## Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/expert-viewpoint-optimizing-breast-cancer-treatment/29832/

Released: 12/30/2024
Valid until: 12/30/2025
Time needed to complete: 1h 32m

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

---

# Expert Viewpoint: Optimizing Breast Cancer Treatment

**Announcer:**
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

**Dr. Gradishar:**
This is CME on ReachMD. I'm Dr. Bill Gradishar, and with me today are Dr. Erica Mayer and Dr. Peter Schmid. Our discussion today will focus on practical considerations when applying treatment guidelines when tailoring treatment for patients with early- and late-stage breast cancer.

We'll start in the early-stage breast cancer setting. Erica, can you tell us about how you optimize therapy for early-stage breast cancer based on the current NCCN Guidelines?

**Dr. Mayer:**
Thanks. Well, it's very important for our treatment decisions in medical oncology to be data-driven. And we are so fortunate that we have a wealth of clinical trial data that represents decades of work. NCCN Guidelines are really a wonderful resource that reflect the most cutting-edge data, and importantly, they are updated very frequently as we have such a rapid pace of development and new agents and new drug approvals.

So, for example, with the recent approval of the CDK4/6 inhibitor ribociclib in the adjuvant setting for high-risk hormone receptor-positive, HER2-negative breast cancer, this approval is already reflected in the current version of NCCN Guidelines, which is great to have that very immediately reflected in our guidance.

Personally, I find it very helpful to review NCCN Guidelines in my practice so I can confirm that my treatment decision-making is congruent with the most current data.

How are you using guidelines in your practice?

**Dr. Gradishar:**
Well, I guess I have a vested interest in guideline development, because I'm the chair of the NCCN Guidelines. But with that said, whether they're the ESMO guidelines or St. Gallen guidelines, whatever guidelines, ASCO guidelines, we try to develop them based on evidence that's available through clinical trials and best clinical decision-making. And we try to distill all that information and hopefully come up with what is the most optimal therapy for a given patient situation.

So all that said as a preamble, we try to abide by the guidelines as much as we can, and that's true both in the early- and late-stage setting. The early-stage setting, as Erica just discussed, is getting more and more complicated as other therapies enter into that space. And by that, I'm referring to partnering endocrine therapy with CD4/6 inhibitors in the early-stage setting, also in select patients, the utilization of PARP inhibitors. And of course, we have to think about how we integrate immunotherapy in early-stage disease setting as well.

So all of those things are integral to optimizing the care for any given patient. And when we look to the guidelines, we don't think of them as cookbook, so to speak, where we're formulaic and simply following what the guidelines, say, but trying to apply the evidence that was generated from clinical trials to best practices in applying therapy to a given patient.

So again, every patient is individual. We have to look at them not only from the standpoint of their disease, but we have to take into account also what their overall condition is, what their comorbidities are, and then make a decision about whether what's on the guidelines is appropriate for that given patient.

What are the challenges in translating the guidelines into clinical practice? For example, can there be formulary or insurance restrictions?

**Dr. Mayer:**
Although the guidelines are very comprehensive and very data-driven, there do remain some gaps and limitations based on available evidence. So, for example, many of our trials that are really very interesting may be somewhat of a pilot phase 2 study or have other kind of innovative trial designs that help us address important questions, but they may not generate data that's at the level that could be included in official NCCN guidance. And this may potentially limit applicability.

So, for example, there's data from the NeoPACT study, which has explored the efficacy and safety of a non-anthracycline preoperative regimen for triple-negative breast cancer. These are very interesting and important data, but they are not reflected in NCCN guidance, and thus, this regimen may not actually be covered by payers. And this creates some difficulties in clinical practice. So, ultimately, we do see that payers may require inclusion of specific regimens or agents in NCCN Guidelines, and if they're not represented, it can limit our ability to offer these to our patients.

What are your thoughts on this?

**Dr. Gradishar:**
So we try to apply the guidelines as best we can. And of course, one of the obstacles or challenges we sometimes have is getting insurance coverage, and we have to abide by the guidelines. Oftentimes, in the US anyway, NCCN Guidelines are very much a roadmap for insurance companies to provide coverage. It's not uncommon, if there are nuances to a given patient, where we have to often talk to medical directors and go through a lot of hoops, so to speak, to try and get a given therapy approved. This is oftentimes most common when new therapies enter the guidelines. In other words, we have to make sure that the insurers understand that what we're offering the patient is based on evidence that resulted in a change in the guidelines.

The guidelines, as Peter will talk about as well, are updated very frequently based on the emergence of new data. We go to meetings very frequently, international and national meetings, where the most recent data from large clinical trials are presented. And if the data is robust, it may change the guidelines in a very quick fashion. Oftentimes, as an example, with the NCCN Guidelines, we'll have calls within a week of the meeting completing, and oftentimes, the most important data is not only presented at the meeting, but it's common these days for there to be a publication that is actually synchronized with the presentation. So we will look at whether the level of evidence is sufficient and make changes to the guidelines almost in real time. And sometimes the insurers aren't aware of that. We have to make them aware of that. And we also, within our own institutions, we sometimes have the formulary playing catch-up, so to speak, when new things emerge very quickly.

Erica, how do you balance treatment selection based on the current guidelines and patient preference?

**Dr. Mayer:**
So we're very fortunate in breast cancer that we do have situations where we have the ability to make choices, and we have more than one option available for patients. These are times when shared decision-making and really spending time working on patient education are really key.

So, as an example, we now have two approved CDK4/6 inhibitors in the adjuvant setting. That's abemaciclib and ribociclib, and both of these agents are very appropriately mentioned in the current NCCN guidance as options. Now, there are differences in how we use these agents, including the specific approved population for whom they are eligible, the duration of time that we use each agent, the side effect profile. So this is really a perfect time when we need to use patient education, and we need to use shared decision-making to make the best decision for a specific patient when both of these agents are potential options for us.

So, of course, despite all of our available data, there are still some gaps in our clinical knowledge when treatment selection is not entirely clear. So here's an example. Data from the RESPONDER trial suggests that there is benefit to adjuvant chemotherapy in addition to adjuvant endocrine therapy for all premenopausal patients with node-positive, hormone receptor-positive breast cancer, regardless of

oncotype score.

However, the RESPONDER trial did not specifically collect data on the potential contribution to this chemotherapy effect of chemotherapy-induced ovarian suppression, or amenorrhea, which we know is a very potent and effective treatment for hormone receptor-positive breast cancer. And so, it becomes very difficult to understand how much benefit from chemotherapy seen in the trial was actually chemotherapy or the secondary impact of amenorrhea.

So this is a gap in our knowledge until we have data from the ongoing NCTN offset trial, which is looking at this question prospectively. But it's difficult for NCCN guidance to really capture the subtlety as the available phase 3 data don't necessarily help provide support for the clinical gray area. So here's where it's really important to really review all the data with patients and make a shared decision and treatment.

**Dr. Gradishar:**
Thanks, Erica, for an excellent discussion.

Peter, I'll turn you now and ask you how you're using the NCCN Guidelines in the UK for metastatic breast cancer. And I think the way the question is crafted is probably a bit too US-centric, I should say, because my guess is that you're not abiding or going to the NCCN Guidelines to make treatment decisions in the UK. So I'm curious what guidelines you do use and how you employ them perhaps on a day-to-day basis, or not?

**Dr. Schmid:**
Yes, thank you, Bill. You're absolutely right. Guidelines are often focused on a certain region. And although we look at the NCCN Guidelines, we also largely focus on the ESMO guidelines. But there's huge overlap between ESMO guidelines, ASCO guidelines, or NCCN Guidelines. And I think I would always focus on where most guidelines overlap. But of course, we can find subtle nuances where those guidelines may be different. For example, if we look at triple-negative breast cancer, metastatic disease, first line, in Europe we have two drugs approved, two checkpoint inhibitors approved, pembrolizumab and now atezolizumab. In the US, it is only one. So consequently, the guidelines are slightly different because we can choose between the different checkpoint inhibitors based on biomarker selection. Or if you go for second-line TNBC therapy in metastatic disease, again, the ESMO guidelines weight slightly differently and give a maybe a stronger weight at the moment to sacituzumab govitecan and use trastuzumab deruxtecan in a different line. But these are sort of subtle nuances, if I may say so.

Looking at HER2-positive metastatic breast cancer, again in a second-line setting, the NCCN Guidelines are very clear that trastuzumab deruxtecan, at the moment, would be the treatment of choice. Whereas, the ESMO guidelines, rightly or wrongly, are still bringing in brain metastases and whether one should consider tucatinib or trastuzumab deruxtecan, although I think we can discuss whether the recent data with DESTINY-Breast12 may change their view, and maybe guidelines will be adjusted.

**Dr. Gradishar:**
Yeah, and I would echo those comments exactly. And I think one of the reassuring things about guidelines is you have experts, whether they're in Europe, whether they're in the United States, they're largely looking at the same data. And the reassuring thing is they come to the same conclusions, by and large. And as you pointed out, there are nuances between the guidelines. Certain drugs may be approved in one part of the world and not in others or in one country versus the other. So there are caveats that if you don't have the drug, you can't use the drug.

But what the guidelines do provide is other options for patients should that drug not be available. And I think the dynamic nature of guidelines is that they're not static. And that really highlights the fact that, number one, in order to stay up to date on how we treat patients optimally, it's very challenging for the average clinician out in the community to really stay abreast with everything that's going on. Guidelines help provide that scaffold or framework for thinking about things, and it really gives us an opportunity to update people very quickly so they have a reference that is up to date so they can apply that data to their patients.

Peter, how do you base your treatment selection on guidelines while taking into account regulatory or formulary considerations? So again, this may get to the issue of, to at least some extent, the availability of drugs that may be approved in one place but not in another.

**Dr. Schmid:**
And I think that is a challenge and actually something that's even in front of patients; we haven't got a clear answer to this. Take, for example, the antibody-drug conjugates in second- and third-line ER-positive, HER2-negative breast cancer, where the guidelines are very clear, both ESMO and NCCN, that trastuzumab deruxtecan in HER2-low is the second-line strategy. And then in later lines we've got, for example, sacituzumab govitecan. There are some parts of Europe where both ADCs are currently not reimbursed in ER-positive breast cancer. So you've got a clear guideline recommendation, but we can't offer that to patients.

Now, fortunately, the guidelines, as you pointed out, provide alternatives if that is the case. And I think there are hardly ever situations where you won't find an answer within the guidelines; you just have to choose and apply. And the same way we have to look at the patient in front of us, at her pretreatment, at the characteristics of her cancer, the behavior of the cancer, and you can treat within the guidelines and still treat poorly if you don't look at the patient and work out when is treatment A better than treatment B, although they're both listed in the guidelines.

And I think that's where treatment of metastatic breast cancer still is a form of art that isn't just delivered in a recipe book, as you said earlier. It's guidance for us, but the guidance needs to be applied, shared decision-making with the patients, ideally in a multidisciplinary environment to then choose the right treatment at the right time for the right patient.

**Dr. Gradishar:**
Right. Excellently put. Your answer actually leads me to the next question, which is if there are specific patient profiles or clinical scenarios that aren't articulated clearly in the guidelines – because typically in the guidelines, we have stage of disease, tumor, whatever the molecular markers of the tumor are, and then we have treatment choices. But what it doesn't take into account are functional status, comorbidities, other things.

So how do you integrate that when you're thinking about a treatment recommendation?

**Dr. Schmid:**
Yes. So again, one of the key determinants is the pretreatment. And, for example, if you look at first-line endocrine therapy, where we will have and have an increasing number of patients who already had CDK4/6 inhibitor in the adjuvant setting, and it is currently unclear, not well-reflected because we haven't got data in the guidelines how to do this. So we have to interpret the data with caution but try to work out whether we still believe there's a benefit from those therapies. Similar situations, for example, in triple-negative breast cancer, where immune therapy has moved into the neoadjuvant setting. But what are we doing with patients when they have disease recurrence and have prior immune therapy?

So there are scenarios where we just haven't got the data. If you haven't got the data, the guidelines can't be absolutely clear, and we need to be cognizant of those limitations and then work in a sensible way. It comes back to the parameters, analyzing pretreatment of patients, their current status. I often look at the disease pattern and the disease dynamics. It’s a difference whether a patient has two very slowly growing bone metastasis or rapidly growing visceral disease involving lung and liver. And you may choose different strategies, even if on paper you could choose the same treatment for those patients. The patient's views are obviously critically important as well. And I think multidisciplinary input, as I said earlier, is also very helpful.

**Dr. Gradishar:**
Yes. And I agree. I think the guidelines, again, are not formulaic. They have as a background, as you nicely put, consideration of the patient in front of you. And we all know that an 80-year-old patient coming in a wheelchair is very different than a 60-year-old patient or a 40-year-old patient in many cases. And we have to take into account not only what their probable longevity is, but what their tolerance of a given therapy is. And that's partially our decision, but of course, the patient weighs in on this too. And there are many different nuances that you touched on too. We have patients that have hormone receptor-poor disease that aren't strictly called triple-negative disease, yet we know they behave like triple-negative disease. And those may be patients where, if we can get an immune therapy in the early-stage setting, we may choose to do it, even though it's not rigorously by the guidelines.

All right, thank you, Peter and Erica, for providing an excellent discussion on this important topic. And I'd like to thank the audience for joining us today. We hope you found this discussion useful for your practice. Thank you.

**Announcer:**
You have been listening to CME on ReachMD. This activity is provided by Prova Education and is part of our MinuteCE curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.