INTERVIEW

William J Gradishar, MD

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Tracks 1-10

Track 1 **Case discussion:** A 60-year-old woman with Stage I, ER-positive, HER2-negative BC initially treated with adjuvant anastrozole presents with an asymptomatic liver metastasis

Track 2 Viewpoint on the results of the Phase III PALOMA-3 trial: Fulvestrant with or without palbociclib in ER-positive, HER2-negative mBC after disease progression on prior endocrine therapy

Track 3 **Case discussion:** A 65-year-old woman with ER-positive mBC receives everolimus/exemestane

Track 4 Management of everolimus-associated mucositis

Track 5 **Case discussion:** A 42-year-old woman with newly diagnosed TNBC experiences a near-complete response to neoadjuvant eribulin/carboplatin on a clinical trial

Track 6 Impact of HER2 and estrogen receptor status on decisions regarding the use of neoadjuvant chemotherapy

Track 7 Perspective of NCCN Breast Committee Chair on the use of (neo)adjuvant pertuzumab

Track 8 **Case discussion:** A 42-year-old woman with a 2.8-cm, ER-positive, HER2-negative BC, a negative sentinel node and an Onco*type* DX® 21-gene Recurrence Score® of 8

Track 9 Application of Onco*type* DX in early-stage, node-positive BC

Track 10 Results of the Phase III Intergroup S0307 study of bisphosphonates as adjuvant therapy for primary BC

Select Excerpts from the Interview

Tracks 2-4

DR LOVE: Would you comment on your clinical experience with palbociclib?

DR GRADISHAR: The data with palbociclib are impressive (1.1, 1.2; page 4), and my experience has been that patients receiving palbociclib don't notice much in terms of side effects. Where the quality of life changes — and I say this somewhat tongue in cheek — is for the physician because rather than administering endocrine therapy and saying, "See you in 3 months," we're saying, "You're receiving palbociclib. You need to come back in 1 month." So we have to be more vigilant about monitoring blood counts regularly.

Neutropenic fevers have been uncommon. Patients do develop asymptomatic neutropenia, but we haven't had to hospitalize anyone. We haven't documented any infections, but for a fair number of patients we've held or reduced the dose. Most of our patients, if not all, have tolerated palbociclib well.

DR LOVE: We are accustomed to sequencing endocrine therapies. Would it make sense to continue the CDK inhibitor and switch the endocrine therapy?

DR GRADISHAR: That's a question I hope we'll address in the future. Trials are evaluating continuing everolimus and switching endocrine therapy. We don't have any data yet, but a similar argument could be made for palbociclib. Using it continuously could be reasonable, but at this time we stop.

I believe with time more patients will receive palbociclib up front and everolimus will be pushed back simply on the basis of tolerability. Patients experience more problems with everolimus. Some have clearly benefited from the combination with hormone therapy, but they can develop mouth sores, peripheral edema and pneumonitis. In many cases we reduce the dose of everolimus from 10 mg to 5 mg to be able to continue therapy. We use the corticosteroid mouthwashes, and they help minimize the symptoms of the mouth sores.

DR LOVE: Do you envision combining adjuvant endocrine therapy with a CDK inhibitor in the future?

DR GRADISHAR: Trials are under way. Another important question is, are we always obligated to use dual therapy? I believe a case can be made for endocrine monotherapy for certain patients with indolent disease.

Track 7

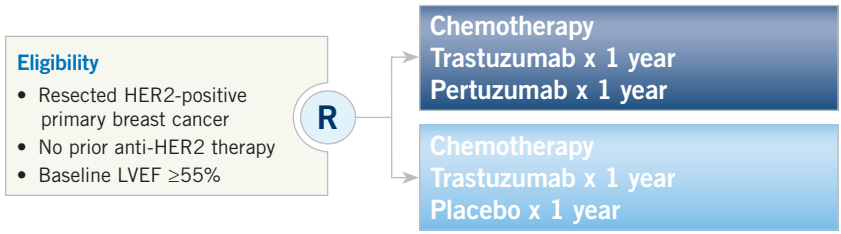
DR LOVE: As chair of the NCCN Breast Cancer Guidelines Panel, would you discuss the debate regarding the use of adjuvant pertuzumab and how it has affected your practice?

DR GRADISHAR: The debate centered on the fact that pertuzumab was FDA approved for use preoperatively within certain criteria — tumors larger than 2 centimeters or with positive nodes. So we had a license to use it in that setting, but in the adjuvant setting we're lacking the data that will come from the APHINITY trial, evaluating pertuzumab-based adjuvant therapy (3.1).

3.1

APHINITY: A Phase III Trial of Pertuzumab in Addition to Chemotherapy and Trastuzumab as Adjuvant Therapy for Patients with HER2-Positive Primary Breast Cancer

Protocol ID: NCT01358877 **Enrollment:** 4,805



LVEF = left ventricular ejection fraction

Primary endpoint: Invasive disease-free survival

www.clinicaltrials.gov. Accessed October 2015.

However, the group believes that if you see a patient postoperatively who would have been a candidate for preoperative pertuzumab, that patient should have the same opportunity to receive the agent after surgery. The language is purposely a little vague about the duration, but we did suggest in the NCCN guidelines that it would be reasonable to administer pertuzumab postoperatively. If you elected to do that, you could administer it for a similar duration to what you would use preoperatively.

I have personally administered adjuvant pertuzumab to a couple of my patients. However, both were prepared to pay for the treatment themselves and are now doing so. But I am not overly eager to administer it for a full year, at least until we have data from the APHINITY study.

Track 10

DR LOVE: Would you discuss the results of the long-awaited SWOG-S0307 study of bisphosphonates as adjuvant therapy for primary breast cancer (Gralow 2015)?

DR GRADISHAR: This was a trial of 3 different bone-targeted agents — zoledronic acid, ibandronate and clodronate. All of the efficacy parameters were perfectly superimposable. No difference was observed among the 3 arms.

The toxicity was also comparable. The incidence of osteonecrosis of the jaw was slightly higher among patients who received zoledronic acid, but the difference was about half a percentage point. So I don't want to say the trial was a "wash," but it didn't tell us that one agent is better. A majority of patients who participated in the trial indicated a preference for oral bisphosphonate formulations. The author concluded that these oral agents should therefore be made available in the United States.

DR LOVE: The hope was that using zoledronic acid would result in less disease recurrence. Do you believe these results negate that idea?

DR GRADISHAR: That effect would be difficult to identify in this trial. Some advocates believe that bisphosphonates can affect disease recurrence in breast cancer, but it's debatable. I have not seen any data that address the issue definitively. ■

SELECT PUBLICATIONS

A randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. NCT01358877

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). **Adjuvant bisphosphonate treatment in early breast cancer: Meta-analyses of individual patient data from randomised trials.** *Lancet* 2015;386(10001):1353-61.

Gianni L et al. **Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): A randomised multicentre open-label phase 2 trial.** *Lancet Oncol* 2012;13(1):25-32.

Gralow J et al. **Phase III trial of bisphosphonates as adjuvant therapy in primary breast cancer: SWOG/Alliance/ECOG-ACRIN/NCIC Clinical Trials Group/NRG Oncology study S0307.** *Proc ASCO* 2015;**Abstract 503**.

Turner NC et al. **Palbociclib in hormone-receptor–positive advanced breast cancer.** *N Engl J Med* 2015;373(3):209-19.

Turner NC et al. **PALOMA3: A double-blind, phase III trial of fulvestrant with or without palbociclib in pre- and post-menopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy.** *Proc ASCO* 2015;**Abstract LBA502**.