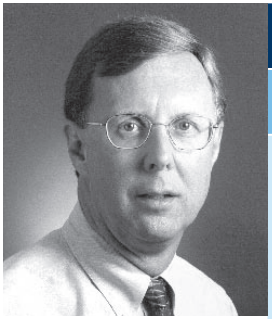


INTERVIEW

C Kent Osborne, MD

Dr Osborne is Dudley and Tiny Sharp Chair in Cancer Research, Director of the Dan L Duncan Cancer Center, Director of the Lester and Sue Smith Breast Center and Professor of Medicine and Molecular and Cellular Biology at Baylor College of Medicine in Houston, Texas.

Tracks 1-12

Track 1 Emerging role of PARP inhibitors in the treatment of BC and other solid tumors

Track 2 Association between DNA repair signature and response to anthracyclines in TNBC

Track 3 Objectives of the ASCO/College of American Pathologists guidelines for ER testing with immunohisto-chemistry (IHC)

Track 4 Discordance in measurement of ER between primary BC and metastatic disease after hormonal therapy

Track 5 Analysis of the BIG 1-98 trial: Up-front letrozole versus switching from tamoxifen to letrozole or vice versa

Track 6 Potential mechanisms of tumor resistance to endocrine therapy

Track 7 Differing mechanisms of acquired resistance to trastuzumab and lapatinib in HER2-positive BC

Track 8 Potential explanation for the apparent benefit of adjuvant trastuzumab for patients with HER2-normal BC

Track 9 EMBRACE trial: Improved survival with eribulin mesylate (E7389) compared to physician's choice of treatment for patients with previously treated locally recurrent BC or mBC

Track 10 Prognostic and predictive value of the Onco*type* DX assay for postmenopausal women with ER-positive, node-positive BC who are receiving chemotherapy

Track 11 Defining the role of sentinel lymph node resection compared to conventional axillary lymph node dissection in BC

Track 12 Value of IHC in the evaluation of lymph nodes of patients with lobular BC

Select Excerpts from the Interview

Track 9

DR LOVE: What are your thoughts on the study presented at ASCO this year on the novel agent eribulin mesylate (3.1)?

DR OSBORNE: Eribulin mesylate is a new chemotherapeutic agent that is derived from a marine sponge and works as a microtubule inhibitor. We participated in the trial, and the data appear promising (Twelves 2010; [3.2]). A survival advantage was evident among patients with advanced breast cancer who had previously received a median of four regimens. Typically our

standard chemotherapy drugs do not show a survival advantage in this setting, so that was interesting. In view of this, I would be interested in seeing its activity in earlier lines of therapy compared to other standard agents.

3.1

EMBRACE: An Open-Label, Global Phase III Study Comparing Eribulin Mesylate to Treatment of Physician's Choice (TPC) in Locally Recurrent or Metastatic Breast Cancer

Accrual: 762

Eligibility

Locally recurrent or metastatic breast cancer

- Two to five prior chemotherapies
- Received two or more chemotherapy regimens for advanced disease

Prior anthracyclines and taxanes

R

2:1

Eribulin mesylate 1.4 mg/m²; 2-5 min IV days 1, 8 q21d

TPC*

* Any monotherapy (chemotherapy, hormonal, biologic) or supportive care

Twelves C et al. *Proc ASCO* 2010;**Abstract CRA1004**.

3.2

EMBRACE Phase III Study: Efficacy Data of Eribulin versus Treatment of Physician's Choice (TPC) in Locally Recurrent or Metastatic Breast Cancer

	Eribulin (n = 508)	TPC[1] (n = 254)	Hazard ratio	*p*-value
Median overall survival	13.1 months	10.7 months	0.81	0.041
One-year survival	53.9%	43.7%	—	—
Median PFS (independent review)	3.7 months	2.2 months	0.87	0.14
Median PFS (investigator review)	3.6 months	2.2 months	0.76	0.002
Overall response	12.2%	4.7%	—	0.0002

[1] No patients on the TPC arm received biologic therapy alone or supportive care.
PFS = progression-free survival

Twelves C et al. *Proc ASCO* 2010;**Abstract CRA1004**.

Track 10

DR LOVE: As a coauthor of the paper published in *Lancet Oncology* that evaluated the Onco*type* DX assay in patients with node-positive breast cancer, would you comment on the clinical implications of this study?

DR OSBORNE: The growing body of data indicating that certain patients with node-positive disease fare well with hormonal therapy alone led us to

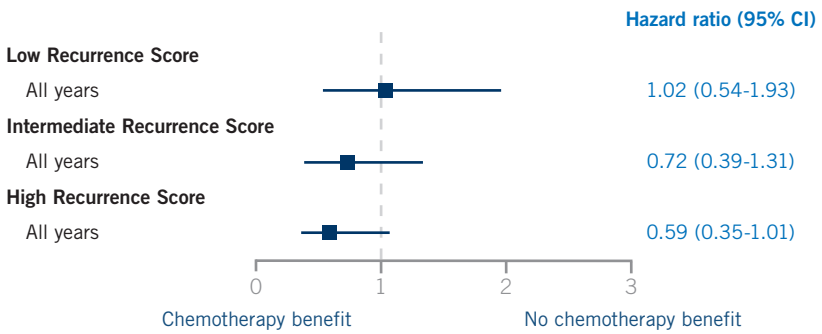
retrospectively evaluate the 21-gene Onco*type* DX assay for approximately 40 percent of the patients who participated in the SWOG-8814 trial.

Our analysis of the Onco*type* DX assay in patients with node-positive breast cancer demonstrated that a much larger proportion of patients who might not receive additional benefit with adjuvant chemotherapy could be identified by the Recurrence Score than by ER and HER2 scores alone (Albain 2010; [3.3]). Patients with low Recurrence Scores don't benefit from chemotherapy, but patients with high Recurrence Scores clearly obtain a substantial benefit (Albain 2009).

It is interesting to note that a strong trend for benefit from adjuvant chemotherapy was evident in patients with intermediate Recurrence Scores, which is different than what was seen in an analysis of patients with node-negative breast cancer (Paik 2004). I must caution that this was a retrospective analysis of a fraction of the larger clinical trial. Therefore, these findings are not definitive, but they are similar to observations that patients with endocrine-responsive tumors don't benefit from chemotherapy. I have changed my practice, and I infrequently use adjuvant chemotherapy for patients with strongly ER-positive, PR-positive, HER2-negative tumors with a low Ki-67 or low Recurrence Scores, even if the nodes are positive. ■

3.3

Disease-Free Survival Hazard Ratios for Tamoxifen Alone versus CAF-T According to Recurrence Risk Group



Albain KS et al. *Lancet Oncol* 2010;11(1):55-65.

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.

Paik S et al. **A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer.** *N Engl J Med* 2004;351(27):2817-26.

Twelves C et al. **A phase III study (EMBRACE) of eribulin mesylate versus treatment of physician's choice in patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane.** *Proc ASCO* 2010;**Abstract CRA1004**.