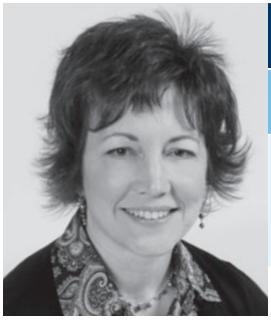

INTERVIEW

Kathy D Miller, MD

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CD 1, Tracks 16-25 — CD 2, Tracks 1-4

CD 1

Track 16 **Second opinion:** Onco*type* DX to guide adjuvant chemotherapy decision-making for patients with limited nodal involvement

Track 17 **Second opinion:** Radiation therapy in older patients with ER-positive BC

Track 18 **Second opinion:** Hormonal therapy versus chemotherapy for patients with advanced ER-positive mBC

Track 19 **Second opinion:** Continuation of trastuzumab in responding patients with advanced HER2-positive mBC

Track 20 **Case discussion:** A 30-year-old woman with recurrent ER-positive, HER2-positive mBC 7 years after completion of adjuvant chemotherapy/trastuzumab on the pivotal NCCTG-N9831 trial

Track 21 Complete response for 2 years with capecitabine/bevacizumab in a patient with ER-positive, "nonfunctional" HER2-positive mBC

Track 22 Impact of chemotherapy partner with bevacizumab for mBC

Track 23 Nanoparticle albumin-bound (*nab*) paclitaxel in the treatment of BC

Track 24 Incorporating eribulin into the treatment algorithm for mBC

Track 25 **Case discussion:** A 68-year-old woman who received adjuvant AC chemotherapy 5 years earlier for Stage I triple-negative BC (TNBC) whose disease recurs with widespread bone metastases

CD 2

Track 1 Potential for false negativity from biomarker assessment on bone

Track 2 Treatment of metastatic TNBC with oral cyclophosphamide and methotrexate on a metronomic schedule

Track 3 Is there a role for a "treatment holiday" in the management of mBC?

Track 4 Consideration of bone-targeted therapy for patients with TNBC and bone metastases

Select Excerpts from the Interview

CD 1, Tracks 16-17, 19

DR LOVE: In which clinical situations have you provided second opinions that commonly differ from those of the first oncologist?

DR MILLER: One issue that comes up frequently is whether or not to administer chemotherapy in the adjuvant setting. We recently had a 43-year-old woman with a Grade I, ER-positive tumor and 1 positive node referred to us for a second opinion by her surgeon, who was surprised that the oncologist had not ordered an Onco*type* DX assay.

The patient had basically been told, "You have a positive node and the standard is that you'll receive chemotherapy," and she was literally scheduled for her first treatment the

day after her second-opinion visit with us. One of my partners at Indiana University talked with her about the Onco*type* DX assay, and they agreed it would be helpful in her treatment decision-making process. She ended up having a Recurrence Score of 6. Now she is not getting chemotherapy.

DR LOVE: Have there been other situations in which there has been disparity between your opinion and what the community oncologist recommended?

DR MILLER: I've recently seen 3 patients with metastatic breast cancer whose local oncologist had suggested that they stop trastuzumab because they'd experienced a great response and the oncologist thought it would be a good time for the patients to take a break. I've suggested maybe not.

One patient was a 32-year-old woman with metastatic disease who'd experienced a complete response to chemotherapy/trastuzumab. Chemotherapy had been stopped due to cumulative toxicity, but the patient continued on trastuzumab alone. She was nearing completion of a total year of trastuzumab and it was suggested that she stop. After some discussion the decision was made to continue trastuzumab.

DR LOVE: Would you discuss some of the data that are available to support this approach?

DR MILLER: The strategy of all past trials was to continue trastuzumab at least until progression. We now have data from trials by Drs von Minckwitz (von Minckwitz 2011) and Kim Blackwell (Blackwell 2010) that indicate continuing or reinstituting trastuzumab after progression on trastuzumab-based therapy improves response, progression-free survival and overall survival (2.1). So if continuing or restarting trastuzumab improves overall survival, it seems hard not to come to the conclusion that arbitrarily stopping it would decrease survival.

DR LOVE: Those are certainly interesting cases. In what other areas do these discrepancies arise?

2.1

Continuation of Anti-HER2 Therapy Beyond Disease Progression in Patients with Trastuzumab-Refractory Metastatic Breast Cancer

	GBG 26/BIG 3-05[1,2]		EGF104900[3]	
	Cape	Cape + T	L	L + T
Median TTP[1] or PFS[3]	5.6 mo	8.2 mo	8.1 wk	12.0 wk
	HR, 0.69; $p = 0.0338$		HR, 0.73; $p = 0.008$	
Clinical benefit rate	54.1%	75.3%	12.4%	24.7%
	$p = 0.0068$		$p = 0.01$	
Median overall survival	20.6 mo	24.9 mo	39.0 wk	51.6 wk
	HR, 0.94; $p = 0.73$		HR, 0.75; $p = 0.106$	
Postprogression survival (PPS)*	13.3 mo	18.8 mo	N/E	
	HR, 0.63; $p = 0.02$			

* PPS according to anti-HER2 treatment versus not as part of third-line treatment
Cape = capecitabine; T = trastuzumab; L = lapatinib; TTP = time to progression; PFS = progression-free survival; HR = hazard ratio; N/E = not evaluated

[1] Von Minckwitz G et al. *J Clin Oncol* 2009;27(12):1999-2006; [2] Von Minckwitz G et al. *Eur J Cancer* 2011;47(15):2273-81; [3] Blackwell KL et al. *J Clin Oncol* 2010;28(7):1124-30.

DR MILLER: Issues arise over the use of radiation therapy after breast-conserving surgery in older patients, specifically those older than age 70 for whom we have randomized trial data evaluating the benefits of breast irradiation after lumpectomy in those with ER-positive tumors (Hughes 2010; [2.2]).

I'm often perplexed as to why patients older than age 70 with T1 or T2, ER-positive tumors who've had a lumpectomy rarely hear about the results from that trial. What they hear is, "You had a lumpectomy. You should receive radiation therapy." I've seen women who are 82 and sick who have not heard of this trial even though they tell me they asked the radiation oncologist 3 times, "Do I really need radiation therapy?" because they were worried about toxicity or having to come back and forth because they don't drive or a younger family member has to take off work to bring them.

So these patients come to me for hormone therapy and often ask, "Do I really need this radiation therapy?" There are trade-offs, of course. Radiation oncologists examine these data and say, "Absolutely, radiation therapy works. There was a lower rate of local recurrence."

The issue is the following: Is the difference so great that radiation therapy should be mandated in this setting, or was the risk of local recurrence in women who didn't undergo radiation therapy in a range such that some women would be comfortable saying, "I just don't see the need. At my age, with my other health issues, with all of the logistics and practicalities involved, that just doesn't make sense to me." ■

2.2

CALGB-9343: 10-Year Follow-Up from a Phase III Study of Lumpectomy and Tamoxifen (Tam) with or without Radiation Therapy (RT) for Older Patients (Age 70 or Older) with Early Breast Cancer

	Tam + RT (n = 317)	Tam (n = 319)	*p*-value
Ipsilateral breast tumor recurrence rate	2%	9%	0.0001
10-year overall survival rate	67%	67%	NS
Breast preservation rate	98%	96%	NS
Distant metastasis rate	95%	95%	NS

Conclusions:

- In older women, the benefits of RT after lumpectomy are small.
- With modern margins and use of aromatase inhibitors, RT will likely have even less benefit.
- Omitting RT in women age 70 or older with clinical Stage I breast cancer is a reasonable alternative.

Hughes KS et al. *Proc ASCO* 2010;**Abstract 507**.

SELECT PUBLICATIONS

Blackwell KL et al. **Randomized study of lapatinib alone or in combination with trastuzumab in women with ErbB2-positive, trastuzumab-refractory metastatic breast cancer.** *J Clin Oncol* 2010;28(7):1124-30.

Hughes KS et al. **Lumpectomy plus tamoxifen with or without irradiation in women age 70 or older with early breast cancer.** *Proc ASCO* 2010;**Abstract 507**.

Von Minckwitz G et al. **Trastuzumab beyond progression: Overall survival analysis of the GBG 26/BIG 3-05 phase III study in HER2-positive breast cancer.** *Eur J Cancer* 2011;47(15):2273-81.

Von Minckwitz G et al. **Trastuzumab beyond progression in human epidermal growth factor receptor 2-positive advanced breast cancer: A German Breast Group 26/Breast International Group 03-05 study.** *J Clin Oncol* 2009;27(12):1999-2006.