INTERVIEW

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Tracks 1-10

Select Excerpts from the Interview

Tracks 2-3

DR LOVE: Would you discuss the efficacy and tolerability observed with enzalutamide in your Phase II trial for patients with advanced androgen receptor (AR)-positive triple-negative breast cancer (TNBC) (Traina 2015; [2.1])?

DR TRAINA: TNBC accounts for about 20% of all breast cancer. Based on the enzalutamide prospective screening, as many as 55% of triple-negative cases had some degree of AR expression. In this study, we observed the first RECIST-confirmed responses elicited by an antiandrogen in TNBC, including a patient with a complete response. Such responses were not observed with bicalutamide in the Phase II TBCRC 011 trial (Gucalp 2013).

We also observed radiographic responses with symptom improvement and resolution of pleural effusions, and the duration of response was quite long. In the trial, the primary endpoint was clinical benefit rate (CBR) at ≥16 weeks, which was 35%. CBR at 24 weeks was also determined, and this was 29%. This suggests that patients are able to have at least stable disease for 6 months with a simple daily oral endocrine option, which in comparison to standard cytotoxics, such as taxanes or platinums, enzalutamide is extremely well tolerated.

In terms of side effects, fatigue was noted on the Phase II trial but not to a large degree. Compared to what has been observed in the prostate cancer setting, use of enzalutamide was not associated with any seizure activity. Some patients experienced a bit of fogginess or cognitive slowdown, but these were simply managed by switching the administration of the drug from morning to evening.

Separate from TNBC, we see high coexpression of AR with estrogen receptor. In ER-positive breast cancer, it's as high as 80% coexpression. As resistance to estrogen-targeted therapies develops, dependence on AR signaling increases, so antiandrogens may have a role in breast cancers that are resistant to antiestrogen therapy. That's one area of interest now in clinical trials.

A Phase II trial of enzalutamide and exemestane in patients with estrogen or progesterone receptor-positive breast cancer is ongoing (NCT02007512). Patients are randomly assigned to receive exemestane in combination with enzalutamide or placebo. We anticipate a report of at least some of the results from that trial this year.

Because ER-positive breast cancer has a luminal-type profile, we believe that mechanisms of resistance involving enzymes such as PI3 kinase or CDK might play a role. A multicenter Phase I/II trial of enzalutamide with or without the PI3 kinase inhibitor taselisib for patients with AR-positive metastatic TNBC is ongoing (NCT02457910). A small Phase II trial by Memorial Sloan Kettering Cancer Center to investigate an AR antagonist in combination with palbociclib is also planned.

2.1

MDV3100-11: Efficacy and Safety Results of a Phase II Trial of Enzalutamide for Patients with Advanced Androgen Receptor (AR)-Positive, Triple-Negative Breast Cancer

		Intention-to-treat (ITT) population according to PREDICT AR status*	
Efficacy	**Evaluable patients** (n = 75)	**AR-positive** (n = 56)	**AR-negative** (n = 62)
CR/PR	8%	9%	3%
CBR at 16 weeks	35%	39%	11%
CBR at 24 weeks	29%	36%	6%
Median PFS	14.7 weeks	16.1 weeks	8.1 weeks
Median OS	NR	NYR	32.1 weeks
TRAEs in ITT (n = 118)	**All grades**	**Grade ≥3**	
Fatigue	34%	5%	
Nausea	25%	0%	
Constipation	8%	1%	
Back pain	2%	1%	
Dyspnea	4%	1%	

CR = complete response; PR = partial response; CBR = clinical benefit rate; PFS = progression-free survival; OS = overall survival; NR = not reported; NYR = not yet reached; TRAEs = treatment-related adverse events

* PREDICT AR is a genomic signature associated with androgen biology to predict response to enzalutamide in triple-negative breast cancer.

Traina TA et al. *Proc ASCO* 2015;**Abstract 1003**.

Track 5

DR LOVE: What are your thoughts on the results of the Phase III Study 301 trial of eribulin versus capecitabine for patients with locally advanced or metastatic breast cancer previously treated with anthracyclines and taxanes (Kaufman 2012, 2015)?

DR TRAINA: In the overall study population, both agents yielded equivalent efficacy. However, in the subset population of patients with TNBC, a trend was evident in favor of eribulin compared to capecitabine. Eribulin is well tolerated. The main side effects are neutropenia and neuropathy. Although the earlier Phase III EMBRACE trial compared eribulin to treatment of physician's choice, that study had no statistical power or ability to compare eribulin to each chosen agent (Cortes 2011).

In my practice, I see less of a problem with neutropenia in earlier lines of therapy. We're able to manage neutropenia with dose reductions and with growth factor support. Eribulin is a reasonable option, but I am uncertain how it compares to paclitaxel as first-line therapy in terms of efficacy.

Track 10

DR LOVE: Can you discuss the results of the prospective trial of the scalp hypothermia system for preventing chemotherapy-induced alopecia in women with Stage I to Stage II breast cancer that were presented at ASCO 2015 (Rugo 2015)?

DR TRAINA: Those results are inspiring, suggesting that the use of the scalp hypothermia system when administering certain (neo)adjuvant chemotherapy regimens, excluding taxanes and anthracyclines, could result in a success rate of approximately 70% in alleviating alopecia to a degree such that women would not require a wig. The downside is that these hypothermal caps are quite laborious and challenging to wear. One of the systems that we've used requires multiple caps. The burden is largely on the patient to bring dry ice in coolers or employ professional "cappers." For those for whom alopecia is a real obstacle, I believe it's a reasonable preventive measure.

The results of this study have been practice changing. We give patients written educational materials about this option and have the resources available so that, if a patient would like to pursue the cold cap strategy, we have the mechanism in place. ■

SELECT PUBLICATIONS

Cortes J et al. **Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): A phase 3 open-label randomised study.** *Lancet* 2011;377(9769):914-23.

Gucalp A et al. **Phase II trial of bicalutamide in patients with androgen receptor-positive, estrogen receptor-negative metastatic breast cancer.** *Clin Cancer Res* 2013;19(19):5505-12.

Kaufman PA et al. **Phase III open-label randomized study of eribulin mesylate versus capecitabine in patients with locally advanced or metastatic breast cancer previously treated with an anthracycline and a taxane.** *J Clin Oncol* 2015;33(6):594-601.

Kaufman PA et al. **A phase III, open-label, randomized, multicenter study of eribulin mesylate versus capecitabine in patients with locally advanced or metastatic breast cancer previously treated with anthracyclines and taxanes.** San Antonio Breast Cancer Symposium 2012;**Abstract S6-6**.

Rugo HS et al. **Clinical performance of the DigniCap system, a scalp hypothermia system, in preventing chemotherapy-induced alopecia.** *Proc ASCO* 2015;**Abstract 9518**.

Rugo HS et al. **Use of the DigniCap system to prevent hair loss in women receiving chemotherapy (CTX) for Stage I breast cancer.** San Antonio Breast Cancer Symposium 2012;**Abstract P2-12-11**.