Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/frontlines-metastatic-breast-cancer/rethinking-frontline-care-in-her2-metastatic-breast-cancer/39714/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Rethinking Frontline Care in HER2- Metastatic Breast Cancer

Dr. May:
This is ReachMD, and I'm Dr. Alexandria May. Today, I'm joined by Dr. Tiffany Traina to talk about unmet needs in HER2-negative metastatic breast cancer and how they're influencing early treatment decisions. Dr. Traina is a breast medical oncologist at Memorial Sloan Kettering Cancer Center in New York.

Dr. Traina, welcome to the program.

Dr. Traina:
Thank you so much.

Dr. May:
Well, let's jump right in, Dr. Traina. When we look at real world data, we see attrition across lines of therapy in both triple-negative and HR-positive metastatic disease. So what does that tell us about the unmet needs our patients are facing?

Dr. Traina:
It's a wonderful question. So what we've seen in real-world data sets is actually somewhat surprising, but consistent: almost half of all patients do not make it to second line therapy. I think that we see that a bit more so in the triple-negative breast cancer population, and this is important information because as time goes on, patients may have a decline in their performance status. They have cumulative toxicity from the treatments we've given before. They may have more complex comorbidities over time. And so I think a really sobering piece of data that is quite consistent is that we cannot make the assumption that patients will have the ability to sequence additional treatments in later lines when almost 40 to 50 percent do not make it to second-line therapy or later.

Dr. May:
And knowing that many of our patients may not reach later lines of therapy, how should we be shifting the way we think about first-line strategy?

Dr. Traina:
I think it's important for us in the first-line setting to be sure we have all the biomarkers we need to be making the right recommendations for our patients. And it's, I think, culturally an approach where we should not think to save a therapy for a rainy day in the future because we can't assume that patient will be able to have a second- or third-line option for treatment.

Again, particularly, this is a greater issue in patients with triple-negative breast cancer than it is with hormone receptor positive. But I think philosophically, I always try to lead with our drugs that have the best efficacy.

Dr. May:
Now, I'd like to zero in on triple-negative disease for a moment. Although we group triple-negative breast cancer under one label, we know it represents a biologically diverse set of diseases. How does that variability influence how you approach first-line treatment selection today?

Dr. Traina:
That's a terrific question. I think calling a tumor triple-negative these days is just insufficient information, and we really must know a few different factors. One, we need to know the PD-L1 status of the tumor itself. About 30 to 40 percent of tumors will be PD-L1-positive, and there is an entirely separate approach to that first-line treatment that incorporates immunotherapy. So we must know the PD-L1 status.

© 2026 ReachMD

I also reflexively think we need to know the germline BRCA mutation status of the patient with triple-negative breast cancer. There's a higher prevalence of BRCA1 mutations in patients with TNBC, and this is relevant because we have really actionable data. If you find a BRCA mutation, we can use oral PARP inhibitors, which work beautifully. They prolong survival and have a much more favorable toxicity profile. So I think it's critically important to define PD-L1 status and BRCA mutation status, and also to be precise about HER2 status because HER2-low may offer opportunities for targeting as well.

Dr. May:
For those just tuning in, you're listening to ReachMD. I'm Dr. Alexandria May, and I'm speaking with Dr. Tiffany Traina about the clinical complexities shaping frontline treatment strategies in HER2-negative metastatic breast cancer.

So Dr. Traina, let's shift gears and talk about HR-positive metastatic disease. We know that endocrine therapy plus CDK4/6 inhibition is standard first-line care for most patients, but after progression, where do you see the greatest unmet needs emerging?

Dr. Traina:
So we've been fortunate to see the impact of adding a CDK4/6 inhibitor to the first line setting, and many patients derive benefit for years in a very well tolerated, often oral endocrine therapy and targeted therapy regimen. Upon progression, the vast majority of patients are still going to be candidates for endocrine therapy, but the choices we make really need to be dictated by biology and mechanisms of resistance at that point.

So I feel that I'm not empowered to even make a recommendation until I have certain genomic information. We need to know if the presence of an ESR1 mutation has emerged or not. I need to know if there's a PI3-kinase, AKT, or mTOR pathway alteration, like a PTEN loss, for example, because these start to enable us to make choices about targeted therapies and which endocrine therapy backbone we're going to use upon progression.

So I think the unmet need is that mechanisms of resistance to endocrine therapy begin to emerge the longer our patients are on estrogen-depriving therapies. And to make the appropriate choices, we really need to know those mutation profiles for the metastases.

Dr. May:
Now, according to real-world data, not all patients undergo comprehensive genomic testing at progression, and some transition directly to chemotherapy without additional targeted endocrine options. So what factors are driving that gap between guidelines and practice?

Dr. Traina:
It's a great question. So, I think first, we need to consider at a time of progression, is this patient a candidate for chemotherapy? And that, these days, is really when somebody truly has large burden of disease and is rapidly progressing—what we would call a visceral crisis.

Because we have so many incredible targeted therapies that are based on biomarker expression, it is so critical that we get that serial repeated molecular testing. And the quickest way is with ctDNA to look for emergence of mutations like ESR1. So, it's interesting to think about why there might be a gap. Perhaps it's an educational gap to recognize that we need to send these assays at the time of each progression. As long as your patient is a candidate for continued therapy, it is worthwhile to resend those ctDNA assays to look for the emergence of those targetable mutations.

It may depend on where clinicians are located, access to testing, cost of testing for some of our patients, and turnaround time, which have all improved over the past months to years as these assays are really critical for making the right guideline driven choices for our patients. So I can imagine there might be some hurdles or barriers, but I see those as diminishing over time because it is so important to have this genomic information to make treatment recommendations.

Dr. May:
Finally, Dr. Traina, given everything we've discussed, from survival attrition to biologic variability and practice gaps, what steps can oncologists take to optimize early-line decision making and reduce missed therapeutic opportunities?

Dr. Traina:
It's a great question. I think it's critically important to always understand the biology of the cancer that we're treating in the moment that we're making a treatment recommendation. And these, in many cases, are quite dynamic changes. So for triple-negative breast cancer, reflexively be thinking about PD-L1 status, germline BRCA status, and even sequencing the tumor because if you find somatic BRCA mutations, that can also be targetable with PARP inhibitors.

In the hormone receptor-positive setting, we have a number of biomarkers to be on the lookout for, and these are dynamics. So at each point of progression, you want to resend circulating tumor DNA. Just because you didn't find a mutation in the beginning doesn't mean it

© 2026 ReachMD

won't emerge over time. So we're looking for ESR1, PI3 kinase, AKT alterations, or PTEN loss; any one of those opens the door to targeted therapies and helps us delay the time to ADCs or chemotherapy, which are great drugs, but have a higher toxicity profile than a simpler endocrine therapy approach. And so delaying that time to the cytotoxics offers our patients maybe many months of higher quality of life.

Dr. May:
With those practical takeaways in mind, I want to thank my guest, Dr. Tiffany Traina, for joining me to discuss how persistent gaps in HER2-negative metastatic breast cancer care are guiding early therapeutic decision making. Dr. Traina, it was great having you on the program.

Dr. Traina:
Thank you so much, Dr. May. I appreciate it.

© 2026 ReachMD