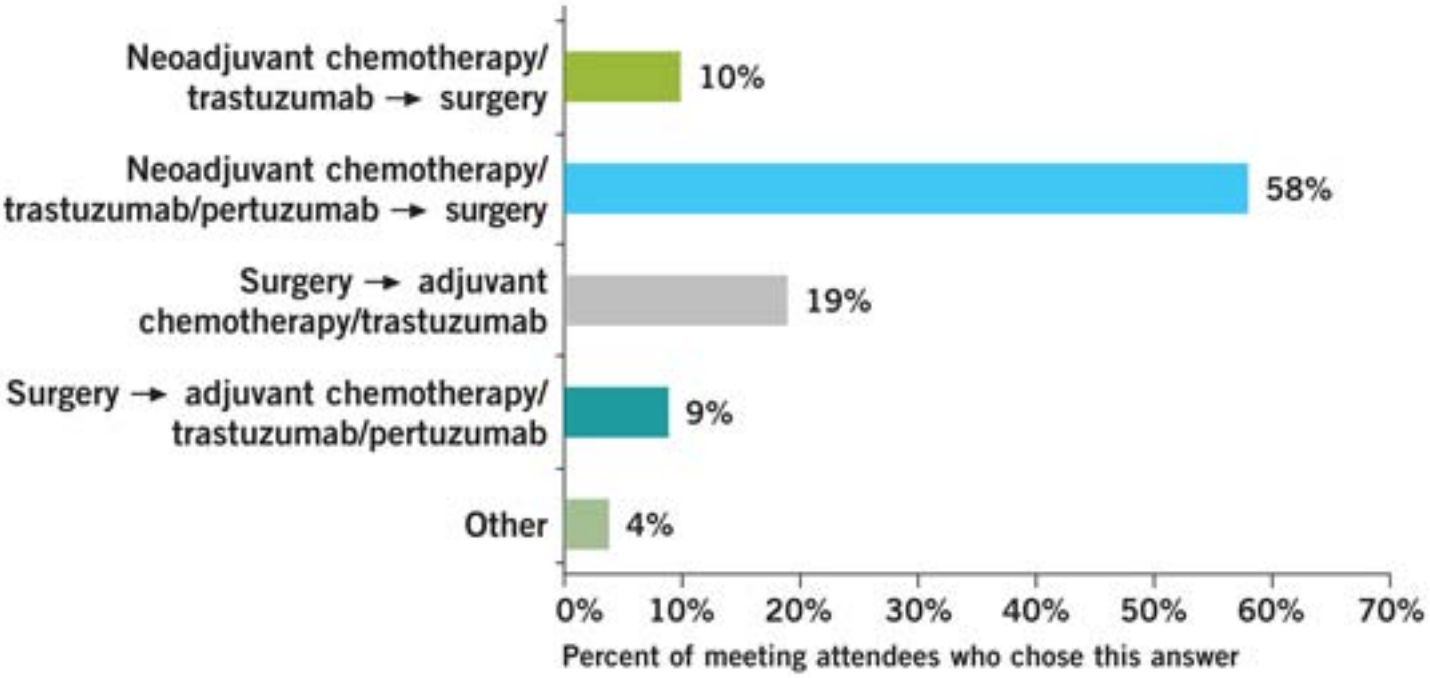
Year in Review

Proceedings from a Multitumor CME Symposium Focused on the Application of Emerging Research Information to the Care of Patients with Common Cancers

Novel Agents and Treatment Strategies for HER2-Positive Breast Cancer — Kimberly L Blackwell, MD

A 60-year-old woman is diagnosed by core biopsy with a 2.2-cm, ER-negative/HER2-positive IDC and clinically negative axilla. The patient is a candidate for breast conservation. What treatment approach would you most likely recommend?



DR LOVE: Certainly, one of the things that we've been talking about a lot in the last couple of years is neoadjuvant therapy for HER2-positive disease, so, Kim, we structured this case to be a little bit provocative. We had a patient, a 2.2-centimeter tumor, but clinically negative axilla, ER-negative, HER2-positive. The patient could get breast conservation right now. It's a small tumor. Do you send the patient to surgery or do you give them neoadjuvant systemic therapy? And, if so, what?

And these answers, Kim, look quite interesting. Most people would use neoadjuvant therapy — even the small tumor — TCHP-type regimen. But, significantly, a fair number of people, maybe a third here, Kim, would send the patient to surgery. Is that an acceptable option in your view, Kim, or really not a good idea?

DR BLACKWELL: I think anything's acceptable in this space. My answer to this question, just to start us off with a more concrete thing, is: I would treat this patient with neoadjuvant therapy, not because she needs us to shrink the tumor, not because the surgeon needs us to make their job easier, but because that is the indication for the utilization of pertuzumab,

which, given its therapeutic index, which is that it works really well and it doesn't add a lot of toxicity, we like to try to get that drug in and offer it to patients. So the reason to treat this patient in the neoadjuvant setting is not the classic reason to treat her in the neoadjuvant setting. It's so that you can offer her what we believe is a very active agent on top of what you would give her anyway.

For those of you who answered 3, 4 or 5, which is "other," that would have been the other "other" answer I would have given. And the only reason I take these women to surgery, especially if they're T1 tumors, is because there are a number of ongoing adjuvant clinical trials, in particular with utilization of drugs like T-DM1. So for these very small, less than 2-cm tumors, patients still have some very good clinical trial options, including T-DM1.

DR LOVE: Ruth, one interesting answer here — we call this the NCCN question because we made it 2.2, right over the 2 centimeters, because, Ruth, as you know, the NCCN made this statement earlier. And actually, Bill Gradishar was with us in New York, talking about it — that it was logical/justifiable to give pertuzumab adjuvantly in a patient who, like this one, met the criteria. Ruth, what are your thoughts about the use of adjuvant pertuzumab? Obviously, it's off label.

DR O'REGAN: I have to say, I don't use it at this point. And I'm kind of surprised the NCCN did that because we don't have the APHINITY study yet. And we learned from Neo-ALTTO and ALTTO that what you see in the preop setting doesn't always translate into the postoperative setting. They are higher-risk patients in APHINITY, so hopefully we'll see a signal. I give neoadjuvant treatment to almost all these patients.

DR LOVE: Skip, I'm going to put out another reason to do neoadjuvant in addition to maybe easier access for pertuzumab. I'm going to say: I put this patient's tumor size into the Memorial nomogram to find out the chance that she has a positive axillary node, and it was 25% to 30%, depending upon exactly what you put in there. So I'm going to say that since, certainly, surgical investigators use postneoadjuvant sentinel node biopsy, that by doing it preop and converting 70% of those node-positive people to node-negative, that you've saved axillary dissection in 15% to 17% of patients. Do you agree with that, Skip?

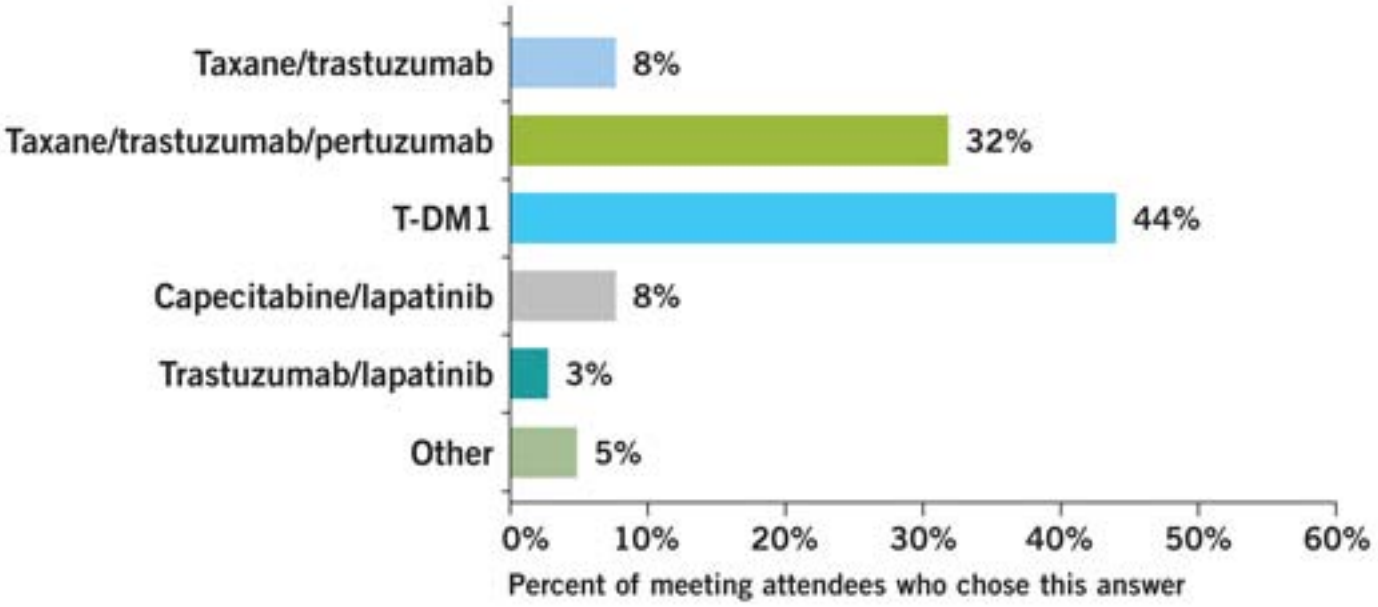
DR BURRIS: Yes, that's a very logical place to go down. And one of the greatest debates we're having right now is: Should we, in fact, push for sentinel node biopsies prior to initiating neoadjuvant therapy? And I think getting the direction of doing that standardly with success of sentinel nodes would be the way to go. But your logic's right in terms of how we need to push that impact.

DR LOVE: Just to get another point of view, Kim, you're working with us on this big neoadjuvant project. We actually have a poster that's coming up in San Antonio, looking at the results of a survey of 70 investigators, and Kim and Terry Mamounas worked with us on this. And we actually found, I think it was, about half of the medical oncology investigators were using pertuzumab, in contrast to Ruth, adjuvantly. What do you think about that as a nonprotocol strategy, Kim?

DR BLACKWELL: I use it across the board. And I think that the reason that the NCCN guidelines included it is because — I think many of us don't want to penalize patients for the option that there might be a benefit for adding pertuzumab in that adjuvant setting. And APHINITY, the study that will confirm adjuvant pertuzumab, is closed to accrual.

Therefore, we as practitioners look at the patient in front of us and say, "What do we think is the state-of-art care?" And for those patients who we don't see preop, that we would have given pertuzumab in the neoadjuvant setting, we don't just give it in the neoadjuvant setting to shrink the tumor. We give it because we think there's a potential benefit. Many of us believe that adding pertuzumab in the adjuvant setting should be considered — that's the wording of the NCCN — simply because we don't have a clinical trial for those patients. And we're in kind of a time gap, where the APHINITY results are not known. So I think it's a very reasonable strategy.

A 60-year-old woman with a 6-cm, ER-negative/HER2-positive tumor and palpable nodes receives TCH/pertuzumab with good response but residual disease at surgery. The patient completes 1 year of trastuzumab and 6 months later develops metastatic disease. What would you most likely recommend?



DR LOVE: Ruth, maybe you can comment on this next question, because we were getting a lot of questions from oncologists about the uncommon — but sometimes this does happen, where a patient with HER2-positive has a fairly early relapse after having received adjuvant or neoadjuvant anti-HER therapy. What do you do about the anti-HER therapy? What do you do about the chemo?

Just to get a little pulse of this — and this is exactly what we've seen in all 3 cities, a real split about how people think this one through — here we presented, Ruth, a patient with a big tumor, gets TCHP, responds, residual disease, gets a year of trastuzumab but then 6 months later has metastatic disease. And you see a real split here between CLEOPATRA and T-DM1. How do you think it through, Ruth?

DR O'REGAN: I do tend to use the CLEOPATRA regimen most times. But she did relapse pretty quickly, so I think, based on MARIANNE, I might consider this patient for T-DM1, actually. I think either of them are reasonable. I think one of the problems we have is that we don't really have any data in the pertuzumab early-stage setting for patients that relapse at this time point. But it makes sense that, since she got those 3 agents from CLEOPATRA before, that maybe you want to go with something different. So I think T-DM1 is totally reasonable.

DR LOVE: Kim, what are your thoughts about it? We hear a lot of questions about chemo partners. And when do you bring back a taxane? A patient's had it a year ago. Now they have progressive disease. Do you use a different taxane? How do you think this through, and what do you think about Ruth's thought about T-DM1?

DR BLACKWELL: T-DM1 should be our initial answer because it's a great drug and it works really well. But this patient is unique in that she had a rapid relapse. I worry a little bit about her HER2 addiction, or her tumor's HER2 addiction. So I ended up answering the CLEOPATRA regimen. I'd give this woman weekly paclitaxel/pertuzumab and trastuzumab, the reason being, in these settings where there's a rapid relapse, I worry a little bit about relying on a drug that really is dependent on HER2 overexpression. That's one reason I would give the CLEOPATRA regimen, or the taxane/trastuzumab/pertuzumab.

The other reason is a very practical one, which is, although we'll get T-DM1 covered in the first-line setting, I try to leave as many options as I can. So there's a biologic reason, which is: I want to throw some chemo on top of the HER2-targeted agents, "free" chemo, in this case weekly paclitaxel, because she did relapse so quickly having our best HER2-targeted agents. And chemo still plays a role in taking care of these patients. Second, it will allow me to maintain as many options for her as possible.

A patient with ER-positive/HER2-positive metastatic disease has a good response to first-line trastuzumab, pertuzumab and docetaxel, and after 6 cycles the docetaxel is stopped. Would you likely add in endocrine treatment at that point or hold off until later in the disease course?