

Question #1: Selection of Therapy for High Volume, Recurrent HER2-Negative Metastatic Breast Cancer

Javier Cortés, MD, PhD
Vall d'Hebron University Hospital
Barcelona, Spain

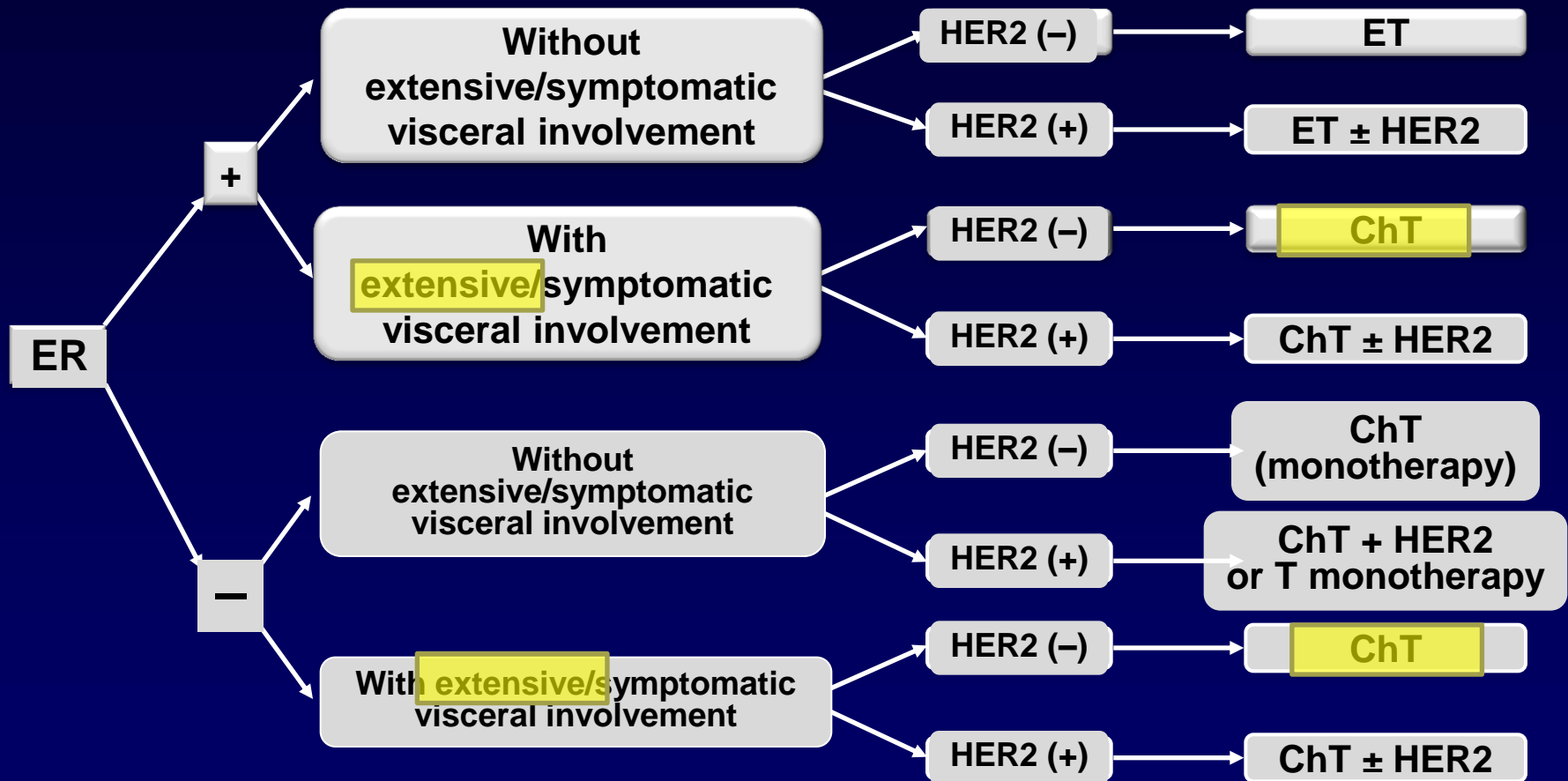
Which of the following outcomes do you feel is the most important when selecting therapy for a “fit” patient who suffers recurrent HER2-negative breast cancer with significant visceral organ involvement but adequate hepatic and renal function?

- 1. Rapid response rate**
- 2. Improved progression-free survival**
- 3. Improved overall survival**
- 4. Least toxicity**

Which of the following outcomes do you feel is the most important when selecting therapy for a “fit” patient who suffers recurrent HER2-negative breast cancer with significant visceral organ involvement but adequate hepatic and renal function?

- 1. Rapid response rate**
- 2. Improved progression-free survival**
- 3. Improved overall survival**
- 4. Least toxicity**

ESMO Guidelines: First-Line Therapy in Advanced Breast Cancer



ChT, chemotherapy; ET, endocrine therapy; T, trastuzumab

Adapted from Cardoso F, et al. Ann Oncol. 2012;23 Suppl 7:vii11-9.

Chemotherapy for Metastatic Breast Cancer

- **Sequential single agents (at MTD) preferred for most patients**
 - Variety of options—no single ‘gold standard’
 - Limited toxicity regimens are generally preferred
- **Combinations appropriate for rapidly progressive, symptomatic disease**
 - Reduction in disease symptoms outweighs potential toxicity
 - May not be a candidate for subsequent therapy if rapid progression continued

Individualized Therapy and Personalized Medicine

Individualized therapy: Estrogen and progesterone receptor status, HER2 status, other targets probably in the near future

Personalized medicine: Comorbidities, age, opinion of the patient

Single-Agent Versus Polychemotherapy in Patients With Advanced Breast Cancer

- **Meta-analysis from abstracted data presented by the Cochrane Breast Cancer Group**
- **43 trials identified up to November 2008**
- **9742 women (55% of them received treatment as first-line therapy)**

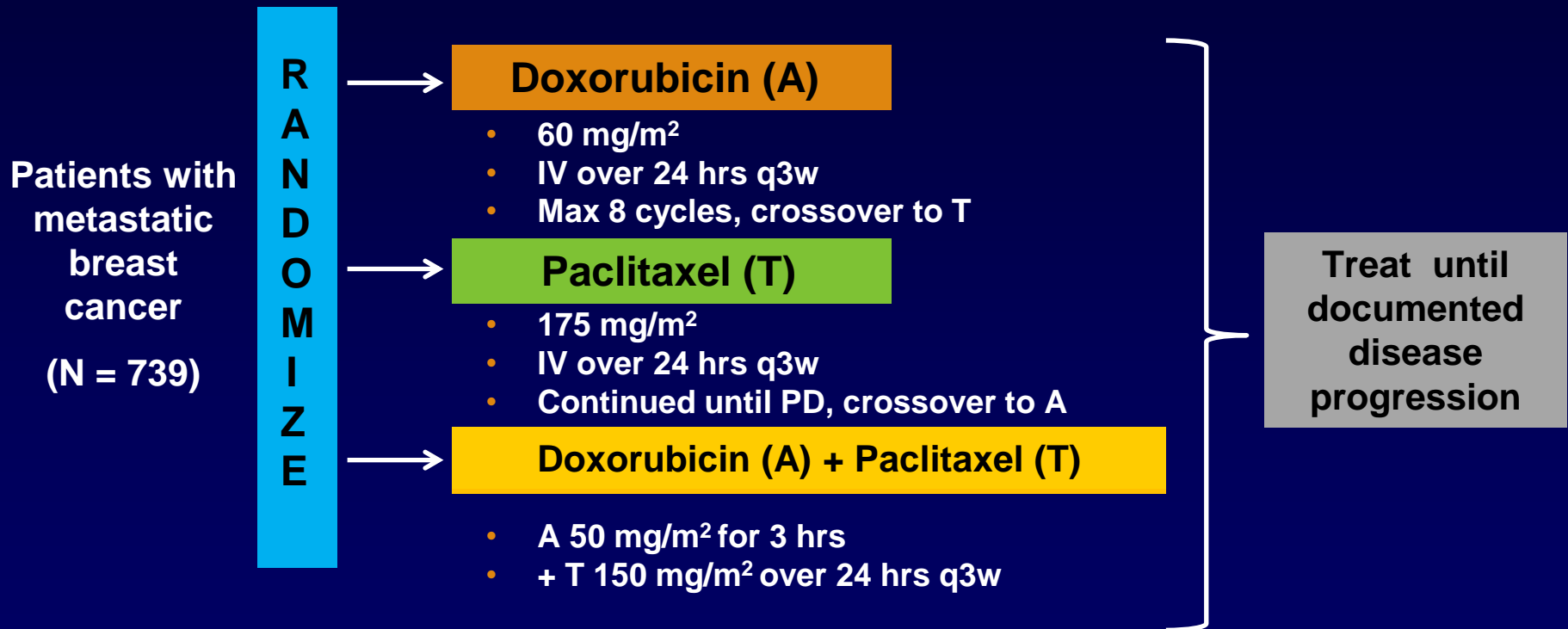
Single-Agent Versus Polychemotherapy in Patients With Advanced Breast Cancer

Polychemotherapy is better than single agent in terms of:

- Response rates (HR = 1.29, 95% CI 1.14-1.45, $P < .0001$)
- Time to progression (HR = 0.78, 95% CI 0.74-0.82, $P < .00001$)
- Overall survival (HR = 0.88, 95% CI 0.83-0.93, $P < .00001$)
- More toxicity with polychemotherapy (nausea, vomiting, leukopenia, alopecia)

An unresolved question is whether combination regimens are more effective than single agents given sequentially.

Doxorubicin vs Paclitaxel vs Doxorubicin/Paclitaxel (ECOG 1193 Phase III Study)



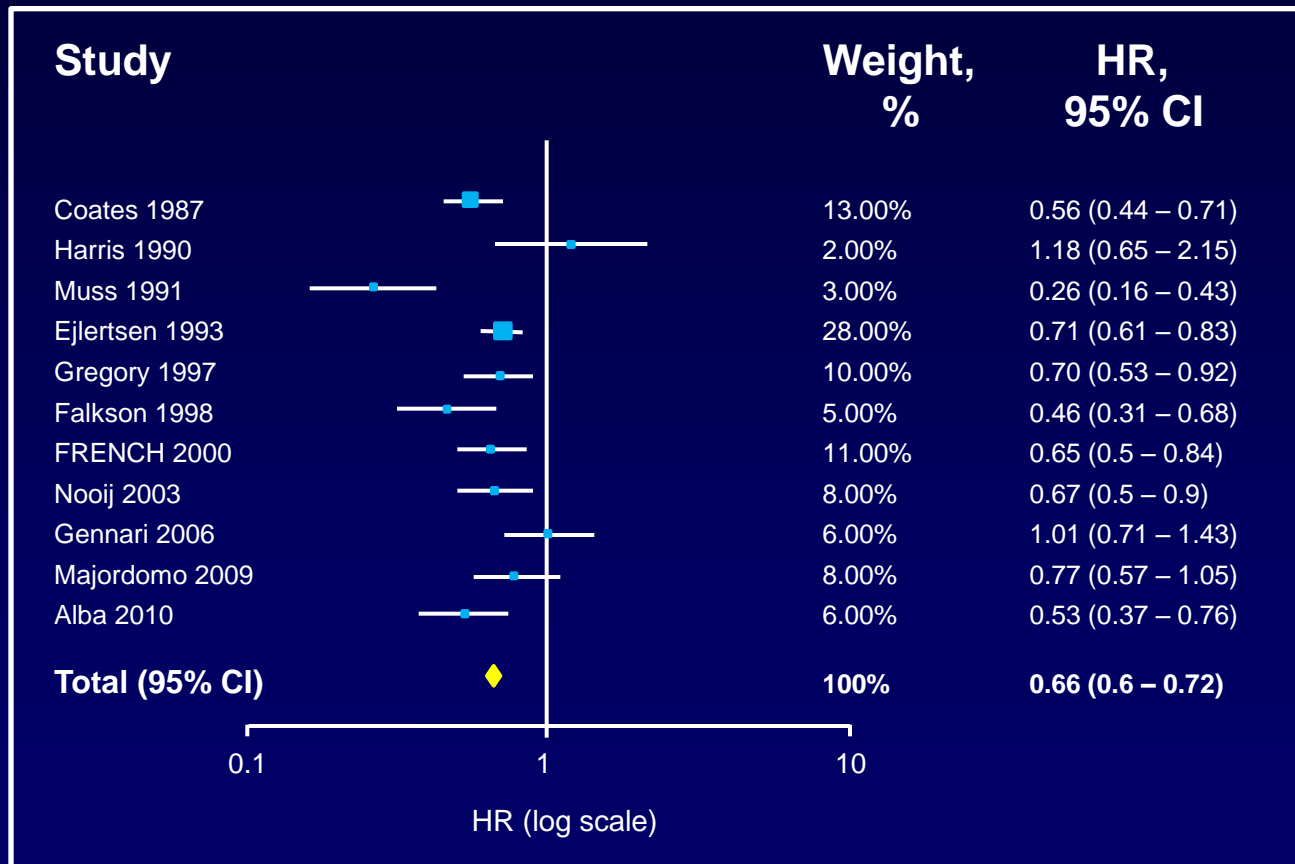
ECOG 1193: First-Line Treatment of MBC

- **ORR**
 - Doxorubicin: 36%
 - Paclitaxel: 34%
 - Doxorubicin→Paclitaxel: 47%
- **TTF**
 - Doxorubicin: 5.8 months
 - Paclitaxel: 6.0 months
 - Doxorubicin→Paclitaxel: 8.0 months
- **Median OS**
 - Doxorubicin: 18.9 months
 - Paclitaxel: 22.2 months
 - Doxorubicin→Paclitaxel: 20 months
- Responses observed in 20% of patients crossing over from doxorubicin to paclitaxel; 22% crossing over from paclitaxel to doxorubicin ($P = \text{NSS}$)

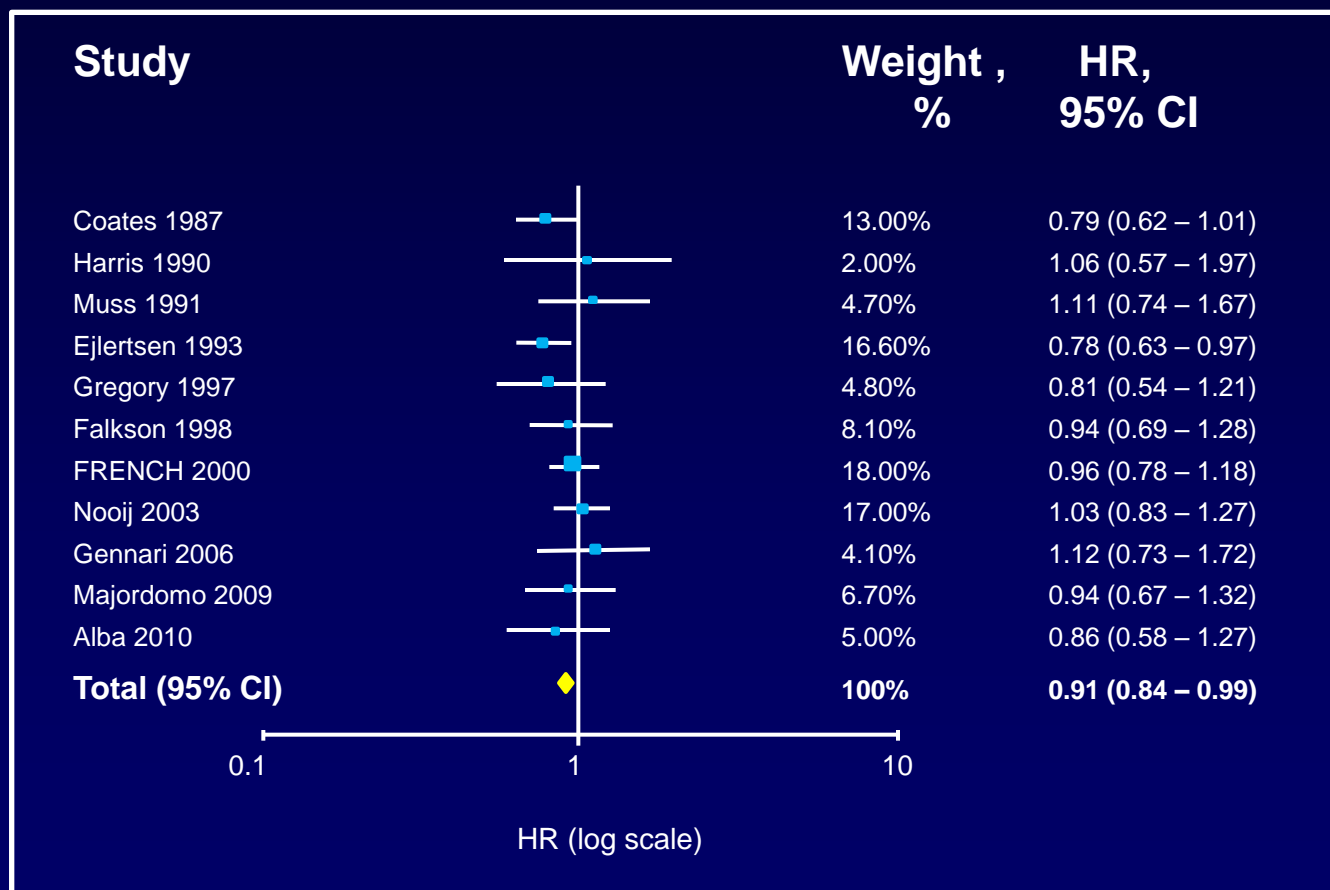
Chemotherapy for Metastatic Breast Cancer

- Sequential single-agent chemotherapy preferred for most patients
- Limits toxicity
- Combinations may be preferred for rapidly progressive symptomatic disease
 - Reduction in symptoms outweighs toxicity
 - Not a candidate for subsequent therapy if continued progression

Longer First-Line Chemotherapy Duration: Substantially Longer PFS (HR: 0.64)

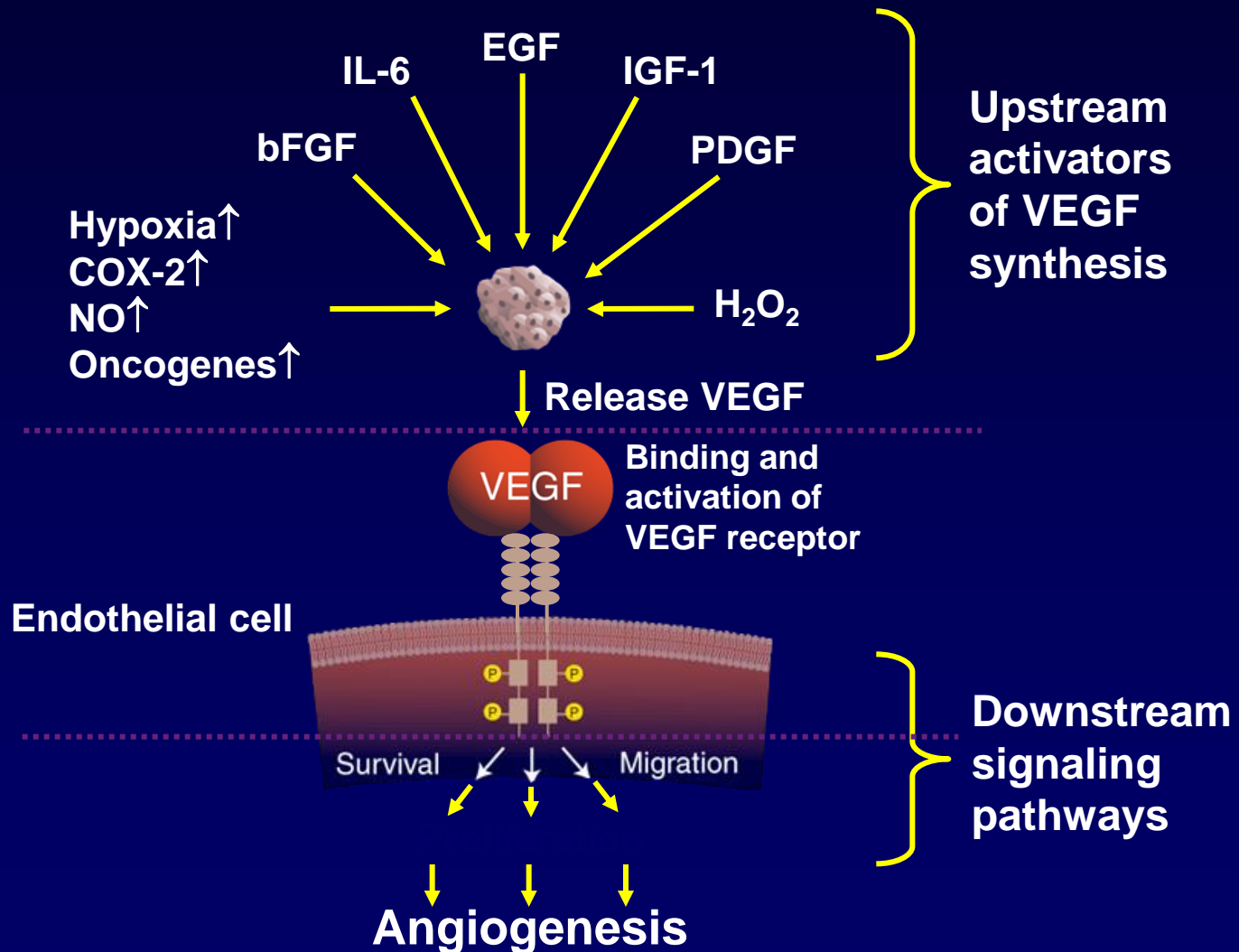


Longer First-Line Chemotherapy Duration: Marginal Effect on OS (HR: 0.91)

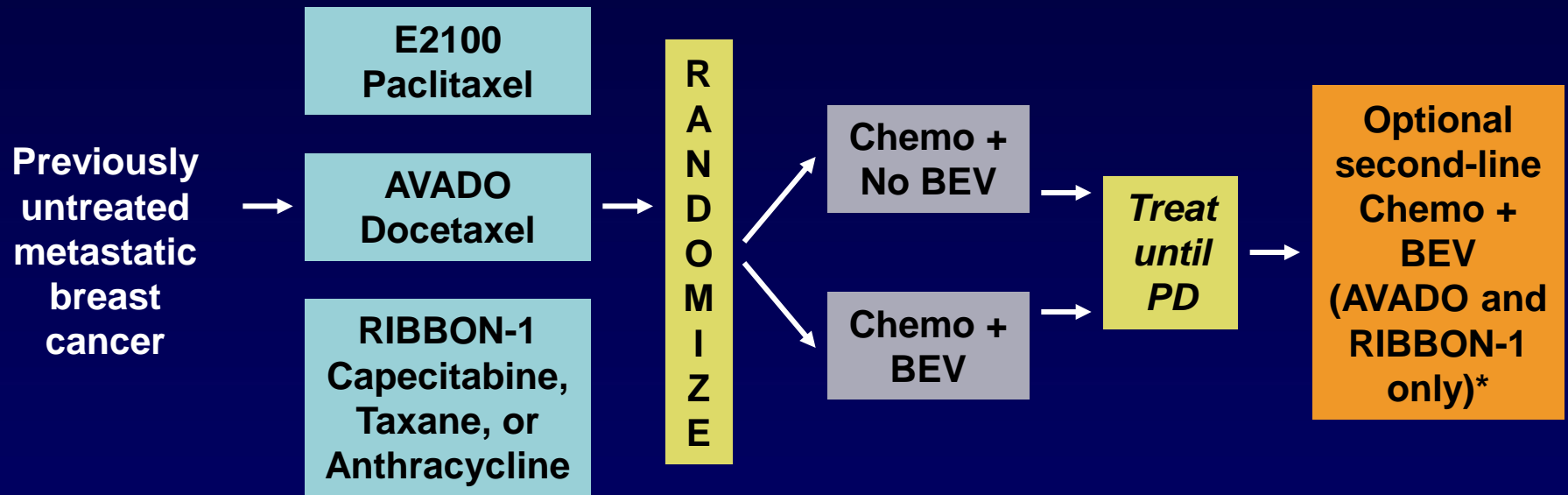


**Do We Have an Alternative
to Polychemotherapy?**

VEGF Is a Key Mediator of Angiogenesis

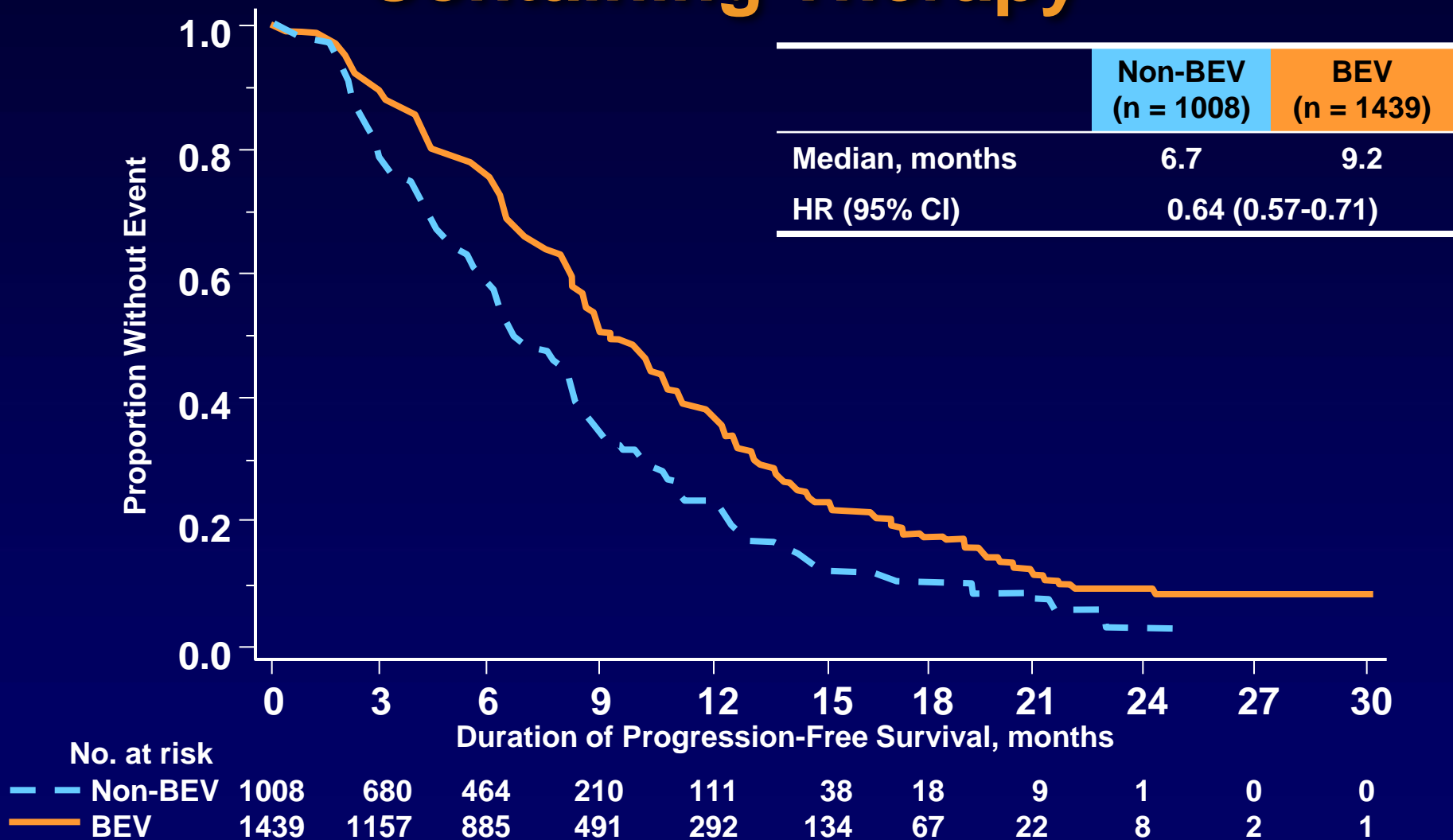


Meta-Analysis of 3 Phase III Trials of Bevacizumab (BEV) in Previously Untreated Metastatic Breast Cancer



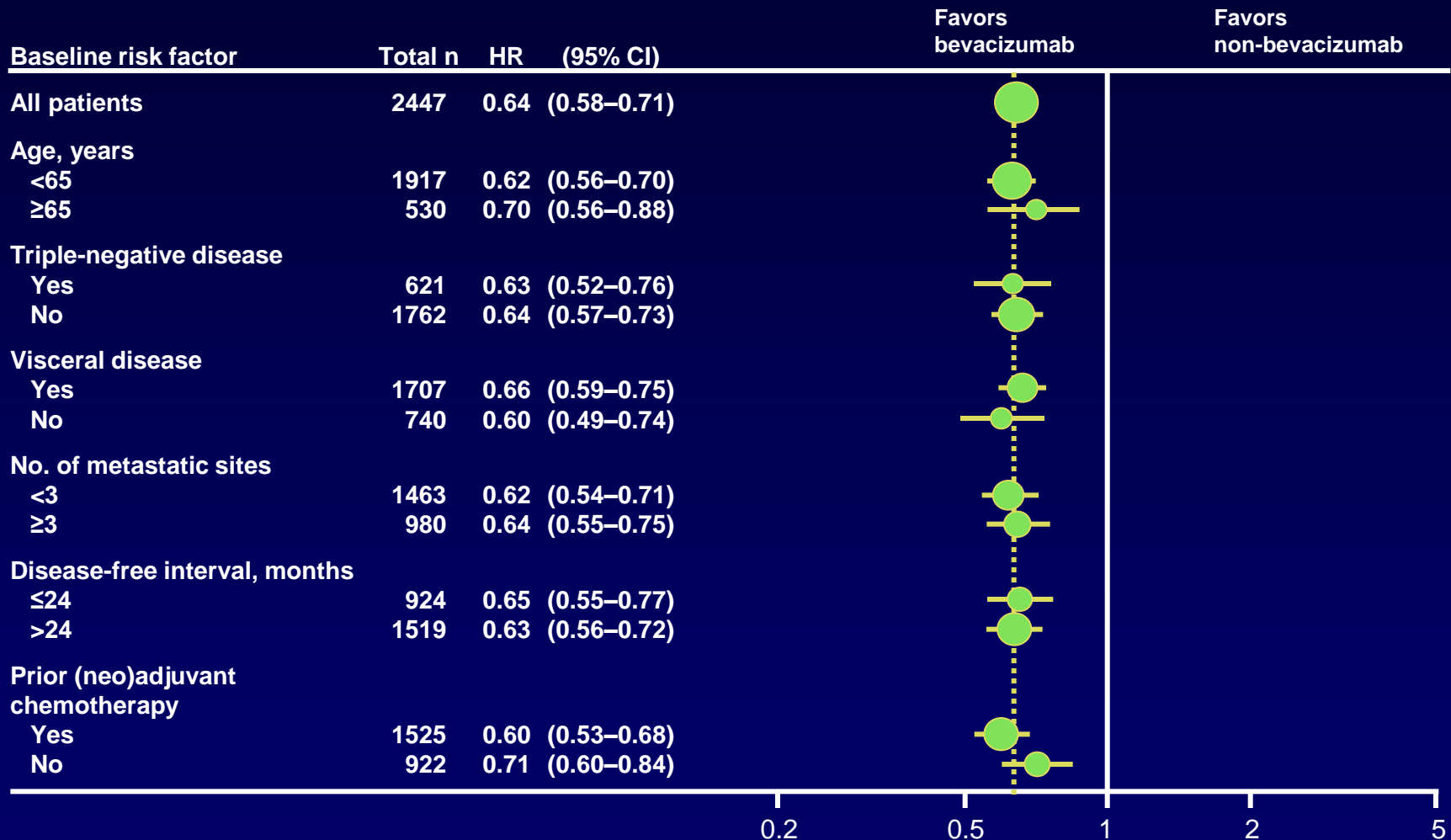
*~50% of patients received bevacizumab at crossover

Meta-Analysis: PFS With Bevacizumab-Containing Therapy

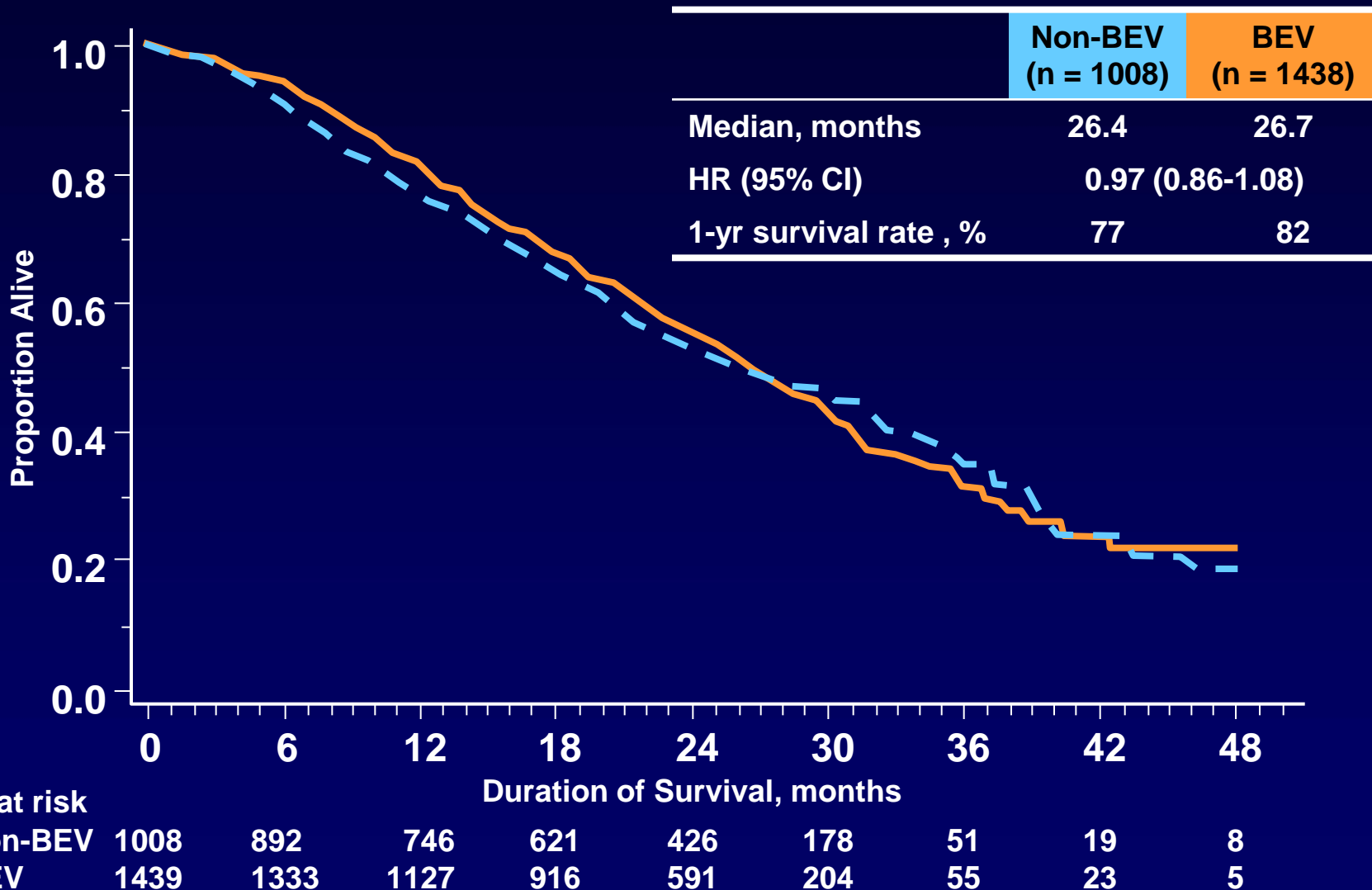


Miles DW, et al. *Ann Oncol.* 2013;24(11):2773-2780.

Meta-Analysis: PFS in Clinically Relevant Subgroups



Bevacizumab Meta-Analysis: OS



My Opinion

Which of the following outcomes do you feel is the most important when selecting therapy for a “fit” patient who suffers recurrent HER2-negative breast cancer with significant visceral organ involvement but adequate hepatic and renal function?

1. Rapid response rate
2. Improved progression-free survival
3. Improved overall survival
4. Least toxicity

RAISING THE BAR IN BREAST CANCER CARE:

Answering Clinically Relevant Questions

