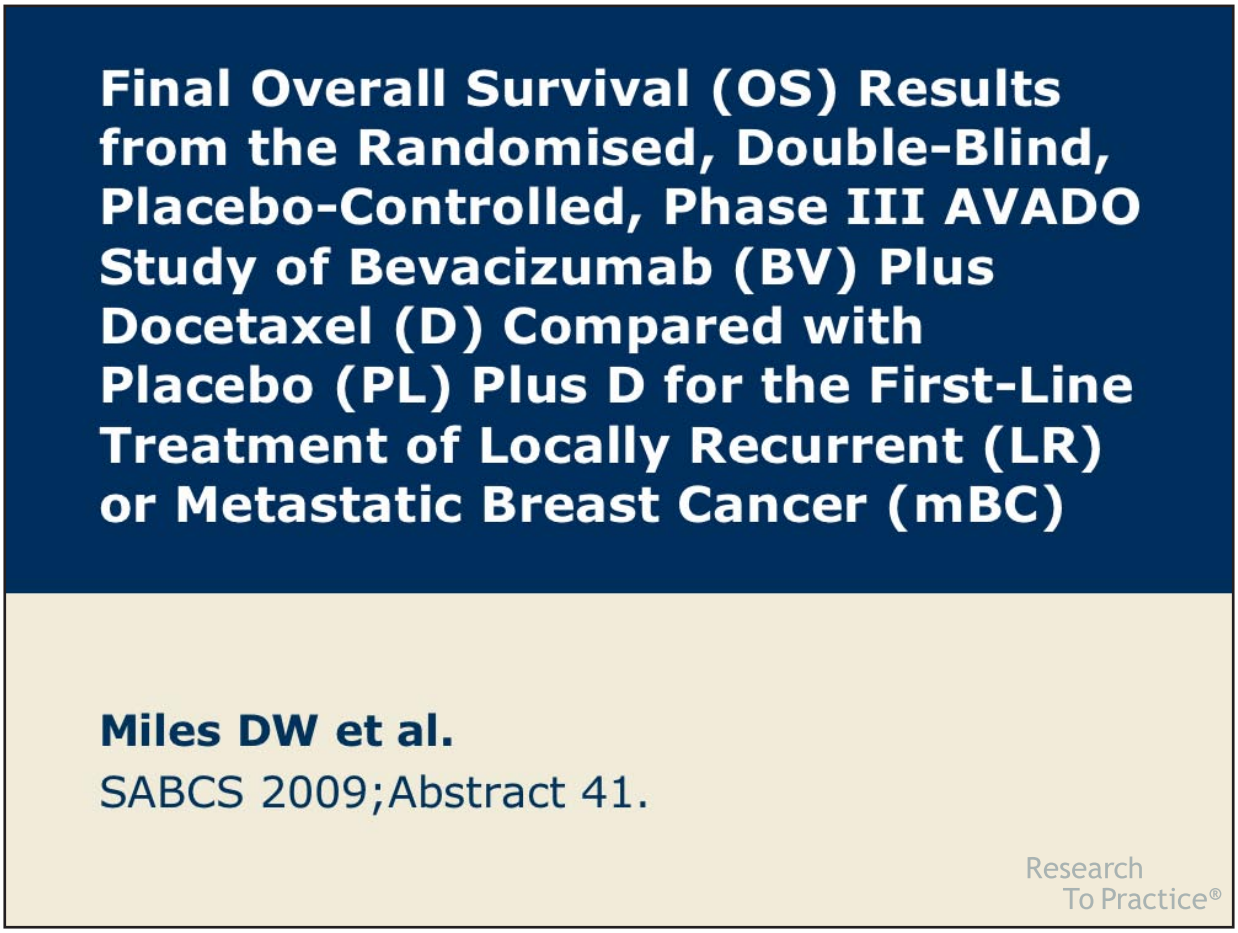
AVADO — Final Overall Survival Results of First-Line Docetaxel in Combination with Escalating Doses of Bevacizumab for HER2-Negative Metastatic Breast Cancer

Presentation discussed in this issue:

Miles DW et al. **Final overall survival (OS) results from the randomised, double-blind, placebo-controlled, Phase III AVADO study of bevacizumab (BV) plus docetaxel (D) compared with placebo (PL) plus D for the first-line treatment of locally recurrent (LR) or metastatic breast cancer (mBC).** San Antonio Breast Cancer Symposium 2009;**Abstract 41**.

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



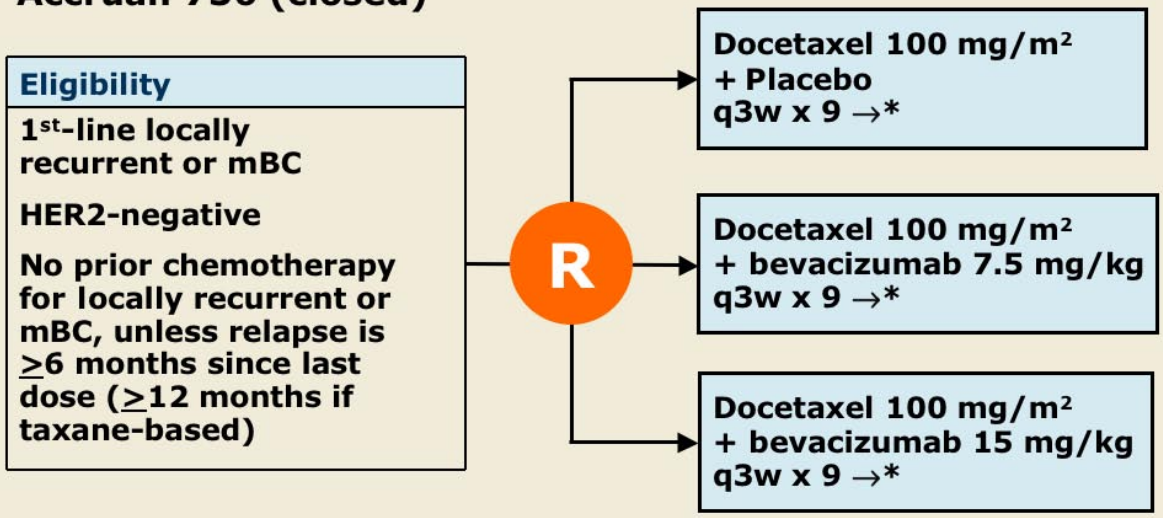
Introduction

- Three Phase III trials (AVADO[1], ECOG-2100[2], and RIBBON-1[3]) have reported positive results with bevacizumab (BV) in the first-line mBC setting ([1]ASCO 2008;LBA1011, [2]NEJM 2007;357:2666, [3]ASCO 2009;1005).
- AVADO demonstrated significantly improved progression-free survival (PFS) with BV plus docetaxel (D) at 10 months follow-up.
  - Median PFS: 8.7 mos (7.5 mg/kg BV + D), 8.8 mos (15 mg/kg BV + D), and 8.0 mos (D + placebo).
- Final overall survival (OS) and updated results of other study endpoints at 25 months follow-up are presented in the current analysis from the AVADO study.

Source: Miles DW et al. SABCS 2009;Abstract 41.

AVADO Study Design

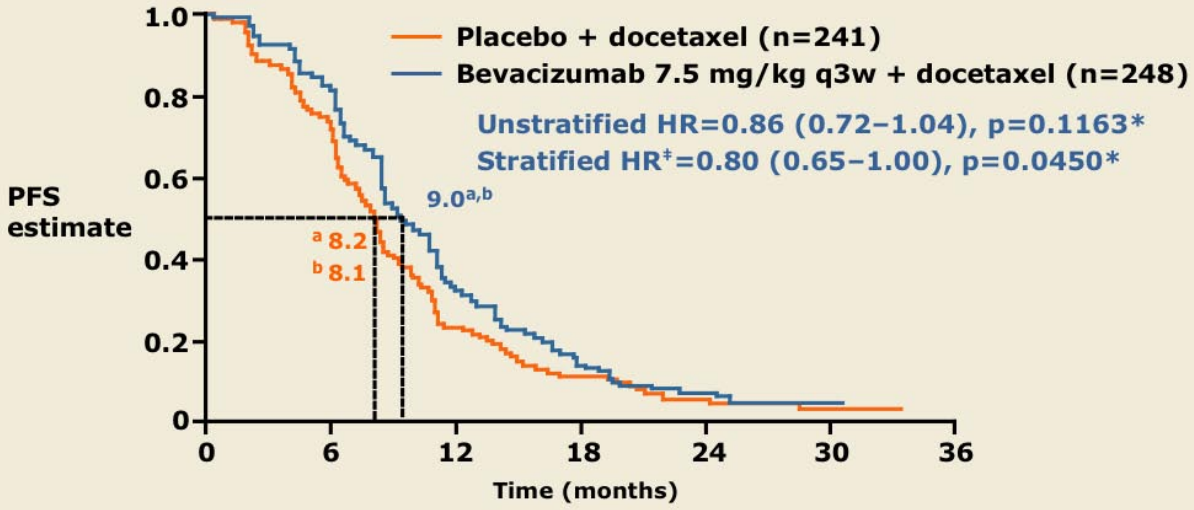
Accrual: 736 (closed)



**Bevacizumab or placebo administered until disease progression*

Sources: Miles DW et al. SABCS 2009;Abstract 41; Miles DW et al. ASCO 2008;LBA1011.

Updated PFS Analysis (Bev 7.5 mg/kg dose)



Intent-to-treat analysis; *p values are of exploratory nature
‡Censored for non-protocol therapy prior to progressive disease;
[a] unstratified; [b] stratified

Source: With permission from Miles DW et al. SABCS 2009;Abstract 41.

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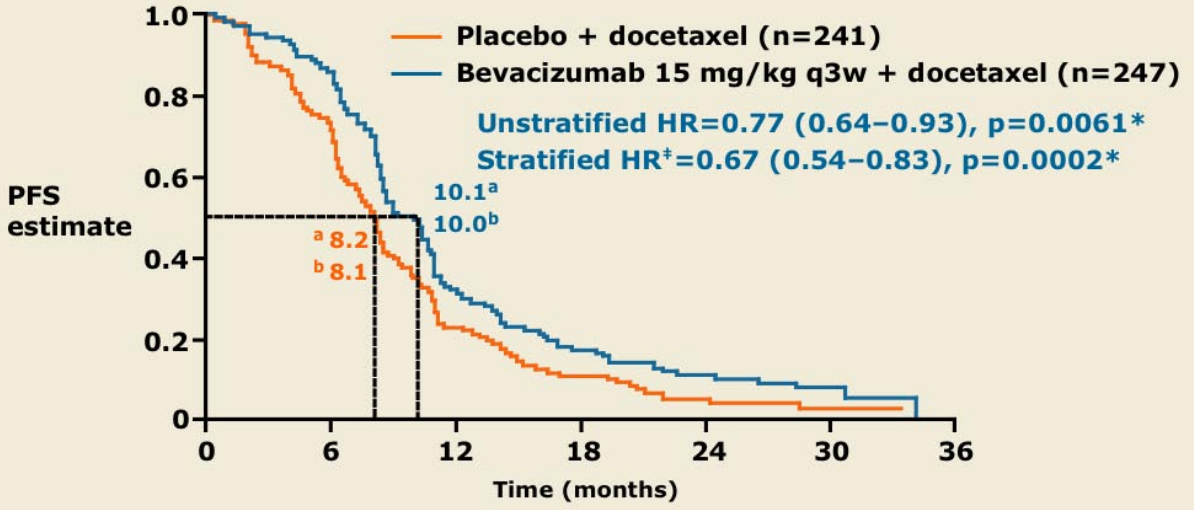
Updated PFS Analysis (Bev 15 mg/kg dose)



Intent-to-treat analysis; *p values are of exploratory nature
‡Censored for non-protocol therapy prior to progressive disease;
[a] unstratified; [b] stratified

Source: With permission from Miles DW et al. SABCS 2009;Abstract 41.

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Updated Efficacy Analysis

	BV, 7.5 mg/kg + docetaxel (n = 248)	BV, 15 mg/kg + docetaxel (n = 247)	Placebo + docetaxel (n = 241)
Median PFS	9.0 mos	10.0 mos	8.1 mos
HR (vs placebo)	0.80*	0.67*	—
p-value (vs placebo)	0.0450†	0.0002†	—
Median OS	30.8 mos	30.2 mos	31.9 mos
HR (vs placebo)	1.05	1.03	—
p-value (vs placebo)	0.7198†	0.8528†	—

*Stratified; † p values are of exploratory nature.

Source: Miles DW et al. SABCS 2009;Abstract 41.

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Updated Efficacy Analysis (continued)

Patients with measurable disease at baseline	BV, 7.5 mg/kg + docetaxel (n = 201)	BV, 15 mg/kg + docetaxel (n = 206)	Placebo + docetaxel (n = 207)
Overall response rate (ORR)	55.2%	64.1%	46.4%
p-value (vs control)†	0.0739	0.0003	—
Intent to treat population	**(n = 248)**	**(n = 247)**	**(n = 241)**
1-year survival rate	81%	84%	76%
p-value (vs control)†	0.198	0.02	—
Patients still at risk (n)	195	201	178

† p values are of exploratory nature.

Source: Miles DW et al. SABCS 2009;Abstract 41.

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Select Adverse Events ≥ Grade 3

	Bev, 7.5 mg/kg + docetaxel (n = 252)	Bev, 15 mg/kg + docetaxel (n = 247)	Placebo + docetaxel (n = 231)
Febrile neutropenia (%)	15.1	16.6	11.7
Hypertension (%)	0.8	4.5	1.3
Bleeding (%)	1.2	1.2	0.9
Wound-healing complications (%)	0.4	0.4	0.9
Venous thromboembolic events (%)	1.6	1.2	3.5
GI perforation (%)	0.4	0.4	0.9

Source: Miles DW et al. SABCS 2009;Abstract 41.

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Conclusions

- First-line BV (15 mg/kg) plus docetaxel significantly improves PFS and overall response rate compared to docetaxel alone in patients with HER2- mBC.
  - PFS: 10.0 mos vs 8.1 mos
  - ORR: 64.1% vs 46.4%
- Addition of increasing doses of BV to docetaxel therapy has a limited impact on the existing docetaxel safety profile.
- No difference in OS was observed between the study arms.
- Exploratory analysis in patients receiving post-progression treatment suggests that the use of 2nd-line BV with chemotherapy may influence OS (data not shown).

Source: Miles DW et al. SABCS 2009;Abstract 41.

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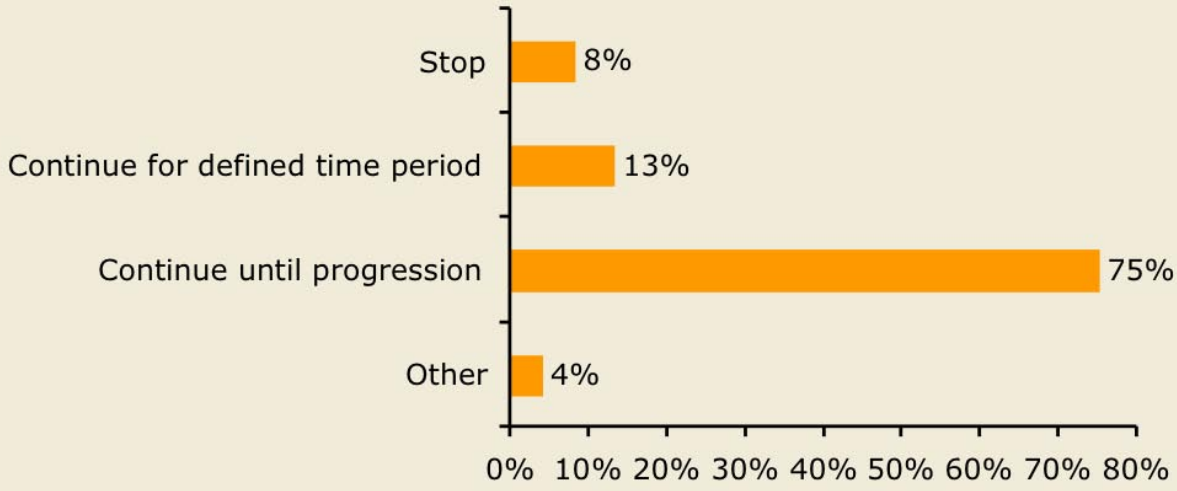
A 45-year-old responds to 1st-line paclitaxel and bevacizumab for mBC. Paclitaxel is discontinued due to toxicity.

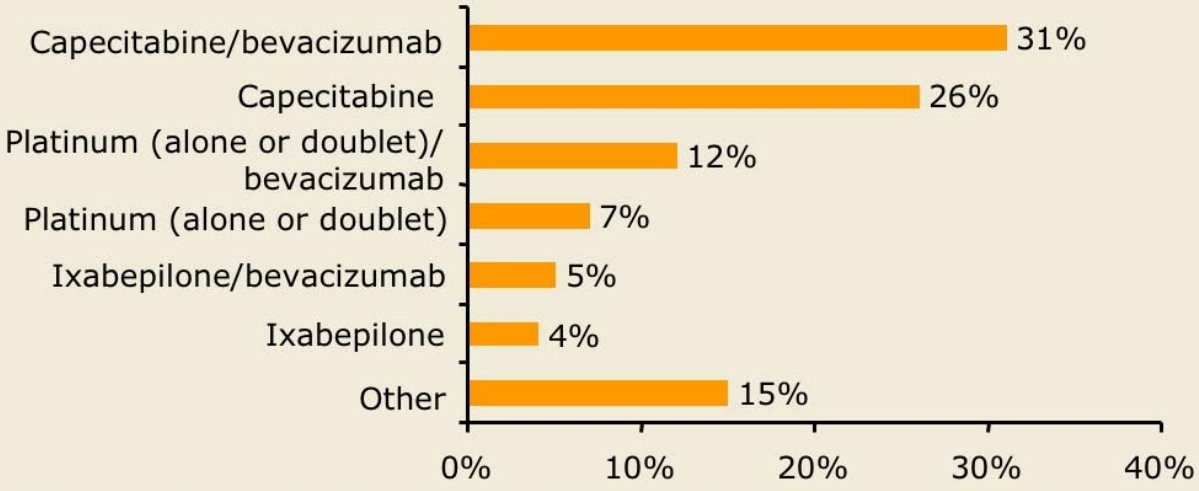
What would you do about the bevacizumab?



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

A 75-year-old with node+ trip neg BC presents with symptomatic metastases after completion of AC → T 2 years ago.

What would you likely recommend if patient is not eligible for a clinical trial? (Check all that apply)



If the patient were eligible for a Phase III trial randomizing to gem/carbo alone or with a PARP inhibitor (BSI-201) 86% would recommend enrollment.

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