INTERVIEW

Nicholas J Robert, MD

Dr Robert is Associate Chair of US Oncology Research Network's Breast Cancer Committee and Chairman of the Cancer Committee of Inova Fairfax Hospital's Cancer Center in Fairfax, Virginia.

Tracks 1-11

Track 1	**Case discussion:** A 73-year-old woman with TNBC experiences relapse five years after initial adjuvant dose-dense chemotherapy and enrolls on a clinical trial of iniparib (BSI-201) with chemotherapy
Track 2	Use of bevacizumab in the management of metastatic BC
Track 3	Clinical trial strategies for investigating PARP inhibitors in early BC
Track 4	Perspective on the choice of HER2-directed therapy in the adjuvant setting for HER2-positive early BC
Track 5	Biology and biomarker-driven personalized therapy for BC
Track 6	**Case discussion:** A 55-year-old woman with ER-positive, HER2-negative metastatic BC receives multiple hormonal therapies followed by enrollment on the RIBBON 1 trial of capecitabine/bevacizumab
Track 7	Antitumor efficacy of fulvestrant and relation to the dose used
Track 8	Use of the Onco*type* DX assay in patients with ER-positive, node-negative or node-positive BC in the adjuvant and neoadjuvant settings
Track 9	Treatment for patients with HER2-positive recurrent BC and prior exposure to trastuzumab
Track 10	Eribulin as a novel antitubular agent with efficacy in BC
Track 11	Challenges with overall survival as the primary endpoint for first-line therapy in metastatic BC

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you tell us about your patient with TNBC?

DR ROBERT: This is a 73-year-old woman who initially presented with T2N1+ TNBC approximately six years ago. She received dose-dense chemotherapy in the adjuvant setting and experienced relapse four years later with biopsy-proven pleural disease. At the time of disease recurrence she received iniparib with carboplatin/gemcitabine in a randomized Phase II trial (O'Shaughnessy 2011; [2.2, page 8]). Her tolerance to the regimen was excellent, and her disease was controlled for approximately 18 months on iniparib with carboplatin/gemcitabine.

DR LOVE: What treatment would you have recommended off protocol?

DR ROBERT: If she had not enrolled on the iniparib trial, then at the time an alternative for her as a patient with TNBC would have been bevacizumab with weekly paclitaxel. When we incorporate bevacizumab into treatment of metastatic breast cancer, we generally use it in the first line with weekly paclitaxel.

DR LOVE: What do we know about chemotherapy with bevacizumab in patients with TNBC as opposed to those with other subtypes?

DR ROBERT: Several bevacizumab trials have taken place in the first-line metastatic breast cancer setting: ECOG-E2100, AVADO and RIBBON 1. These trials combined different chemotherapy regimens with bevacizumab. When evaluating the TNBC subset, we see enhanced efficacy when bevacizumab is added to chemotherapy (O'Shaughnessy 2010; [5.1]).

5.1

Meta-Analysis of Patients with Triple-Negative Breast Cancer Randomly Assigned in First-Line Trials of Chemotherapy with or without Bevacizumab for Metastatic Breast Cancer

	Bevacizumab + chemotherapy (n = 363)	Chemotherapy alone (n = 258)	HR	*p*-value
ORR	42%	23%	NR	<0.0001
Median PFS	8.1 months	5.4 months	0.649	<0.0001
12-month survival rate	70.9%	64.8%	NR	0.1140
Median OS	18.9 months	17.5 months	0.959	0.6732

HR = hazard ratio; ORR = objective response rate; NR = not reported; PFS = progression-free survival; OS = overall survival

O'Shaughnessy J et al. San Antonio Breast Cancer Symposium 2010;**Abstract P6-12-03**.

Track 8

DR LOVE: Would you comment on the data combining clinicopathologic factors with the Onco*type* DX RS that were presented at San Antonio (Tang 2010)?

DR ROBERT: My takeaway from the presentation is that we are still left with the current RS and the modification of the RS did not translate to be useful in the clinic.

With that said, until we have the results of the TAILORx trial, in a patient with an intermediate RS, a number of other clinical factors — such as age, tumor size and tumor grade — come into play.

In the case of a lower-grade, smaller tumor in an older patient with an intermediate RS, we are more comfortable administering endocrine therapy alone.

My older patients — that is, those who are postmenopausal — usually decline the idea of pursuing even a short course of adjuvant chemotherapy if they hear of any doubt about additional benefit with the adjuvant chemotherapy approach in the clinical setting.

Track 10

DR LOVE: Would you discuss what we know about eribulin?

DR ROBERT: Eribulin is a unique analog of the marine sponge natural product halichondrin B and is a potent mitotic inhibitor. Our group was involved in the pivotal randomized Phase III EMBRACE trial, which randomly assigned patients to eribulin or physician's choice.

The results of the trial showed improved outcomes on the eribulin arm (Twelves 2010; [5.2]). On the basis of the results of this trial, the drug was approved by the FDA and now adds to the armamentarium against metastatic breast cancer. ■

5.2

EMBRACE Trial: Eribulin versus Treatment of Physician's Choice (TPC) for Patients with Previously Treated Locally Recurrent or Metastatic Breast Cancer

Endpoint (ITT population)	Eribulin	TPC	Hazard ratio	*p*-value
Median OS (n = 508, 254)	13.1 mo	10.6 mo	0.81	0.041
Median PFS* (n = 508, 254)	3.7 mo	2.2 mo	0.87	0.14
ORR* (CR + PR) (n = 468, 214)	12.2%	4.7%	—	0.002
CBR* (CR + PR + SD) (n = 468, 214)	22.6%	16.8%	—	—

* Independent review

ITT = intent to treat; OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; CBR = clinical benefit rate; SD = stable disease ≥6 months

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

SELECT PUBLICATIONS

O'Shaughnessy J et al. **Iniparib plus chemotherapy in metastatic triple-negative breast cancer.** *N Engl J Med* 2011;364(3):205-14.

O'Shaughnessy J et al. **Meta-analysis of patients with triple-negative breast cancer (TNBC) from three randomized trials of first-line bevacizumab (BV) and chemotherapy treatment for metastatic breast cancer (MBC).** San Antonio Breast Cancer Symposium 2010;**Abstract P6-12-03**.

Tang G et al. **Comparing the prediction of chemotherapy benefit in patients with node-negative, ER-positive breast cancer using the recurrence score and a new measure that integrates clinical and pathologic factors with the recurrence score.** San Antonio Breast Cancer Symposium 2010;**Abstract S4-9**.

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**.