### Genetics

- Clues
  - *BRCA1*
  - Young patients
  - Specific ethnicity (African studies)

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### Slide 9.

**Dr. Winer:** And just 1 last question before getting to the patient perspective. George what is your sense, is this about race or is this about environment?

**Dr. Sledge:** I suspect that we are dealing to a significant degree with genetics rather than environment here. That's a bias and perhaps not a bias that everyone shares, but certainly the *BRCA1* mutation story would point us in that direction. The fact that it's younger women would point us in that direction. In general, genetic diseases are more common in younger patients and the fact that it's related to a particular ethnicity certainly would suggest that the African studies, as opposed to the African-American studies, are indeed suggesting a higher risk of triple-negative breast cancer.

## Patient Perspectives

**Dr. Winer:** So Liz, 10 or 15 years ago, and I have been around long enough to have been a breast cancer doctor 10 and 15 and 20 years ago, we talked about breast cancer. We didn't talk about the subtypes of breast cancer. We knew there was a difference between ER-positive and ER-negative breast cancer (sort of), but talking about HER-2-positive disease and ER-positive disease and triple-negative disease was something that just wasn't part of our language. So now when patients hear about these subtypes of breast cancer and they hear about triple-negative breast cancer, my sense is that this is a term that often strikes fear in peoples' hearts, but what is your sense?

## Triple-Negative Breast Cancer: *Patient Perceptions*

- Traumatic diagnosis
- The "bad" breast cancer
- The most dismal prognosis
- Less hope of good therapy

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### Slide 10.

**Elizabeth S. Frank, EDA:** I think it's a very, very traumatic diagnosis to hear. I think people associate -- if they know anything about breast cancer and I think people associate death with breast cancer to begin with. But if they are a little bit knowledgeable about breast cancer, then the thing that I hear as a survivor is "I have the 'bad' breast cancer." So I think it's really thought about as the cancer with the most dismal diagnosis and the one with less hope of a really good therapy. So it's a tough diagnosis to get right now.

**Dr. Winer:** Some number of women with triple-negative breast cancer, a greater number of women with triple-negative breast cancer than other subtypes, do have these inherited abnormalities like *BRCA1* mutations, which then raise implications in terms of family members and maybe you could comment on that.

## Inherited Abnormalities and Family Matters

- Siblings
  - What about family members who don't want to know?
- Children
  - When and what to tell them?

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### Slide 11.

**Ms. Frank:** Actually I think that's a really interesting question because those of us who are *BRCA1*, one of the things that we think about is what do we do about our children, and what do we do about our sisters and our brothers? We may have relatives that really

don't want to hear about some kind of a genetic mutation and I think that can cause real problems within a family. Then there really is a rather confusing message to our children. What do you tell them, when do you tell them, and what do they need to know? So I think these are all issues that we think about.

## Treatment

**Dr. Winer:** And later maybe we'll have a chance to get into something about screening but at the moment I want to return to treatment because we know that this seems to be a diagnosis that is more feared, but I guess the other question is, should it be and what do we know about treatment for women with newly diagnosed triple-negative breast cancers?

**Newly Diagnosed Early-Stage  
Triple-Negative Breast Cancer:  
*Treatment***

- Surgery ± radiation therapy
- Adjuvant systemic cytotoxic therapy
  - Taxanes
  - Dose-dense or weekly regimens
- Novel targeted agents?



### Slide 12.

And first I think we should focus on women who have early-stage breast cancer and by that I mean stage I or stage II breast cancer where the breast cancer is clearly operable. A woman is going to have either a lumpectomy and radiation or a mastectomy and she is worried that the cancer is potentially going to come back. What do we know about the effectiveness of treatment in that setting? So George, do you want to start there?

**Dr. Sledge:** The first thing to say is that treatment can be very effective and treatment, as in all stages of breast cancer, depends on biologic factors but it also depends on how large is the tumor, whether it has involved the lymph nodes, and those will determine prognosis for many women. But in terms of local control of the disease, and that's to say treatment such as lumpectomy and radiation, breast-conserving surgery, and mastectomy, in general, we offer similar options to a woman with a triple-negative breast cancer as we do to any other woman. And local regional therapy is, of course, incredibly important for those women. Similarly, when we look at women in terms of systemic disease, the prevention of overt metastatic disease through the use of adjuvant systemic therapy, we have clear and compelling evidence that the recent generation's improvement in chemotherapy have been improvements for triple-negative breast cancer. And indeed if any group has benefited the most from advances in chemotherapy, it has probably been the triple-negative population. For instance, the addition of the taxanes in the 1990s, and the use of dose-dense or weekly chemotherapies in this decade certainly have improved both disease-free and overall survival for patients with triple-negative breast cancer. And I think there is also, as I'm sure we'll get to in a few minutes, a growing sense that we're going to have novel targeted agents that may be of benefit to these women, both in the advanced and in the local disease setting.

## Standard Adjuvant Treatment for Triple-Negative Breast Cancer - Stage II (*not investigational*)

- Anthracycline + taxane
  - Dose-dense regimen
  - Weekly regimen

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### Slide 13.

**Dr. Winer:** Outside of a clinical trial, because this is very important for women with triple-negative breast cancers to know and for their doctors to know, a woman is not participating in a clinical trial and let's say she has stage II breast cancer with a 2-cm cancer and 1 positive lymph node, what is the standard adjuvant treatment that she should receive?

**Dr. Sledge:** Well in my clinic, certainly that patient would receive anthracycline and taxane-based chemotherapy.

**Dr. Winer:** And Lisa?

**Dr. Carey:** The same.

**Dr. Winer:** I think it's fair to say that is really true across the country in terms of that being the standard treatment and whether it's one anthracycline and taxane-based regimen vs another, it probably doesn't make a huge difference to any of us. We each have our favorite perhaps in terms of the regimen that we're most comfortable giving, but we don't know that one is better than the other. George?

**Dr. Sledge:** I would qualify that a little, which is to say that we certainly know that regimens that involve either dose-dense chemotherapies or weekly chemotherapies, we know from large well-conducted prospective randomized trials give an improvement in disease-free and overall survival.

**Dr. Winer:** True. So I was assuming that everyone was up to speed there, but in terms of exactly how you give it and which agent may be a little less critical. But then there are newer agents that have been talked about, agents like the platinums. In any given week I feel like there are at least 1 or 2 e-mails that come in either from a patient or from a doctor describing a patient with newly diagnosed triple-negative breast cancer saying "don't you think I should give this patient Taxol [paclitaxel] and carboplatin or Taxotere [docetaxel] and cisplatin" or some such thing... What do you tell those people?

## Treatment for Triple-Negative Breast Cancer: *Common Fallacies*

- Other drugs/regimens (ie, other than anthracyclines and taxanes) are more effective
- Current regimens (eg, anthracyclines, taxanes) are ineffective
- Prevention strategies are not effective for individuals with inherited mutations

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### Slide 14.

**Dr. Carey:** I think we're victims of our own successes in some respects. There has been so much research into ways that we might get better at this and we talk about it so much that there is an assumption that we know of something better than the drugs that we have, and an assumption the drugs we have don't work. And I think those are 2 fallacies that it's important to take care of because it is true that the modern chemotherapies, this is not a dismal disease, modern adjuvant therapy is very effective in reducing the risk of it coming back. And many of these patients are cured, just as they are with all the other subtypes. Moreover you're talking about the people who have inherited risks, prevention strategies work for this and work very well. So in early breast cancer, you know using standard approaches is entirely appropriate. It works and if you don't give standard approaches you may, in fact, do more harm than good by introducing a novel therapy that we don't know has a role to play.

## Screening and Access

**Ms. Frank:** Building on what you were saying Lisa, the thing that I think about is screening does help but one of the things we want to make sure of is that everybody has access to screening and we know that's not true.

## Screening and Access: *Issues and Barriers*

- Age – women at highest risk may be too young for standard screening
- Access to screening/treatment may be difficult geographically, financially, logistically


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**Slide 15.**

**Dr. Winer:** That absolutely is true and in particular we know that some of the women who are at greatest risk of developing triple-negative breast cancer, young African-American women, may be women who, number 1 aren't generally screened because they're not old enough to be screened in many situations, although ideally they should be getting clinical breast examinations. And beyond that, they may not have access even if they are of an age where they would be screened, so they are in their early 40s or some such thing. They may not have access to get screened and that is clearly something that is very important.

### Effect of Triple-Negative Status on Treatment Decisions

- ER/PR-positive or HER-2-positive disease — much benefit will be derived from endocrine therapies or trastuzumab, respectively
  - Less benefit with chemotherapy
  
- Triple-negative disease — *most benefit with chemotherapy*
  - Third-generation regimen (anthracycline + taxane)



**Slide 16.**

In terms of decision-making about chemotherapy, is your decision-making different in a patient with triple-negative breast cancer than in a patient with ER- positive breast cancer? Say you are faced with a woman who has stage I triple-negative breast cancer as opposed to stage I ER-positive breast cancer. How does that affect the chemotherapy choices?

**Dr. Carey:** It's all about risk, right? So if you have a certain risk of a cancer recurring and you know that your endocrine therapy is already going to cut that in half, then the chemotherapy is less important and the benefit is lower. In triple-negative [disease], since everything that we have relies on the chemotherapy benefit, then the benefit and the importance of it is greater for any particular stage of tumor.

**Dr. Winer:** So it's fair to say that your threshold for using a third-generation regimen, one of these more intensive anthracycline/taxane regimens, your threshold for using that is somewhat lower in a patient with triple-negative disease than in perhaps the ER-positive setting. So if you have somebody with stage I triple-negative breast cancer, you are going to be a little bit more inclined to add more chemotherapy.

**Dr. Carey:** Right, because that's what you have compared to either the ER-positive or the HER-2 positive group.

## Triple-Negative Breast Cancer: *Burden of Disease*

To undergo modern, intensive, weekly adjuvant chemotherapy regimens, patients need...

- Flexible employment policies and hours
- Transportation
- Physical mobility
- Financial arrangements (health insurance)
- Childcare and/or other family arrangements

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### Slide 17.

**Ms. Frank:** So you have a therapy that involves a little more support, right? You have to have a patient who has access and ability to get to a hospital weekly, who can financially afford it, and who might have small children. So I think that the burden of the disease actually is pretty high, or can be pretty high on a population that is going to have a hard time affording a really high cancer burden.

**Dr. Winer:** That's clearly true, and this is, of course, where advocacy can come in and some of the organizations can try to help people get through all of this. The 4 of us were all at a retreat earlier this week, or a think tank that was sponsored jointly by the Triple-Negative Breast Cancer Foundation and Komen [Susan G. Komen for the Cure®]. And I think what was remarkable about that is it was the second retreat we've had. Lots of ideas were shared and 10 years ago we never talked about triple-negative breast cancer. The very idea that we're sitting around talking about it hopefully means that there will be many more answers in the years ahead. But to get there we need trials, and maybe we can talk just a little bit before we close about some of the exciting new agents that are being looked at here.

## Future Directions

Of course it's easier to talk about exciting agents when we feel like we know more about biology and we're also still struggling to learn more about the biology of triple-negative breast cancer. Lisa, maybe you can start and tell us a little bit about some of the clues in terms of the biology of triple-negative breast cancer, and George can talk a little bit about a few of the trials.

## Biologic Clues to Novel Treatment Approaches for Triple-Negative Breast Cancer

- Platinum compounds
  - Target DNA repair pathways?
  - Particularly effective for *BRCA1* disease (preclinical data)
- More genomic instability in these tumors

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### Slide 18.

**Dr. Carey:** The first question has to do with the platinum agents, which of course is chemotherapy. We tend to think we have smart drugs and then we think of chemo and I guess by default those become dumb drugs. But in reality, chemotherapy may be more targeted than we give it credit for. The preclinical studies and studies largely from *BRCA1* mutations show that platinum drugs and DNA-damaging drugs in fact can be very effective if you lose certain DNA repair pathways and *BRCA1* loss actually does augment sensitivity to DNA-damaging agents in the preclinical sense. There are some clinical data in support of this, again largely in people who actually carry a mutation -- an inherited mutation of *BRCA1*. Because of that association between basal-like breast cancer and women who carry a *BRCA1* mutation, there is an assumption that *BRCA1* is somehow abnormal even in sporadic noninherited forms of basal-like breast cancer. But frankly that hasn't been proven yet, which is why we are all cautious about the assumptions we make about these drugs. But that's why the platinum agents have become something that is being tested regularly as a backbone for these trials.

**Dr. Winer:** And again, *BRCA1* is involved in DNA repair.

**Dr. Carey:** Yes, as is *BRCA2*.

**Dr. Winer:** As is *BRCA2* and you lose that second copy of *BRCA1* in a cancer that arises for the most part in a woman with a *BRCA1* mutation and then you lose that ability to repair DNA, making drugs like the platinum theoretically that much more effective.

**Dr. Carey:** Exactly.

**Dr. Winer:** But again more theory than practice, particularly outside of the setting of people with mutations.

**Dr. Carey:** Right and there are similarities. There is research that suggests that there are some very real similarities between *BRCA1*-associated basal-like breast cancer and sporadic basal-like breast cancer but it's not at all a settled thing that the *BRCA1* pathway itself is deranged in a way that can be targeted with these drugs, but that's going to be tested.

**Dr. Winer:** I guess it's fair to mention that compared to other breast cancers, including HER-2-positive breast cancers and high-grade ER-positive breast cancers, there is just generally more genomic instability in these cancers. There is chromosome loss, there is chromosome gain, the genome is just -- if you will, just a bit of a mess.

**Dr. Carey:** Right, which again may get to it not having DNA repair working very well.

## Investigational Targeted Treatment Approaches

- Antiangiogenic agents
  - Efficacy in advanced/metastatic disease
  - Intergroup E5103 (early disease)
- PARP inhibitors (advanced disease)
- EGFR, c-KIT inhibitors
- MAP-kinase inhibitors
- mTOR inhibitors

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### Slide 19.

**Dr. Winer:** George, what about some of the trials that are going on now that we would like to encourage doctors and patients to think about?

**Dr. Sledge:** We certainly already have evidence in the advanced disease setting that 1 new class of drugs, antiangiogenic agents, may be of benefit for women with triple-negative breast cancer. I also add, of course, that it's of benefit for women with other breast cancer subtypes, but in large clinical metastatic trials we have evidence of that and that has led to the development of early-stage trials such as the breast cancer Intergroup's E5103 trial, which is looking at whether or not the addition of anti-vascular endothelial growth factor therapy can actually improve disease-free and overall survival for women with early triple-negative breast cancer, among other cancers. In the advanced disease setting we have so many new agents being looked at in triple-negative breast cancers that it's difficult to know almost where to start. In addition to the chemotherapy approaches that we have heard about, altering DNA repair mechanisms in particular with what are known as poly(ADP-ribose) polymerase (PARP) inhibitors looks very exciting. Novel attacks on growth factor receptors such as the epidermal growth factor receptor are being looked at. To date I'd say that this has been an area where we don't have any big signal yet but perhaps have some small signals. Downstream activators of cell growth, such as the MAP-kinase and mTOR are being looked at very actively. You know Eric, there is a certain power to naming things and this is what fascinates many of us. I looked at PubMed recently to try and find out when the first use of the word "triple-negative" breast cancer came into the medical literature and in essence one can't find it before 4 four years ago. The very fact that we have been able to name this and isolate it as a population worthy of study I think will advance the study of this type more than anything else anyone could imagine. That is exciting.

**Dr. Winer:** I agree entirely. Not only does it bring researchers and clinicians together, but importantly it also brings pharmaceutical companies into the fold because they want to develop drugs for what they realize is a new area. And in terms of clinical trials, not that we want to alarm people, but when women have recurrences of triple-negative breast cancer -- and by recurrences here I mean recurrences outside of the breast to other parts of the body -- so when women have metastatic triple-negative breast cancer, on average, unfortunately, they don't live as long as women with other types of breast cancer. And of course there are exceptions and there are women with triple-negative breast cancer who, in spite of the fact that it has spread, can live for years. But on average, the survival is shorter. And I think that speaks to the fact that we really want to encourage women and their doctors to think about clinical trials earlier rather than later. Running through a number of standard drugs and then looking for a clinical trial probably isn't the approach that we'd all like to see happen. Liz, do you have thoughts about that and how we can encourage that from a patient's standpoint?

## Developing Attractive Clinical Trials

- Translational Breast Cancer Research Consortium
- Cooperative cancer clinical trials groups
- Industry-sponsored trials

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**Ms. Frank:** I think we want to try to develop attractive clinical trials so that we can, as an advocacy community, encourage patients to participate in them. And I think that we do need to, as a group, really brainstorm as to how we accrue to clinical trials at a faster rate because this is a population of people that will benefit and need to benefit from it.

**Dr. Winer:** You know we are all also part of a group called the Translational Breast Cancer Research Consortium, which is a group of 16 different centers that are focused on early-phase clinical trials and we have trials related to triple-negative breast cancer there. There are, of course also trials in the cooperative groups and sponsored by the pharmaceutical companies and other centers but there are a number of trials available and a number of new agents and we really need to look at them and look at them rapidly.

**Dr. Carey:** There are signals of activities in several of these arenas, you know including the kinase inhibitors and antiangiogenesis...

**Dr. Winer:** And the PARP inhibitors potentially.

**Dr. Carey:** That's right. So with all of these things there is actually evidence that gives us hope about these approaches. They are not entirely untested, they are coming quickly. And one of the things that I think is really important is the value of getting tissue and actually looking at the cancers themselves to try and help identify what is heterogeneous even within these triple-negative breast cancers so that you can target them. It's going to be a real challenge for us but one that is likely to help us individualize the therapy for these patients.

## Lessons From Previous Decades

- Value of obtaining tumor tissue for biologic analysis
- Re-analyze results from large trials by tumor subtype
- Risk factors may be different, according to tumor subtype
  - Modifiable lifestyle factors?
- Screening issues may be different for different tumor subtypes

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### Slide 21.

**Dr. Winer:** And finally, you know much of what we know about breast cancer comes from lessons that we learned from clinical trials and from epidemiologic studies 10 and 15 and 20 years ago when not only did the term triple-negative breast cancer not exist, we also didn't think about it that way. We thought about breast cancer. We didn't think about this kind of breast cancer and that kind. And how much of those old lessons do we just have to toss away and just relearn what we know about triple-negative breast cancer? How do we deal with that?

**Dr. Carey:** I don't think you throw them away. We have these wonderful big studies --

**Dr. Winer:** Shift them to the side...

**Dr. Carey:** No, no you keep them but then you have to re-analyze them. You throw away your assumptions and you throw away global results that treat all breast cancers as if it was 1 disease. You go back and you say okay, let's see what's happening within triple negative and what is happening within the luminal subsets. For example, as you know in several of the epidemiologic studies, when they went back and started being a little more sophisticated about the nature of the cancers, it turns out that risk factors may be entirely different for certain subtypes of breast cancer and that may mean that there may be modifiable lifestyle factors if you know who was at risk for each subtype. And I think that actually takes the old data and what we need to do is add onto it, not throw it away.

**Dr. Winer:** I agree with you entirely. And it is a pretty striking lesson that much of what we thought were important risk factors for breast cancer in general may, in the end, not turn out to be such important risk factors for triple-negative breast cancer. For that matter many of the lessons about screening may not hold for triple-negative breast cancer. Not for a second to suggest -- Liz is giving me a look --

**Ms. Frank:** I want better therapy so that the screening will really matter!

**Dr. Winer:** That look is to say "don't you dare suggest that these women not get screening" and we're not suggesting that for a second. But I think that we are also well aware that, more so than in any subtype of breast cancer, there are women with triple-negative breast cancer who present in between mammograms with their triple-negative breast cancer. And I think it's a reminder that a woman who has a lump, even though she has been getting mammograms on a yearly basis and has been very attentive to her breast health, needs to go see her doctor because, in fact these triple-negative breast cancers do present that way with some frequency.

## Lessons From Previous Decades

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### Slide 21.

I think we had a great discussion and I want to thank our 3 panelists, Lisa Carey from the University of North Carolina, George Sledge from Indiana University, and Liz Frank from the Dana Farber Harvard Cancer Center. This has really been a great panel. We've had a wonderful discussion. Thank you for participating in the Medscape Oncology CME Program today. We'd also like to thank you, the audience, for your continued interest in the professional education activities that are supported by Susan G. Komen for the Cure through Medscape.

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### Author

#### Eric P. Winer, MD



Professor of Medicine, Harvard Medical School, Boston, Massachusetts; Director, Breast Oncology Center, Dana-Farber Cancer Institute, Boston, Massachusetts

Disclosure: Eric P. Winer, MD, has disclosed no relevant financial relationships.

#### Lisa A. Carey, MD



Associate Professor, University of North Carolina, Chapel Hill; Medical Director, UNC Breast Center, University of North Carolina School of Medicine, Chapel Hill, North Carolina

Disclosure: Lisa Carey, MD, has disclosed that she has served as an unpaid advisor or consultant for Genentech, Novartis, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer, and sanofi-aventis. Dr. Carey has also disclosed that she has received grants for clinical research from Genentech, Bristol-Myers Squibb, GlaxoSmithKline, and Boehringer Ingelheim.

### **George W. Sledge, Jr, MD**



Ballé-Lantero Professor of Oncology, Indiana University School of Medicine, Indiana, Indianapolis

Disclosure: George Sledge, MD, has disclosed that he has served as an advisor or consultant for Genentech, Bristol-Myers Squibb, sanofi-aventis, and GlaxoSmithKline.

### **Elizabeth S. Frank, EDM**



Patient Advocate -- Breast SPORE, Dana-Farber Cancer Institute, Boston, Massachusetts

Disclosure: Elizabeth S. Frank, EDM, has disclosed no relevant financial relationships.

## **Editor**

### **Margie Miller**

Group Editorial Director, Medscape Hematology-Oncology

Disclosure: Margie Miller has disclosed no relevant financial relationships.

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