INTERVIEW

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Tracks 1-10

Track 1	**Case discussion:** A 55-year-old woman with ER/PR-positive, HER2-negative Stage I BC and an Onco*type* DX RS of 17 who declines chemotherapy and receives tamoxifen followed by anastrozole
Track 2	Prognostic and predictive utility of the Breast Cancer Index for ER-positive BC
Track 3	Evaluation of the Breast Cancer Index in patients with ER-positive, HER2-positive BC for risk of late recurrence and potential benefit of extended endocrine therapy
Track 4	**Case discussion:** A 40-year-old woman with ER/PR-positive, HER2-negative BC and de novo metastatic disease to the bones and liver
Track 5	Effect of primary tumor resection on outcomes for patients with mBC
Track 6	Efficacy of the CDK4/6 inhibitor palbociclib with letrozole as first-line therapy or with fulvestrant as second-line therapy for ER-positive, HER2-negative mBC
Track 7	Incorporation of palbociclib and everolimus into the treatment algorithm for patients with ER-positive mBC
Track 8	Clinical trials with palbociclib or everolimus combined with adjuvant endocrine therapy
Track 9	Discordant expression of hormone receptors in primary and metastatic tumors
Track 10	Activity and tolerability of the novel agents abemaciclib and ribociclib for ER-positive mBC

Select Excerpts from the Interview

Tracks 1-3

DR LOVE: Could you discuss how you integrate the 21-gene Recurrence Score for patients with breast cancer in your practice?

DR O'REGAN: I use the Onco*type* DX assay broadly. I use it for approximately 90% of my patients with node-negative breast cancer. For node-positive disease, I use it often for patients with 1 to 3 positive lymph nodes. My preference would be to enroll these patients with node-positive disease in the SWOG-S1007 (RxPONDER) study, but I will occasionally order it even off study. I believe that the cancer biology rather than the nodal status is important. But I haven't made the jump to do it in patients with many positive lymph nodes because that's not currently accepted. However, I believe that's where we're heading.

DR LOVE: Would you talk about the Breast Cancer Index and how it can be used to predict risk of recurrence and the benefit of extended adjuvant therapy?

DR O'REGAN: The Breast Cancer Index is a combination of the endocrine response biomarker H/I (HoxB13/IL17BR) and the 5-gene molecular grade index. This is the one molecular assay that has been shown to be able to predict which patients with ER-positive, node-negative breast cancer will benefit from extended adjuvant endocrine treatment. The caveat is that it was based on the MA.17 trial in which patients received tamoxifen and were transitioned to letrozole (Sgroi 2013a).

The Breast Cancer Index was also able to predict the risk of recurrence up to 10 years. Up front, like the Recurrence Score, patients can be classified into 3 risk groups — low, intermediate and high. When determining recurrence risk at 5 to 10 years, 2 groups of patients can be identified: the low-risk group is one and the intermediate- and high-risk groups come together. Patients in the intermediate- and high-risk group are more likely to experience a recurrence in years 5 to 10 versus the low-risk group (Sgroi 2013b).

I usually use the Breast Cancer Index to explain to patients why it's important to stay on endocrine therapy rather than to tell them they don't need more endocrine therapy because I'm a little cautious about that.

DR LOVE: Would you discuss the study you presented at ASCO 2015 evaluating the Breast Cancer Index in patients with ER-positive, HER2-positive breast cancer for risk of late recurrence and benefit of extended endocrine therapy?

DR O'REGAN: Before this study, I had always believed that patients with ER-positive, HER2-positive breast cancer who made it to 5 years were unlikely to experience recurrence. This study showed that compared to patients with HER2-negative breast cancer, those with HER2-positive disease had a higher risk of recurrence during years 5 to 10. Also, more patients with HER2-positive tumors benefited from extended endocrine therapy than those in the HER2-negative group (O'Regan 2015; [4.1]).

I hadn't considered using the Breast Cancer Index for patients with ER-positive, HER2-positive breast cancer before this study, but these results indicate that it may

4.1

Evaluation of the Breast Cancer Index (BCI) to Assess Risk of Late Recurrence and Potential Extended Endocrine Therapy (EET) Benefit for Patients with ER-Positive, HER2-Positive Breast Cancer

BCI risk classification	HER2-positive cohort (n = 140)	HER2-negative cohort (n = 1,042)
BCI prognostic	**Risk of late recurrence**	
Low	13%	54%
High	87%	46%
BCI predictive	**Likelihood of benefit from EET**	
Low	32%	62%
High	68%	38%

Conclusions:

- BCI classified a higher proportion of HER2-positive/HR-positive tumors as being associated with high risk for late recurrence and a high likelihood of benefitting from EET compared to those that are HER2-negative/HR-positive. However, a subset of HER2-positive tumors are classified as low risk for late recurrence by BCI.
- A significant proportion of the HER2-positive cohort was predicted to benefit from EET.

O'Regan R et al. *Proc ASCO* 2015;**Abstract 595**.

be helpful in determining which of these patients should continue endocrine therapy beyond 5 years.

Tracks 6-7

DR LOVE: The CDK4/6 inhibitor palbociclib recently received accelerated approval for use as first-line therapy in combination with letrozole for postmenopausal women with ER-positive, HER2-negative mBC. Would you discuss your clinical experience with this agent?

DR O'REGAN: A side effect of concern with palbociclib is neutropenia (Turner 2015). Serious infections can occur. If we administer it in the first-line setting, patients must come in for blood counts by day 15. It's now also recommended that blood counts be checked on day 21 of the first cycles so that the dose can be adjusted if necessary.

A certain subset of patients probably do not need palbociclib in the first-line setting and would fare well with endocrine therapy. We need to define who those patients are because we are changing the whole game plan for them now.

DR LOVE: In what situations would you use palbociclib for a postmenopausal woman who experiences relapse while receiving an adjuvant AI?

DR O'REGAN: The disease-free interval would be the important determining factor. If a patient experienced relapse within 1 or 2 years, I would consider palbociclib. For a late recurrence, I might consider endocrine therapy alone, particularly for an older patient, although we have not observed any indication that older patients experience more toxicity. So for patients with de novo metastatic disease or patients who have a long disease-free interval, I would consider holding palbociclib until later.

DR LOVE: Beyond the first-line setting, how do you incorporate palbociclib versus everolimus in your practice?

DR O'REGAN: I would tend to use palbociclib before everolimus because the efficacy data support palbociclib. That agent has shown positive results in the first-line setting, and we do not have the data with everolimus. However, for a patient who experiences relapse after having received a nonsteroidal AI in the adjuvant setting, either of them could be administered. Palbociclib is not approved outside the first-line setting, so that would be another consideration, although I haven't had a problem obtaining approval since the ASCO meeting. ■

SELECT PUBLICATIONS

Finn RS et al. **The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): A randomised phase 2 study.** *Lancet Oncol* 2015;16(1):25-35.

O'Regan R et al. **Evaluation of the Breast Cancer Index in patients with HER2+/HR+ breast cancer for risk of late recurrence and potential extended endocrine benefit.** *Proc ASCO* 2015;**Abstract 595**.

Sgroi D et al. **Prediction of late disease recurrence and extended adjuvant letrozole benefit by the HOXB13/IL17BR biomarker.** *J Natl Cancer Inst* 2013a;105(14):1036-42.

Sgroi D et al. **Prediction of late distant recurrence in patients with oestrogen-receptor-positive breast cancer: A prospective comparison of the breast-cancer index (BCI) assay, 21-gene recurrence score, and IHC4 in the TransATAC study population.** *Lancet Oncol* 2013b;14(11):1067.

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