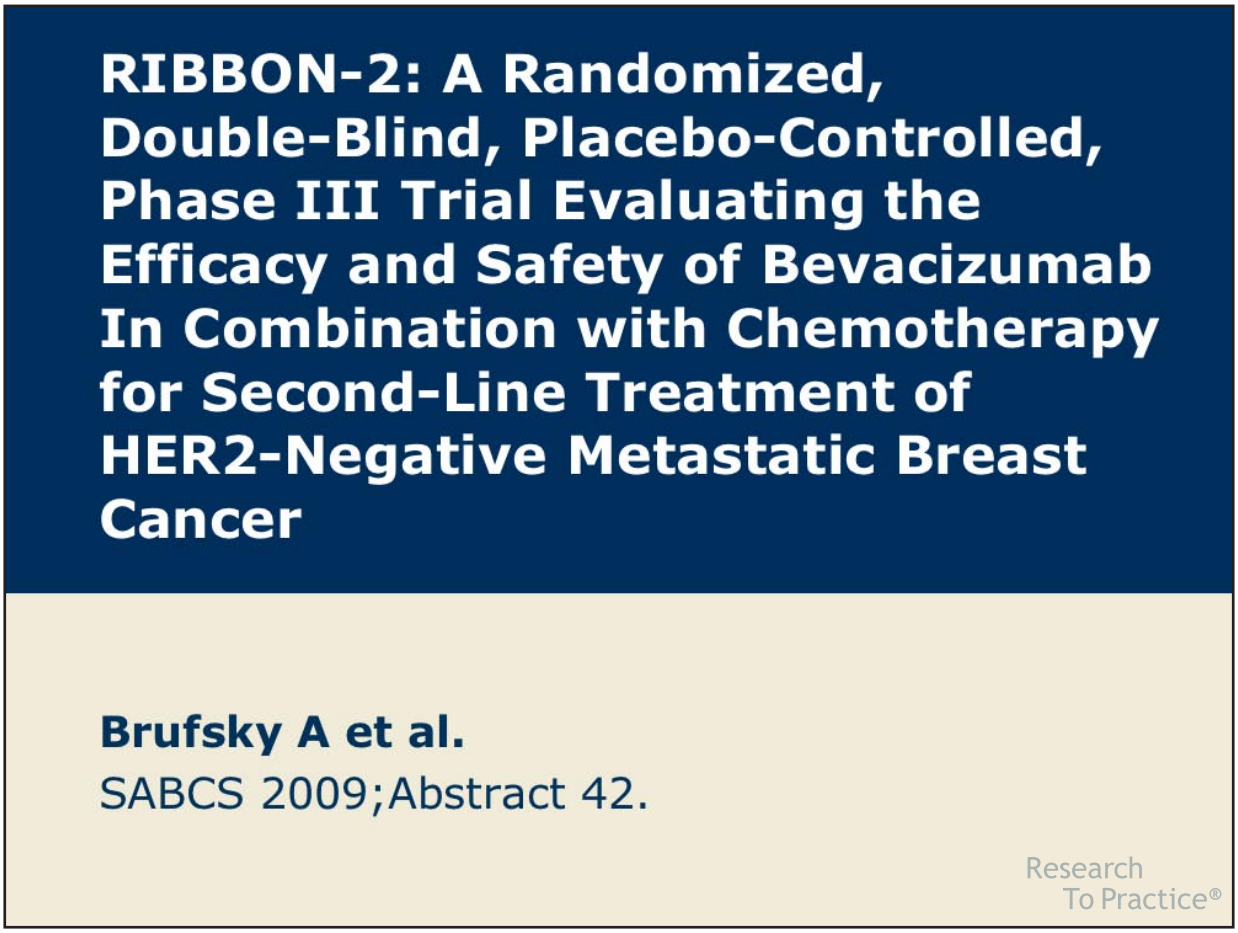
RIBBON 2 — A Phase III Trial of Second-Line Bevacizumab in Combination with Chemotherapy for HER2-Negative Metastatic Breast Cancer

Presentation discussed in this issue:

Brufsky A et al. **RIBBON-2: A randomized, double-blind, placebo-controlled, Phase III trial evaluating the efficacy and safety of bevacizumab in combination with chemotherapy for second-line treatment of HER2-negative metastatic breast cancer.** San Antonio Breast Cancer Symposium 2009;**Abstract 42**.

Editor's comment: At the end of this slide set are several graphics with results from a recent Patterns of Care study of 100 US-based medical oncologists.

Slides from a presentation at SABCS 2009



Introduction

- Phase III trials have reported improved progression-free survival (PFS) with 1st-line bevacizumab (bev) combined with chemotherapy versus chemotherapy alone in the metastatic breast cancer (mBC) setting.
  - ECOG-E2100 PFS: 11.8 mos vs. 5.9 mos (*NEJM* 2007;357:2666)
  - AVADO PFS: 8.8 mos vs. 8.0 mos (SABCS 2009;Abstract 41)
- Phase III AVF2119g trial of bev combined with capecitabine in patients with heavily pretreated mBC did not meet its primary PFS endpoint, but reported a significant increase in the objective response rate (*JCO* 2005;23:792).
- **Current study objectives:**
  - Evaluate the clinical benefit of combining bev with various chemotherapy regimens used to treat patients with mBC in the second-line setting.

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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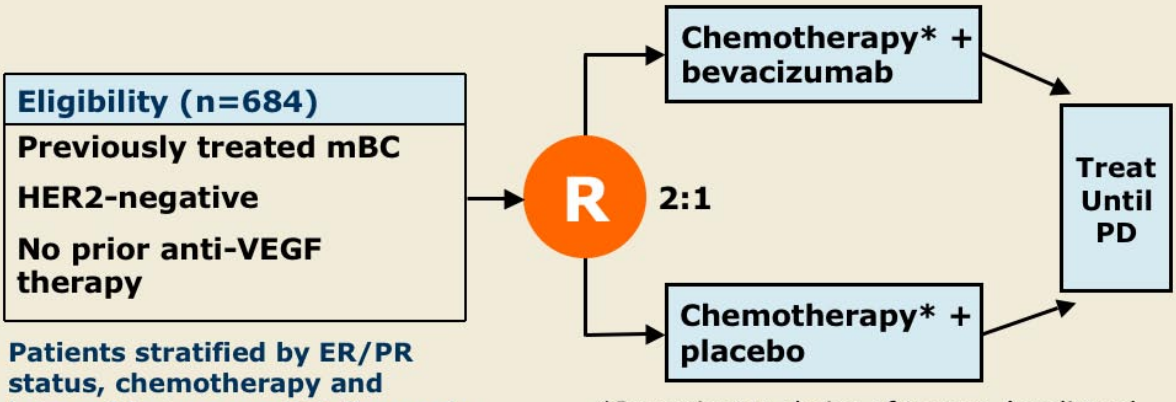
RIBBON-2 Study Design



Patients stratified by ER/PR status, chemotherapy and interval between mBC diagnosis and first disease progression (PD).

**Investigator choice of taxane (paclitaxel, nab paclitaxel, or docetaxel) OR gemcitabine OR capecitabine OR vinorelbine*

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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Efficacy Analysis (Intent-to-treat Population)

	Chemo + bev (n = 459)	Chemo (n = 225)	Hazard ratio	*p*-value
Median PFS	7.2 mos	5.1 mos	0.78	0.0072
Median overall survival *	18.0 mos	16.4 mos	0.90	0.3741
1-year survival rate	69.5%	66.2%	—	—

*Interim analysis at 57% information (315 events).

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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PFS: Cohort Specific Analyses (Intent-to-treat Population)

Cohort	Chemo + bev (n = 459)		Chemo (n = 225)		
	Events	Median (mos)	Events	Median (mos)	Hazard ratio
All subjects (n=684)	372/459	7.2	184/225	5.1	0.78
Chemotherapy					
Taxanes (n=304)	151/201	8.0	84/103	5.8	0.64
Gemcitabine (n=160)	84/108	6.0	43/52	5.5	0.90
Capecitabine (n=144)	87/97	6.9	39/47	4.1	0.73
Vinorelbine (n=76)	50/53	5.7	18/23	7.0	1.42

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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Efficacy Analysis (continued)

	Chemo + bev	Chemo	*p* value
Objective response rate*	39.5%	29.6%	0.0193†
Complete response	2.2%	1.1%	
Partial response	37.3%	28.5%	
Duration of response	7.3 mos	7.5 mos	—

* Includes only patients with measurable disease at baseline.
† p-value for ORR was not significant according to pre-specified limit of 0.01.

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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Select Adverse Events ≥ Grade 3 (Safety Population)

Adverse Event*	Chemo + bev (n = 458)	Chemo (n = 221)
Neutropenia	17.7%	14.5%
Hypertension	9.0%	0.5%
Sensory neuropathy	6.3%	5.9%
Proteinuria	3.1%	0.5%
Febrile neutropenia	2.2%	2.7%
Bleeding events	1.7%	0%
Arterial thrombotic event	0.7%	1.4%

**Shown are only those adverse events with an incidence of ≥1%.*

Source: Brufsky A et al. SABCS 2009;Abstract 42.

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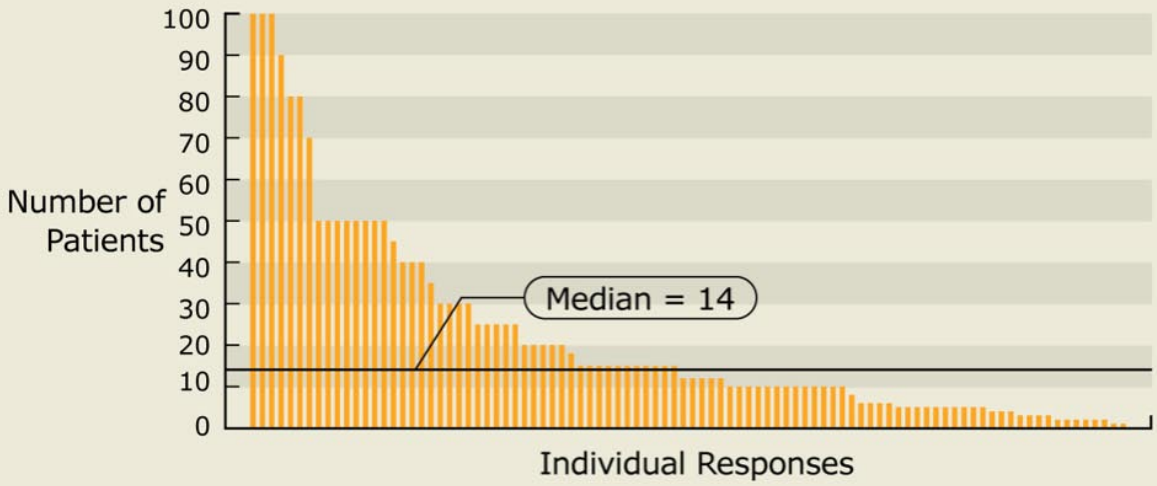
Conclusions

- RIBBON-2 is the first randomized Phase III study demonstrating an advantage for adding bevacizumab to chemotherapy in the second-line metastatic setting.
- RIBBON-2 demonstrated benefit for the combination of bevacizumab with standard second-line chemotherapy versus chemotherapy alone.
  - PFS: 7.2 mos vs 5.1 mos (p = 0.0072)
- PFS results were generally consistent across all chemotherapy cohorts with the exception of a small vinorelbine sub-group.
- Adverse event profile of bevacizumab was consistent with that of previous studies in mBC.

Source: Brufsky A et al. SABCS 2009;Abstract 42.

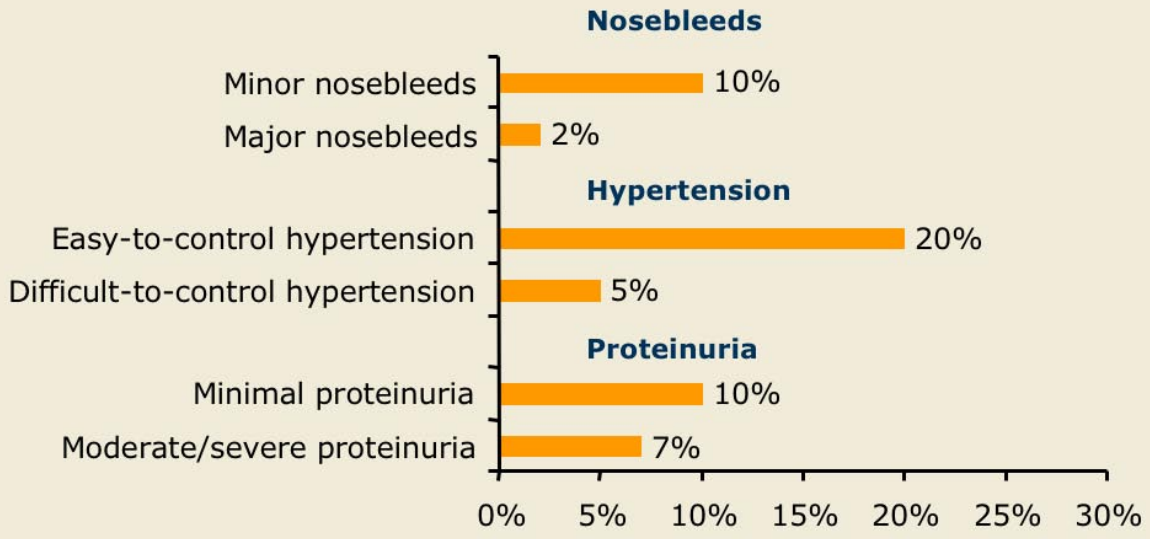
How many cases of breast cancer have you treated with bevacizumab?

Responses from the 96 physicians who have used bevacizumab to treat breast cancer



Source: Patterns of Care in Breast Cancer — Survey of 100 US-Based Medical Oncologists

What proportion of your patients who receive bevacizumab develop the following complications? (Median)



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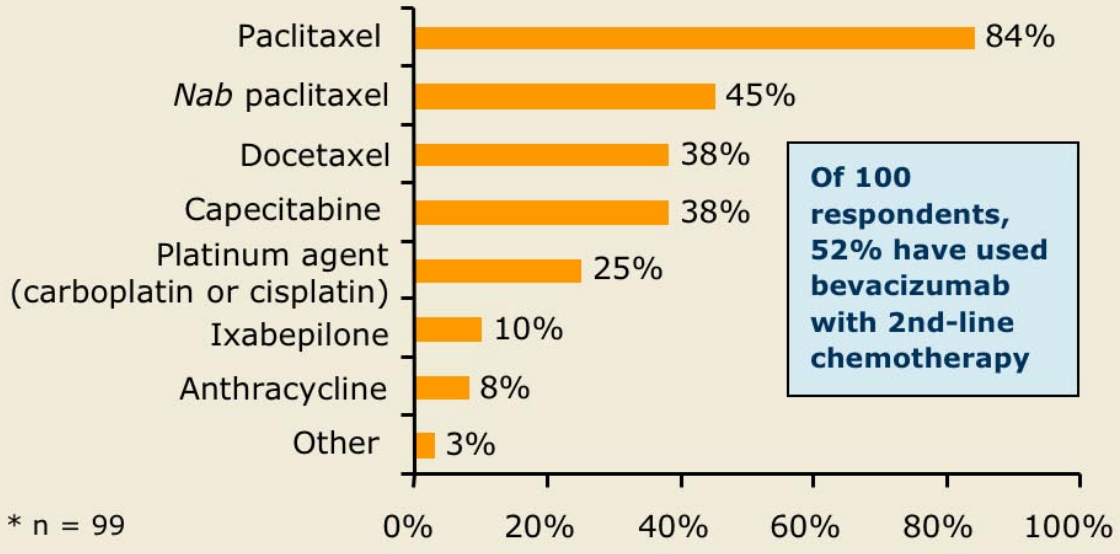
Source: Patterns of Care in Breast Cancer — Survey of 100 US-Based Medical Oncologists

Which chemotherapy agents have you combined with bevacizumab?* (Check all that apply)



* n = 99

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Source: Patterns of Care in Breast Cancer — Survey of 100 US-Based Medical Oncologists