INTERVIEW

Kathy S Albain, MD

Dr Albain is Professor of Medicine at Loyola University Chicago Stritch School of Medicine and Director of the Breast Clinical Research and Thoracic Oncology Programs at Cardinal Bernardin Cancer Center in Maywood, Illinois.

Tracks 1-8

Track 1 RxPONDER: A Phase III trial of adjuvant endocrine therapy with or without chemotherapy for patients with node-positive BC and a Recurrence Score® (RS) of 25 or lower

Track 2 Metabolic syndrome and recurrence within the Onco*type* DX® assay RS risk categories in node-negative BC

Track 3 **Case discussion:** A 55-year-old woman with strongly ER-positive, HER2-negative, T1cN1M0 BC with 2 of 5 positive sentinel lymph nodes

Track 4 Role of molecular profiling assays in BC

Track 5 **Case discussion:** A 46-year-old woman with a 2.5-cm, ER-negative, HER2-positive, node-negative infiltrating ductal carcinoma

Track 6 ATLAS trial results: Continuing adjuvant tamoxifen to 10 years versus stopping at 5 years for ER-positive early BC

Track 7 Results of the Phase III SWOG-S0226 trial of first-line anastrozole with or without fulvestrant for postmenopausal women with ER-positive mBC

Track 8 Clinical experience with first-line treatment with the combination of anastrozole and fulvestrant

Select Excerpts from the Interview

Tracks 1-2, 4

DR LOVE: Would you discuss the ongoing Phase III adjuvant RxPONDER trial?

DR ALBAIN: The RxPONDER trial is evaluating standard adjuvant endocrine therapy with or without chemotherapy for patients with hormone receptor-positive, HER2-negative breast cancer with an Onco*type* DX Recurrence Score (RS) of 25 or lower and with 1 to 3 positive nodes (2.1).

The RxPONDER trial was originally proposed to include patients with any number of positive nodes, but oncologists may be nervous about offering endocrine therapy only and no chemotherapy to a patient with 6 positive nodes and an RS of 2. In this scenario, the biology indicates that the disease will probably be chemotherapy insensitive, no matter how many nodes are positive. Perhaps clinical trials will show that endocrine therapy with everolimus and no chemotherapy is the correct treatment choice.

We are currently deliberating whether to amend the eligibility criteria for the RxPONDER trial now that it's accruing well by including patients with more than 3 positive nodes. These deliberations are under way, and we must wait for the outcome.

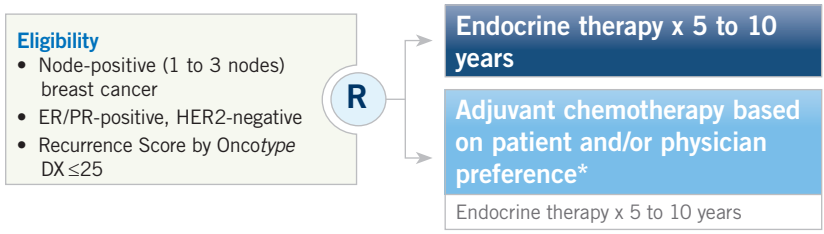
DR LOVE: Would you talk about the design and results of your analysis evaluating the association between metabolic syndrome and the risk of recurrence based on the

2.1

Phase III Randomized Clinical Trial of Adjuvant Endocrine Therapy with or without Chemotherapy in Node-Positive Breast Cancer

Protocol IDs: SWOG-S1007; RxPONDER

Target Accrual: 4,000



* Multiple agents that can be used in various combinations and different schedules, including doxorubicin, epirubicin, 5-FU, cyclophosphamide, paclitaxel, docetaxel and methotrexate

www.clinicaltrials.gov. Identifier NCT01272037, July 2013.

Oncotype DX assay RS for patients with newly diagnosed ER-positive, node-negative breast cancer (Lakhani 2012; [2.2])?

DR ALBAIN: We performed a chart review to determine the relationship between components of metabolic syndrome such as obesity and diabetes and the Oncotype DX RS. We found that although recurrence risk is low in the patient group with the luminal A subtype, a major independent predictor of risk level is the presence or absence of metabolic syndrome. Conducting more aggressive interventional studies may lead to a survival advantage for patients with such tumor characteristics.

We always discuss with patients the benefits of weight loss, diabetes control and exercise. However, a more intensive, prospectively designed approach for this patient population may be warranted. Although this was a small, hypothesis-generating, retro-

2.2

Retrospective Study of Metabolic Syndrome (MS) and Breast Cancer Recurrence within the Oncotype DX Assay Recurrence Score (RS) Risk Categories for Patients with ER-Positive, Lymph Node (LN)-Negative Breast Cancer Treated with Standard Adjuvant Therapy (N = 332)

Oncotype DX risk category	Odds ratio (presence versus absence of MS)	95% CI (odds ratio)
Low risk (RS 0-17)	23.649	2.818-198.435
Intermediate risk (RS 18-30)	3.950	0.984-15.852
High risk (RS 31-100)	0.813	0.063-10.478

Conclusions

- MS is an independent risk factor for breast cancer recurrence among women with low-risk, ER-positive, LN-negative breast cancer treated with standard adjuvant therapy.
- MS has an effect on recurrence for patients with a tumor biology defined by the Oncotype DX assay RS as low risk or, to a lesser extent, intermediate risk.
- No difference in recurrence risk is reported for patients who are at high risk of breast cancer recurrence according to the Oncotype DX assay RS.

Lakhani A et al. San Antonio Breast Cancer Symposium 2012;**Abstract PD10-02**.

spective study, the results are intriguing. We need to validate it with a larger sample size, after which we may be able to propose a new treatment approach.

DR LOVE: Would you comment on other genomic assays being investigated beyond the 21-gene RS?

DR ALBAIN: One is the BluePrint™ assay, which provides the intrinsic breast cancer subtype. Unlike the 21-gene RS, this approach has not been validated in a prospective Phase III trial.

The BluePrint is an 80-gene expression signature that classifies breast cancer into 3 categories: basal, luminal and HER2 types. For patients with breast cancer classified as luminal type with BluePrint, conducting the MammaPrint® assay to assess whether they are at low or high risk of recurrence provides deeper insight into whether they have luminal A- or B-type disease.

We also have the PAM50 assay, which is a paraffin block application of intrinsic molecular subtyping to classify recurrence risk. In the neoadjuvant setting studies indicated that patients at low recurrence risk by the PAM50 assay did not achieve pathologic complete responses (Gomez Pardo 2011). Although all these profiling assays are prognostic, it is uncertain whether they are equally predictive of benefit from chemotherapy.

DR LOVE: Over the 10 years since the Onco*type* DX assay was first developed, many studies have investigated these predictive signatures retrospectively rather than prospectively. What is your perspective on the future clinical approach to validating and expanding on the existing molecular profiling signatures?

DR ALBAIN: The only 2 studies with tamoxifen-only control arms that banked tissue samples were the NSABP-B-20 and SWOG-8814 trials. The newer TAILORx and RxPONDER trials have a rich bank of tumor specimens that will allow studies of the new generation of predictors, which will expand beyond 21 or 70 genes in the near future. We are proposing to conduct a next-generation sequencing analysis of the residual RNA samples from the SWOG-8814 trial. We have enough banked tissue to ask more questions, but we need to be careful about how we expend the remaining resources. ■

SELECT PUBLICATIONS

Albain KS et al. **Prognostic and predictive value of the 21-gene Recurrence Score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial.** *Lancet Oncol* 2010;11(1):55-65.

Dowsett M et al. **Comparison of PAM50 risk of recurrence score with Onco*type* DX and IHC4 for predicting risk of distant recurrence after endocrine therapy.** *J Clin Oncol* 2013;[Epub ahead of print].

Gomez Pardo P et al. **PAM50 intrinsic subtyping and pathologic responses to neoadjuvant trastuzumab-based chemotherapy in HER2-positive breast cancer.** *Proc ASCO* 2011;**Abstract 554**.

Goncalves R, Bose R. **Using multigene tests to select treatment for early-stage breast cancer.** *J Natl Compr Canc Netw* 2013;11(2):174-82.

Lakhani A et al. **Metabolic syndrome and recurrence within the 21-gene Recurrence Score assay risk categories in lymph node negative breast cancer.** San Antonio Breast Cancer Symposium 2012;**Abstract PD10-02**.

Mamounas EP et al. **Association between the 21-gene Recurrence Score (RS) and benefit from adjuvant paclitaxel (Pac) in node-positive (N+), ER-positive breast cancer patients (pts): Results from NSABP B-28.** San Antonio Breast Cancer Symposium 2012;**Abstract S1-10**.

Ramsey SD et al. **Integrating comparative effectiveness design elements and endpoints into a phase III, randomized clinical trial (SWOG S1007) evaluating Onco*type* DX-guided management for women with breast cancer involving lymph nodes.** *Contemp Clin Trials* 2013;34(1):1-9.