



## Breast Cancer Research Highlights From ASCO 2017

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**Andrew Schorr:**

Andrew Schorr on location in Chicago at the American Society of Clinical Oncology meeting, the ASCO meeting, and of course there's always a lot that's discussed about breast cancer here. So if you or a loved one is living with breast cancer, you want to pay attention now as we talk with a leading expert and researcher in the field.

That's Dr. Steven Isakoff who is from Massachusetts General Hospital Cancer Center and get the latest and what it may mean for you. So, first of all, thank you for being with us.

**Dr. Isakoff:**

My pleasure. Thanks for inviting me.

**Andrew Schorr:**

So we are in the so-called age of precision medicine. Not all breast cancer is alike, and certainly women learned that, whether they were HER2-positive or triple-negative or ER-positive. So where are we now with strategies of knowing what are we dealing with for a certain woman, and what are the right treatments for them?

**Dr. Isakoff:**

Sure. So there's been somewhat of an evolution over the last 15 years when we first realized that breast cancer was not one disease. Initially, we separated it based on estrogen receptor and HER2 and progesterone receptor, but I think in the last 10 years or so we really realized that even among those subgroups breast cancer really gets subdivided even further. At the moment, we don't have a good clinically validated way to separate that, meaning there's no clinical test to say you are this particular subgroup, but in the research setting we're actually doing quite a bit to try and understand this.

For example, in the triple-negative subgroup, if you think about it, that's really a type of breast cancer simply defined by missing three receptors, ER, PR and HER2. But really it's a very heterogeneous group, and there have been a number of different groups who have looked at how can we use molecular subtyping to really distinguish these into different groups. And through one of these particular research-level versions, there are some that may be more sensitive to certain chemotherapies like platinum, there may be some that may be sensitive to androgen-receptor therapy, which is actually a prostate cancer therapy that we can use. There are some that may be more responsive to a pathway called PI3 kinase inhibitors. And so even in the triple-negative group there are probably five or six further subtypes.

In the estrogen-positive subgroup, at a very high level we've now begun to understand at least two subgroups, Luminal A and Luminal B, but for sure there will be other subgroups.

And in the HER2-positive subgroup, for a long time we thought all HER2-positive was the same. We now see many studies showing difference in response rates certainly in the early stage but also in the advanced stage between ER-positive, HER2-positive, ER-negative, HER2-positive, and there almost for sure will be further subgroups there.

In particular, we're thinking about immunotherapy, and there will be subtypes of HER2-positive and triple-negative where immunotherapy may be very effective, and we're trying to understand those subgroups.

The other area where this becomes very important is in our targeted therapies now. It's becoming not routine at every center, but at our center and at many centers we are routinely in the advanced setting sending tumors to be sequenced and to try and understand the different specific genetic mutations that might have been driving the development of that particular cancer not inherited in families but a change that happened to cause that particular cancer.

And we now have a number of targeted therapies, many in clinical trials, some moving very forward towards being approved that really target those specific mutations. And similar to what we've seen in lung cancer with mutations such as ALK mutation, A-L-K, which is an only very small sliver of patients, but when those patients get treated with the right drug they have tremendous responses.

And I think we're learning now in breast cancer as well if you have a PI3 kinase mutation, if you have an AKT mutation, if you have one of a number of other mutations, we now have targeted drugs in development to really attack those. One of the ones that was brought up at this meeting, for example, was in the BRCA carrier population with PARP inhibitors, the olaparib (Lynparza) study, the OlympiAD study with olaparib was a very encouraging study for that. That's a very selected subtype, but that also fits in with the concept of precision medicine.

So I think we've made really quite tremendous progress, and many people would say the sort of current thinking is we're no longer at the beginning of the beginning, but we're sort of at the end of the beginning. But we still have a long way to go, but we're making a lot of good progress.

**Andrew Schorr:**

Okay. First of all, that's great progress, but now women and their family members hear kind of this alphabet soup of mutations you've talked about and say, well, oh, my God, how can my doctor and I know what's right for me at this point? Now, you are at a major research center, but people see this everywhere. What are the questions that you would suggest that family members and women ask so that they get what could be used now, either approved therapies or even access to trials?

**Dr. Isakoff:**

So at a minimum, at a very high level if you meet criteria for genetic testing for germline mutations in BRCA, we think that that's actually very important. That has implications for platinum chemotherapy and hopefully soon for PARP inhibitor therapy.

At the next level, we always—whenever I meet with a patient I always discuss several options, and high among them in addition to standard chemotherapy or endocrine therapy it's clinical trials. That's really the only way we move the field forward. So I would recommend that any patient who is visiting with their physician at the time of needing to think about a new therapy it's always good to ask are there any clinical trials particularly for my kind of cancer?

There are a number of commercial entities that are offering genetic testing of tumors, and in large part they all do very similar things. We don't generally recommend that for routine testing, because as of now at least in breast cancer there are very limited drugs approved. However, if access to a clinical trial is possible, then that may be a very worthwhile thing, because it can guide the patient towards looking for a particular trial. And there are organizations that we've worked very closely with to try and help patients get to a clinical trial and not make geography be the only barrier to that. So we would certainly encourage people to look.

One thing I would say about clinical trials is 20 years ago clinical trials were often thought of as the treatment of last resort. That is completely the opposite now. And many of our trials where we're using targeted therapies, and we might have identified a target, we are trying to get these into patients early, because we've seen such dramatic responses. All of the proper studies still need to be done, but we really try and encourage people not to think of clinical trials as oh, no, there's nothing left for me but instead oh, wow there's something targeted for me. Let's try that. Because all the standard things will always, always be available.

**Andrew Schorr:**

That's very hopeful. Well, I want to just reinforce that. I've been in two clinical trials, not for breast cancer but for other cancers, and I believe I'm here today because of that. And we meet at Patient Power all the time people who have greatly benefited and had access to tomorrow's medicine today.

So, two things: Ask about trials, close analysis of your situation, when appropriate, genetic testing to know does it match up with either what's available now or what's coming. Thank you so much, Dr. Isakoff from Massachusetts General Hospital Cancer Center.

On location in Chicago, I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

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