INTERVIEW

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Tracks 1-15

Track 1 Association between molecular subtype of BC and clinical outcome

Track 2 Effect of the Onco*type* DX RS on treatment selection for patients with ER-positive, node-negative or node-positive BC

Track 3 Clinical use of the Onco*type* DX assay for patients with ER-positive early BC

Track 4 Utility of the MammaPrint assay in clinical practice

Track 5 Patient compliance, treatment-related symptoms and secondary resistance with endocrine therapy

Track 6 Inhibition of the phosphatidylinositol 3-kinase pathway as a therapeutic target in patients with ER-positive BC

Track 7 Phase II study of low- versus high-dose estradiol therapy in ER-positive, AI-resistant mBC

Track 8 Emerging data with the estrogen receptor downregulator fulvestrant alone and in combination with anastrozole for ER-positive mBC

Track 9 Perspective on administration schedule of high-dose fulvestrant

Track 10 Heterogeneity in the pharmacology among PARP inhibitors under development

Track 11 Perspective on the clinical use of bevacizumab as first- and second-line therapy for mBC

Track 12 Novel mechanisms of action of the nontaxane microtubule inhibitor eribulin mesylate in mBC

Track 13 Role of anthracyclines in the treatment of HER2-positive early BC

Track 14 Therapeutic options for patients with HER2-positive mBC previously treated with trastuzumab

Track 15 Treatment options when transitioning patients with ER-positive mBC from endocrine therapy to chemotherapy

Select Excerpts from the Interview

Tracks 8-9

DR LOVE: Would you summarize the key current data sets with fulvestrant in advanced breast cancer and where we are moving with this drug?

DR ELLIS: The so-called "FIRST" trial compared fulvestrant 500 mg to anastrozole as first-line treatment for advanced breast cancer (Robertson

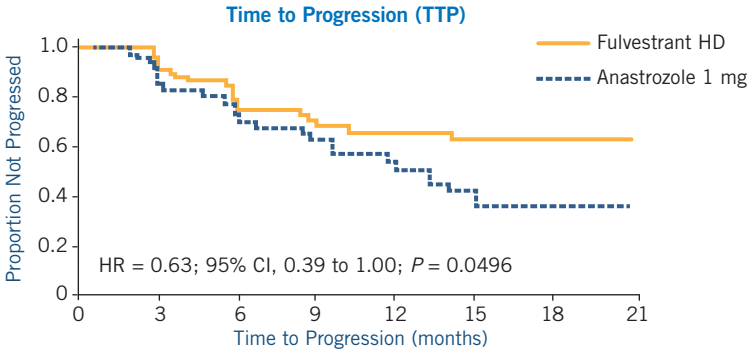
2009; [4.1]). Another study evaluated two doses of fulvestrant in the second-line setting. Evidence from the dose response curve indicated that increasing from 250 mg to 500 mg appeared to be of clinical benefit (di Leo 2010; [4.2]). So both of those trials suggest that the higher dose is more active. Moving forward I believe fulvestrant will be a good partner for combination therapy. I believe we'll be administering more high-dose fulvestrant and evaluating fulvestrant in combination with a variety of signal transduction inhibitors, including the PI3 kinase.

DR LOVE: How do you currently approach fulvestrant dosing in your practice outside of a protocol setting?

DR ELLIS: I'm not convinced the loading dose makes any difference because the curves don't break in favor of the higher dose until two or three months. I administer 500 mg on day one, 500 mg on day 29 and don't bring the patient back in for that extra dose at 14 days. Patients seem to tolerate this approach well.

4.1

FIRST Study: Fulvestrant 500 mg versus Anastrozole for ER-Positive Advanced Breast Cancer



Primary endpoint	Fulvestrant HD (n = 102)	Anastrozole 1 mg (n = 103)	*p*-value
Clinical benefit rate (CBR)*	72.5%	67.0%	0.386

* CBR = complete response + partial response + stable disease ≥ 24 weeks

"The high CBRs for fulvestrant HD and anastrozole of 72.5% and 67.0%, respectively, confirm the high clinical efficacy of both agents. Furthermore, results from the analysis of the primary end point (CBR) indicated that fulvestrant HD was at least as effective as anastrozole. The secondary end points further confirmed the activity of fulvestrant HD in this setting, most notably median TTP, which was estimated to be 60% longer in patients treated with fulvestrant HD compared with TTP for those treated with anastrozole, a statistically significant difference. DoR and DoCB data also favored fulvestrant HD. This is the first clinical trial to compare fulvestrant with anastrozole in first-line advanced breast cancer and to show that another endocrine agent may be more effective than a third-generation AI in this setting."

Robertson JFR et al. *J Clin Oncol* 2009;27(27):4530-5.

4.2

CONFIRM: A Phase III Trial of Fulvestrant 250 mg versus Fulvestrant 500 mg in ER-Positive Advanced Breast Cancer

	Fulvestrant 500 mg (n = 362)	Fulvestrant 250 mg (n = 374)	Hazard ratio	*p*-value
Median progression-free survival	6.5 months	5.5 months	0.80	0.006
Clinical benefit rate*	45.6%	39.6%	—	—

* Clinical benefit rate = complete response + partial response + stable disease ≥ 24 weeks

Di Leo A et al. *J Clin Oncol* 2010;28(30):4594-600.

Track 11

DR LOVE: What are your thoughts on the overall survival data meta-analysis of bevacizumab and first-line chemotherapy presented at ASCO 2010, and what's the bottom line in terms of how you put together the effect of this agent and its clinical utility?

DR ELLIS: We've discovered that bevacizumab doesn't have single-agent activity in breast cancer and is an obligatory chemotherapy partner. We need more research on bevacizumab to understand the correct population in which to use it. I believe, based on the data, that for patients who need a rapid response — such as those who have visceral crisis, lung and liver disease with increasing LFTs or shortness of breath — a bevacizumab-based regimen seems to yield a benefit faster.

This might be the patient population we should focus on to ascertain if a survival benefit exists with bevacizumab, as all the trials performed in Europe and the United States included a number of patients with more indolent disease for whom death from breast cancer was not a near-term likelihood. Thus survival was difficult to show. ■

SELECT PUBLICATIONS

Di Leo A et al. **Results of the CONFIRM phase III trial comparing fulvestrant 250 mg with fulvestrant 500 mg in postmenopausal women with estrogen receptor-positive advanced breast cancer.** *J Clin Oncol* 2010;28(30):4594-600.

O'Shaughnessy J et al. **A meta-analysis of overall survival data from three randomized trials of bevacizumab (BV) and first-line chemotherapy as treatment for patients with metastatic breast cancer (MBC).** *Proc ASCO* 2010;**Abstract 1005**.

Robertson JFR et al. **A comparison of fulvestrant 500 mg with anastrozole as first-line treatment for advanced breast cancer: Follow-up analysis from the 'FIRST' study.** San Antonio Breast Cancer Symposium 2010;**Abstract S1-3**.

Robertson JF et al. **Activity of fulvestrant 500 mg versus anastrozole 1 mg as first-line treatment for advanced breast cancer: Results from the FIRST study.** *J Clin Oncol* 2009;27(27):4530-5.