Transcript Details

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Navigating Metastatic Breast Cancer Care: Key Factors in Decision-Making

Announcer:
Welcome to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. On this episode, we'll hear from Dr. Paolo Tarantino, who's a medical oncologist and Clinical Research Fellow in the Breast Oncology Program at Dana-Farber Cancer Institute and Harvard Medical School. He'll be discussing therapy sequencing in metastatic breast cancer. Here's Dr. Tarantino now.

Dr. Tarantino:
So there's several important factors that impact treatment choices in the first, second, and third-line settings for metastatic breast cancer. The key factor is the subtype of the disease. And we now know that breast cancer is a heterogeneous disease, and so we always first look at the estrogen receptor status of the disease and the HER2 status of the disease, and we divide the tumors in three buckets. For the ER+/HER2- tumors or luminal tumors, usually, in this case, we try to start with a type of endocrine treatment, usually combined with some kind of targeted agent. And we do this usually for several lines, one to two to three, before we move to cytotoxic treatments. And in fact, in other diseases—for instance, HER2+ breast cancer—we always start with some HER2-targeted agents, usually combined with chemotherapy, and then we always keep the HER2 blockade in subsequent lines. In triple-negative breast cancer, since we do not have targets like ER or HER2, we mostly use chemotherapy, sometimes with additional immunotherapy. So the key factor really is a subtype of disease, but of course, we have other factors, such as the burden of disease, if it's rapidly progressing, and of course, patients preferences are always critical in every treatment decision.

It's extremely important to discuss in settings where we don't have head-to-head comparisons within different drugs how to navigate treatment choices based on different guidelines, clinical characteristics, and the patient profile. One important aspect is the magnitude of benefit, and so even when we don't have head-to-head comparisons, we can do cross-trial comparison. We're not supposed to do it, but we need to do it in order to make treatment decisions, and we can estimate the magnitude of benefit from each drug compared to the standard of care in terms of progression-free survival and overall survival.

And then we have other aspects. We have the toxicity profile that often differs between different options and the schedule of the drugs that differ, and so it's always important to be aware of the data and present the data to the patients whenever more than one drug is available and to try to tailor the treatment choice according, first of all, to the efficacy of the drug that has been observed in the trials, and then the toxicity profile and the schedule that most suits every patient. And our patients are very heterogeneous. You have patients who would favor to do more rather than less, patients who instead would like to minimize the side effects as much as possible, patients who live close to the center and can come in every week to receive treatment, and patients who live far and prefer treatment every three or four weeks. And having different treatment options, even if they're not compared head-to-head, allows us to really tailor treatments according to the patient profile and preference.

So it is good news to have many options, but we need to adapt to more uncertainty. And unfortunately, we cannot always have randomized data to decide for certain treatment options, but we need more and more to adapt to evolving guidelines, which is why, for instance, ESMO adopted the living guidelines that can be updated constantly. And the more new drugs enter the market, the more we gain experience with these, and it becomes easier to also understand how to prevent and manage side effects with these new options and make sure that the patients gain all the benefit from them without suffering too many side effects.

Recently, we have been establishing some different paradigms. In some settings, for instance, we do something that is more like a maintenance treatment, and so we give initial induction and then maintenance and only switch once again after progression. And then there are some clinical trials that are now trying to switch treatment before actual progression of disease when there is a certain marker

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of resistance observed in the circulating tumor DNA, so at the blood draw, and this is the case, for instance, of the SERENA-6 trial. There is switching endocrine treatment based on the emergence of ESR1 mutations in the blood. This is still not standard of care, so for the moment we usually switch treatment type upon progression of disease on CT scans or in general on imaging—this is a standard in oncology—and we do try to switch around the mechanism of action of the drug, but it is not an absolute rule. And so we are starting also to sequence drugs that have a similar mechanism of action, such as topoisomerase I ADC, and this comes with challenges, but we do have trials that are trying to fill the gaps and teach us somehow how to best sequence even drugs that have similar mechanisms of action.

Announcer:
That was Dr. Paolo Tarantino talking about navigating therapy sequencing in metastatic breast cancer. 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!

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