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Clinical Decision-Making in Metastatic Breast Cancer: Optimizing Sequencing Choices

Ms. Baker:
This is *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ms. Ashley Baker, and joining me to discuss how we can optimize therapy choices for patients with metastatic breast cancer is Dr. Giancarlo Moscol, who is an Associate Professor in the Department of Breast Medical Oncology at the University of Texas MD Anderson Cancer Center in Houston.

Dr. Moscol, thanks for being here today.

Dr. Moscol:
Absolutely. Nice meeting you, and thank you for the opportunity to participate.

Ms. Baker:
To start us off, Dr. Moscol, how do you typically approach first-line treatment selection in metastatic breast cancer?

Dr. Moscol:
Sure. Well, I think that this needs to be a shared decision process. So you need to consider different variants—for example, the tumor profile, the receptor status, the percentage of estrogen and progesterone positivity, the HER2 expression, and patient-derived factors like menopausal status, the burden of disease, how many organs are involved, and the previous lines of therapy, if any, that the patient may have received in the past.

I also consider goals of care. Is the patient willing to be treated just with a palliative intent? Are we trying to maybe help her bridge to pursue any other life milestones that the patient is looking forward to? And how well prepared is the patient and the family to maybe be exposed to a little more toxicity in order to gain maximum clinical benefit?

Ms. Baker:
And when you're evaluating second or third-line options, what key clinical or biologic factors come into play?

Dr. Moscol:
Whenever we talk about second-line treatment is when I start reflecting on the presence of any actionable mutations. So by rule of thumb, what I like to do is, upon metastatic diagnosis, get a biopsy of the most distant lesion. I go ahead and run next-generation sequencing to see if there any alterations, and then I try to reflect on these findings upon progression. So when the patient goes into second-line, for example, for ER-positive, we may end up having some alterations that we can now target—for example, PIK3CA, ESR1, BRCA1, BRCA2, and AKT, among others. So I think that as the time passes by, we're seeing more importance in being able to identify these mutations and then offer treatments that are more targeted to the patients.

Real-world data is helpful because it allows you to get a closer look to the day-to-day experiences of the patients. So, for example, it gives you a better sense and understanding about the tolerability of a new regimen or how burdensome the logistics to monitor for toxicity could be. They can also help us better understand the impact that some toxicities may have—for example, in the frequency or the need to have more continuous lab checks or checkups for hyperglycemia other end-organ damage. But still, I think one of the biggest caveats is that we cannot really try to compare or replace reported efficacy that comes from real-world evidence because it will not have the same weight and impact as the results from phase 3 randomized controlled trials.

Ms. Baker:
For those just tuning in, you're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Ms. Ashley Baker, and I'm

speaking with Dr. Giancarlo Moscol about therapy sequencing in metastatic breast cancer.

So, Dr. Moscol, after disease progression, how do you decide whether to continue with a similar therapeutic approach or switch mechanisms of action?

Dr. Moscol:
So I think that's a very important question. I would say it mostly depends on the pattern of relapse. So if the patient has only oligometastatic disease—so they're only showing very early signs of progression in one or two spots, very limited burden of disease, and not really having symptomatic progression—then under those circumstances, I think it will be very reasonable to try to switch to a different agent within the same class.

For example, if the patient was on a first-line CDK4/6 inhibitor, I may try to switch to a different CDK4/6 inhibitor that has a broader coverage and then alter the endocrine backbone. A good example of this would be what was done in the postMONARCH setting when patients were switched from palbociclib to abemaciclib, for example, and then you replace fulvestrant as the endocrine backbone.

On the other hand, if the patient has clear evidence of symptomatic progression—so we're talking multiple new metastases over bone, over lung, or over liver and the patient is having symptoms associated to this—I usually prefer to switch the treatment to a completely new strategy. So I prefer to switch the mechanism. I prefer to go with a drug that has a different target and potentially a different payload.

Ms. Baker:
And how are newer agents like antibody-drug conjugates and novel targeted therapies changing your approach to treatment sequencing?

Dr. Moscol:
I think they're making a very big impact. Right now, we recognize that about 20 to 25 percent of the first-line patients who are diagnosed with estrogen receptor-positive metastatic disease likely have what is called refractory disease. So this is a very specific group of patients who tend to have a quick progression that happens in the first 12 months of the use of the CDK4/6 inhibitors. And for this very specific group of patients, there are likely different biologic features. So the disease has developed other pathways or other systems, and the cancer does not only truly grow on the estrogen receptor pathway.

So I believe that for this group of patients, it makes sense. Instead of trying to manipulate the estrogen receptor pathway with a second or third-line treatment, it makes more sense to me to recommend switching to either chemotherapy or to antibody drug conjugates. And the decision to go with one agent versus the other is usually based on the presence of different receptors. In breast cancer specifically, it will depend on the presence of HER2 expression. If the patient is HER2 low or HER2 ultra low, then we will have the option to offer an agent like trastuzumab deruxtecan. Otherwise, I would prefer to switch them to chemotherapy, like capecitabine, in order to rescue them back.

Ms. Baker:
As we approach the end of our program, Dr. Moscol, do you have any key takeaways you'd like to share on how we can best approach treatment sequencing in metastatic breast cancer?

Dr. Moscol:
Sure. So I think it's important to understand the tempo of the disease. Is the disease accelerating or decelerating? Is the patient having any symptomatic recurrence, or is this an indolent and oligometastatic progression?

It's also going to be important that we fully understand the molecular characterization of the disease. In the near future, I expect we're going to be getting more and more targeted agents. So running a genomic comprehensive panel from the beginning and then pretesting upon progression is going to help us get more data and potentially offer more options that are not going to be chemotherapy related and, with that, try to expand and improve the quality of life of patients and also give them a little more survival.

I would say, finally, when in doubt, I think there's no shame in calling a colleague that may have a little more experience in the field to try to gain their insights.

Ms. Baker:
Those are great insights for us to think on as we come to the end of today's program, and I want to thank my guest, Dr. Giancarlo Moscol, for joining me to discuss decision-making in therapy sequencing for metastatic breast cancer.

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

Dr. Moscol:

Thank you. Look forward to speaking to you soon. Take care.

Ms. Baker:
You've been listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of Metastatic Breast Cancer* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.