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## Oncologist Recommendations for Patients with Hereditary Breast Cancer

Announcer:

You're listening to *Breaking Boundaries in Breast Cancer*, sponsored by Lilly.

Dr. Nacinovich:

Mutations and penetrance breast cancer susceptibility genes such as BRCA1 and BRCA2 increase the risk of breast cancer more than 4-fold, but despite this sobering recognition, the guidelines for treating mutation carriers with newly diagnosed breast cancer have been lacking, and many clinicians remain uncertain as to how and when to best incorporate surgical radiation and systemic therapies for these patients. On today's program we'll dive into the latest recommendations issued by the expert panel representing 3 major oncology societies in this pursuit of optimal care for patients with hereditary breast cancers.

Welcome to *Breaking Boundaries in Breast Cancer* on ReachMD. I'm Mario Nacinovich, and here to share his insights is Dr. Anthony Dragun, Professor and Chairman of the Department of Radiation Oncology at Cooper Medical School of Rowan University and Chief of the Radiation Oncology at MD Anderson Cancer Center at Cooper University Hospital.

Dr. Dragun, welcome to the program.

Dr. Dragun:

Thank you very much, Mario. I appreciate it. Happy to be here.

Dr. Nacinovich:

To start, let's get a level set on the issue of uncertainty around treatment for these patients. Why has it been so challenging up to this point to standardize treatment practices for patients with hereditary breast cancers?

Dr. Dragun:

It's been challenging to coordinate a lot of recommendations. I would say that each one of the specialties had developed their own set of guidelines based on their own view of the medical literature in their own scope of practice, but this most recent guidelines task force was really the first opportunity to get representatives from the 3 specialties—surgical oncology or breast surgery, medical oncology and radiation oncology—into the same room to hammer out some recommendations on how to treat these patients in areas where our specialties overlap, and I believe it's extraordinarily helpful because most breast cancer patients are now treated in a multidisciplinary setting. It's really important that the different specialties are knowing what each other is doing and all on the same page.

Dr. Nacinovich:

With that background, tell us a little bit more about this multidisciplinary consensus panel you are part of and its mission. From what I understand, the objective was to examine the current state of the data and then offer updated management guidelines. Certainly, that's no small task.

Dr. Dragun:

Yeah, I would say that it's no small task because it's somewhat of a moving target. The penetration of the field of genetics in cancer in general, and in breast cancer especially, has been higher and higher in recent years, and we've seen more and more patients being referred for genetic counseling and genetic testing. We have some of these genes that represent hereditary breast cancers that we know a lot about and some that are emerging. And so this panel was put together—and I was really honored to be a part of it as a radiation oncologist—but it was put together to bring together people who had this in their scope of practice and their interest from the different perspectives of the different specialties. The background was that we were all tasked to meet together, both in multiple in-

person meetings and virtually, review the literature, call out what were the strongest studies and try to put aside some of the studies that were still somewhat questionable, get the best available data and bring it all into one place and then clarify it for the average practitioner so that there was almost a triage of what the best available data is and being able to push that out to tell people who are taking care of these patients in practice what we know and what we don't know to help guide them and make the best decisions for their individual patients.

Dr. Nacinovich:

So let's move on to some of the key treatment recommendations for the indexed cancers which came out of this systematic review. Starting with surgical management, there were some new considerations around breast-conserving therapies versus mastectomies, weren't there?

Dr. Dragun:

I wouldn't say that these were new, but there was some clarification on them, specifically as they came to the availability of breast-conserving surgery for patients with some of these hereditary breast cancers. I think the panel was looking to provide some clarification on whether patients with hereditary breast cancers are eligible for breast-conserving therapy to begin with. I think that as some of the data was coming out on hereditary breast cancers, the field was generally drifting toward a perspective on hereditary breast cancers that they should all be treated with mastectomy, and that's not necessarily the truth. The literature doesn't necessarily bear that out. While these patients have a higher risk of lifetime breast cancer, both from the perspective of the indexed cancer, which is the breast cancer that they're seeing their specialist for at that time, as well as a risk of contralateral breast cancer, meaning breast cancer on the opposite breast, treating the indexed breast cancer with breast-conserving surgery and radiation therapy is an option for these patients. It's just a more complicated option that requires some more robust surveillance of the contralateral breast.

Dr. Nacinovich:

What about the role of nipple-sparing mastectomies? How do they factor into these guidelines?

Dr. Dragun:

Well, it's not directly in my specialty in radiation oncology, but the surgical oncologists and breast surgeons on the panel did clarify that nipple-sparing mastectomy is a reasonable oncologic approach for both the treatment of the indexed cancer and the treatment of any contralateral prophylactic mastectomy that might be considered so that when surgeons are making those decisions, they can make them based on whether the patient is eligible for a nipple-sparing breast procedure if she hadn't had a hereditary gene mutation, which I also think is a good clarification of the guidelines.

Dr. Nacinovich:

For those just tuning in, you're listening to *Breaking Boundaries in Breast Cancer* on ReachMD. I'm Mario Nacinovich, and joining me today is Dr. Anthony Dragun to discuss the treatment and management for patients with hereditary breast cancer. So, Dr. Dragun, earlier you discussed the surgical management of hereditary breast cancer, but if we turn to radiation therapy, how did the guidelines shift or update positions with respect to best practices for these patients?

Dr. Dragun:

Yeah, so this is the area of my greatest interest being a radiation oncologist, and having seen some of these patients over time, there's always a question, number 1: Should a patient be treated any differently based on her hereditary breast cancer status with radiation therapy? And the answer is largely no. Number 1, the kind of doses and the kind of areas that you would treat on somebody who has a hereditary breast cancer shouldn't be any different than patients with a nonhereditary breast cancer. That's number one. The indication for giving radiation therapy should be made based on the disease. Number 2, there are some hereditary breast cancer genes of lower penetrance that the medical literature has shown may have a higher risk of toxicity or side effects from radiation therapy.

Dr. Nacinovich:

Can you speak further to the new positioning around toxicity risks for radiation exposure and which patients should receive or avoid radiation therapies?

Dr. Dragun:

Yeah, so some of these hereditary mutations carry with them the risk of somewhat higher toxicity from radiation. The easy answer to that is that patients with BRCA1 or BRCA2 mutations don't seem to have a higher risk of toxicity to radiation, so they should be treated appropriately with radiation. There's another set of genetic mutations called the p53 mutation, or Li-Fraumeni Syndrome, and those patients really can't be treated with radiation therapy. Their risk of toxicity is too high. Then there are some of these genes in the middle which the data is mixed. There seems to be a suggestion that there could be a slightly higher risk of radiation toxicity or side effects for patients with ATM mutations. However, the toxicity risks are not high enough to justify the omission of radiation therapy. It's just that clinicians need to be on the lookout for some of the risks that those patients may have. And that's not all that different from some other

medical comorbidities that patients may have to put them at a higher risk for radiation toxicity.

Dr. Nacinovich:

And on the medical management side, did the consensus group change recommendations around any of the systemic therapies?

Dr. Dragun:

Yes, in medical oncology many of the recommendations talked about the substitution of different chemotherapeutic drugs at some point in time along the course of the treatment of patients, especially when we're talking about patients who are genetic carriers who have metastatic breast cancer where platinum chemotherapy is shown to be very effective, and so there are some recommendations or guidance for substitutions of some more effective therapies than others, and then there are other recommendations where some therapies may be helpful but the data isn't clear.

Dr. Nacinovich:

On the subject of subsequent or new cancer risks to the ipsilateral and contralateral breasts respectively, where did these guidelines land?

Dr. Dragun:

I would say that even after these guidelines the majority of patients, especially with BRCA1 and 2 mutations, tend to opt for bilateral mastectomy. However, the panel did want to open up the pathway as a legitimate pathway for patients to undergo breast-conservation surgery and radiation therapy of the indexed breast cancer and close surveillance of the contralateral breast and the ipsilateral breast after treatment. Now in the era of MRI, that surveillance has been made much more robust, and so the panel wanted to make clear that that is a legitimate option for patients to have and that their outcome from their cancer should be just as good and just as strong as those with nonhereditary breast cancers; it's just that the surveillance becomes that much more important because of their risk of subsequent cancer. So, if you have a patient who for whatever reason cannot undergo robust surveillance with breast MRI, then they're likely best served with bilateral mastectomy.

Dr. Nacinovich:

Before we wrap up, Dr. Dragun, do you have any additional takeaways you'd like to impart to our audience regarding these updates?

Dr. Dragun:

I think that... Going back to my initial statement that the genetic understanding of cancer and breast cancer specifically is a moving target, and it's something that's constantly evolving, and there are lots of genes that are emerging that are clarifying our understanding of how different breast cancers behave, I think that it will be important for panels like this to be convened in the future to keep on top of some of the changes and some of the evolving data so that in a multidisciplinary setting we can continue to update these recommendations and make sure that they're fitting the times.

Dr. Nacinovich:

Those are all great things for us to keep in mind. And as that brings us to the end of the program, I want to thank my guest, Dr. Anthony Dragun, for shedding some light on hereditary breast cancers and the new recommendations for optimal care of these patients.

Dr. Dragun, it was great having you on the program.

Dr. Dragun:

Thank you. It was my pleasure.

Announcer:

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