

# Comprehensive Cancer Center Vienna

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## **Are Patients Being Treated Better Within the Frame of Clinical Trials? „YES“**

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# Advantage of Treatment within a Clinical Trial

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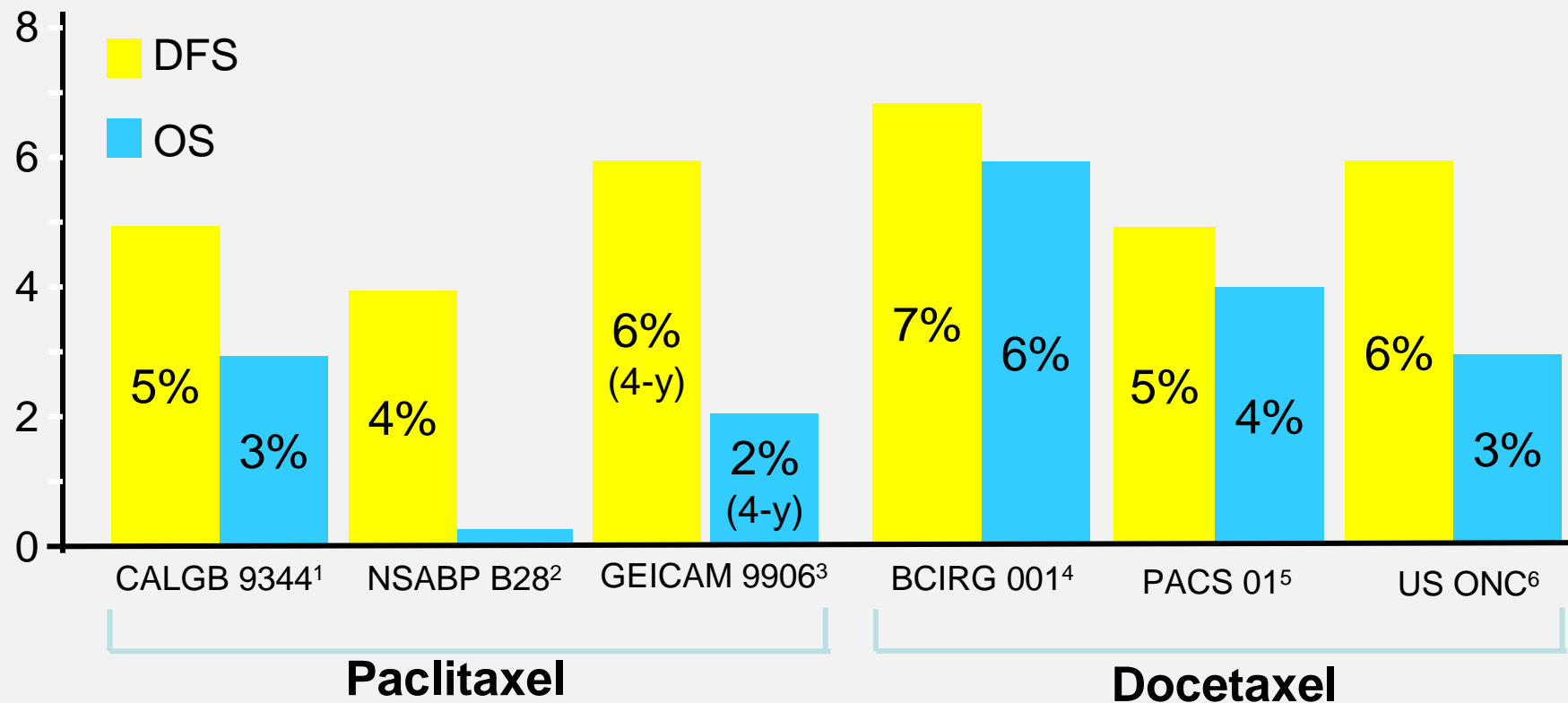
**1. Access to Innovative Drugs or Drug Combinations**

**1. Guideline-Adherence in Medical Care Including the Control Arm**

**1. Continuation with Study Drug in Case of Efficacy**



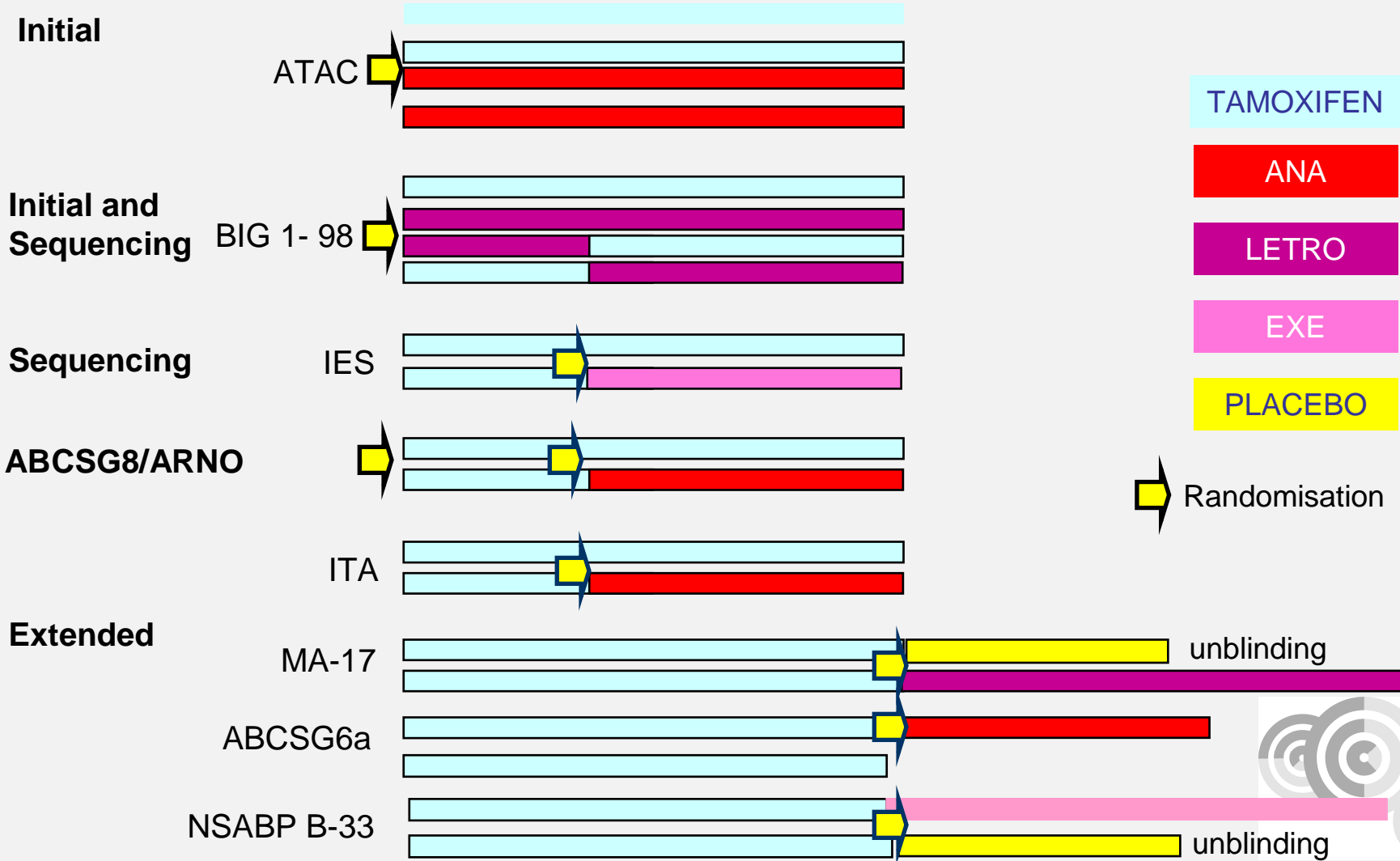
# Adjuvant Trials with Taxanes: Absolute 5-year Benefit over Comparator



DFS, disease-free survival;  
OS, overall survival

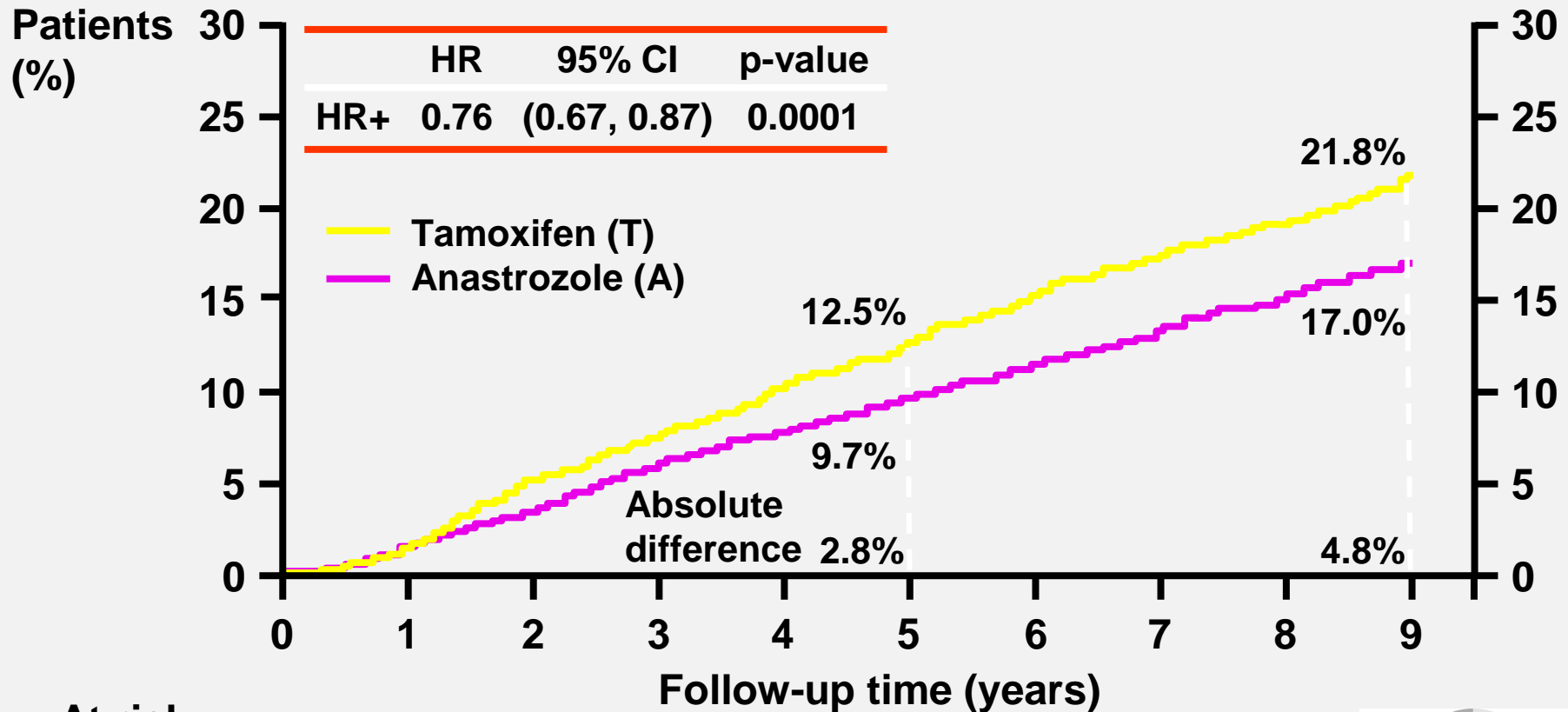
1. Henderson IC et al. J Clin Oncol 2003;21:976–83; 2. Mamounas EP et al. ASCO 2003. Abstract 12; 3. Martin M et al. SABCS 2005. Abstract 39. 4. Martin M et al. N Engl J Med 2005;352:2302–13; 5. Roché H et al. SABCS 2004; Abstract 27; 6. Jones S et al. J Clin Oncol 2006;24:5381–7

# Trials of Adjuvant Aromatase Inhibitor Trials in Postmenopausal Patients.



# ATAC Trial: Time to Recurrence

## HR+ patients



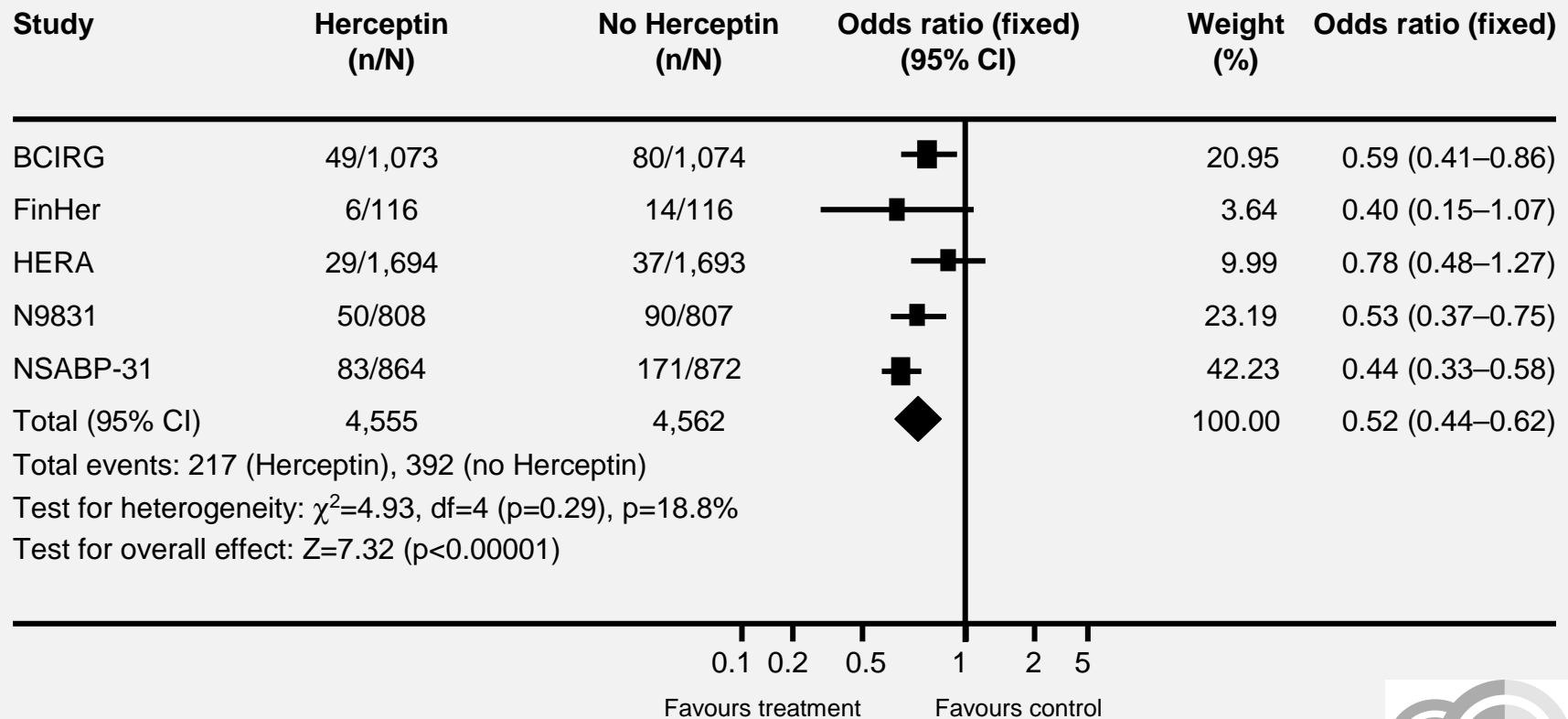
At risk:

A	2618	2541	2453	2361	2278	2159	1995	1801	1492
T	2598	2516	2400	2306	2196	2075	1896	1711	1396



# Trials of Adjuvant Trastuzumab in Her-2/neu Overexpressing Breast Cancer

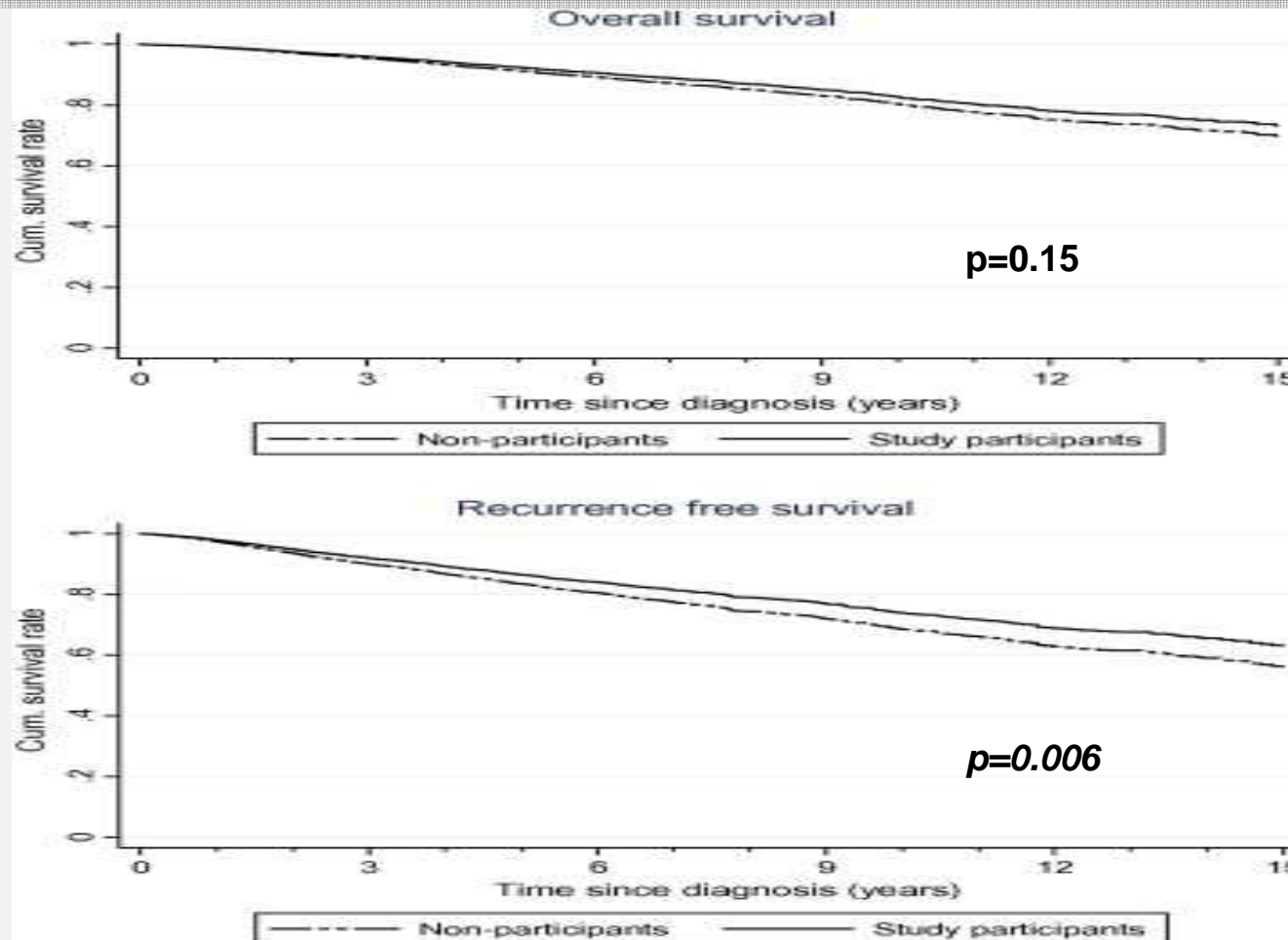
## Meta-analysis of Herceptin adjuvant trials<sup>1</sup>



<sup>1</sup>Viani G, et al. BMC Cancer 2007;7:153

## Overall and Recurrence-Free Survival for 1255 Study Participants vs. 8178 Non-Participants in the Retrospective BRENDA Trial.

Adjusted for age, year of diagnosis, patient treated at University Department Ulm, nodal status, grading, hormone receptor status, menopausal status, erb-2-status and comorbidity, as well as for missing data on the latter two variables.



L. Schwentner , R. Van Ewijk , C. Kurzeder , I. Hoffmann , J. König , R. Kreienberg , M. Blettner , A. Wöckel

Participation in adjuvant clinical breast cancer trials: Does study participation improve survival compared to guideline adherent adjuvant treatment? A retrospective multi-centre cohort study of 9433 patients

European Journal of Cancer 2012

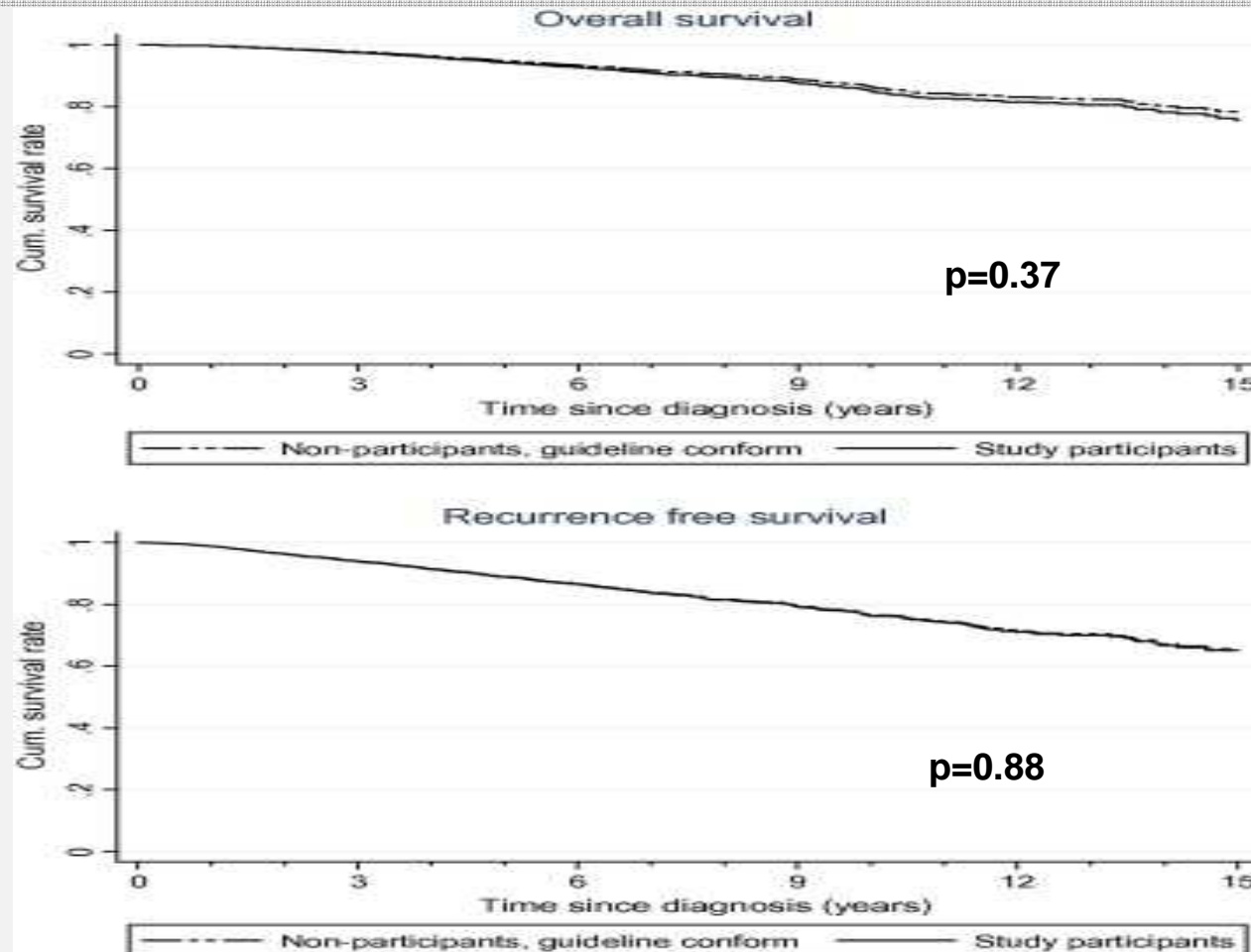
<http://dx.doi.org/10.1016/j.ejca.2012.08.011>



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## Overall and Recurrence-Free Survival for 1255 Study Participants vs. 4888 Guideline Conform Non-Participants (BRENDA Trial).

Adjusted for age, year of diagnosis, patient treated at University Department Ulm, nodal status, grading, hormone receptor status, menopausal status, erb-2-status and comorbidity, as well as for missing data on the latter two variables.

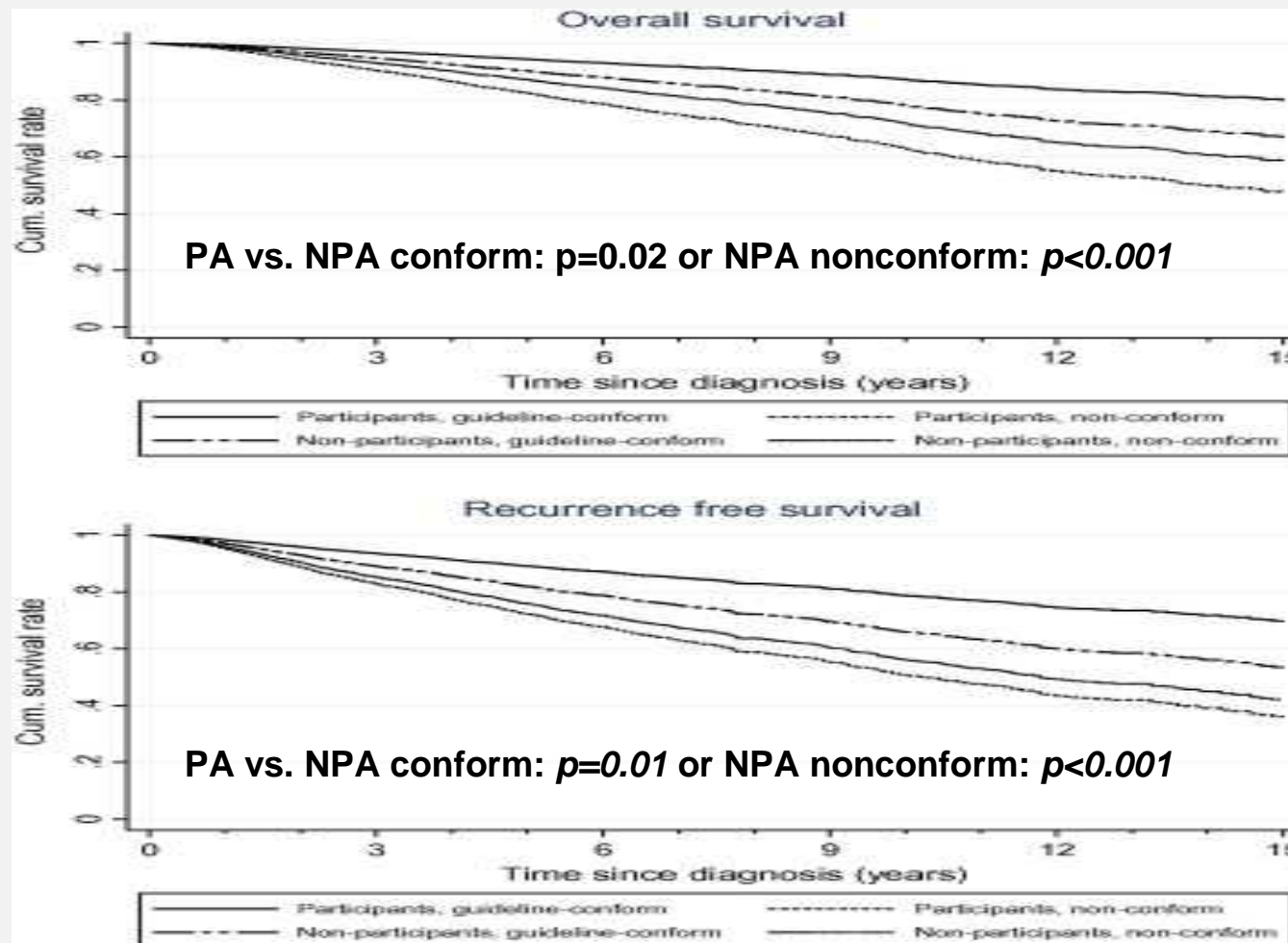


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<http://dx.doi.org/10.1016/j.ejca.2012.08.011>



## Overall and Recurrence-Free Survival for Study Participants vs. Guideline Conform Non-Participants Stratified to Guideline Adherence for All Groups (BRENDA Trial).

Adjusted for age, year of diagnosis, patient treated at University Department Ulm, nodal status, grading, hormone receptor status, menopausal status, erb-2-status and comorbidity, as well as for missing data on the latter two variables.



Participation in adjuvant clinical breast cancer trials: Does study participation improve survival compared to guideline adherent adjuvant treatment? A retrospective multi-centre cohort study of 9433 patients  
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# Guideline Violations in the BRENDA Trial

<u>Treatment</u>	<u>Study Participants</u> n=1255	<u>Study Non-Participants</u> n=8178	<u>p</u>
Radiotherapy	3.3%	9.4%	<0.001
Surgery	15.9%	13.1%	0.007
Endocrine Therapy	8.0%	11.9%	<0.001
Chemotherapy	5.0%	18.0%	<0.001



# **Weaknesses of the BRENDA Trial**

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## **1. Retrospective.**

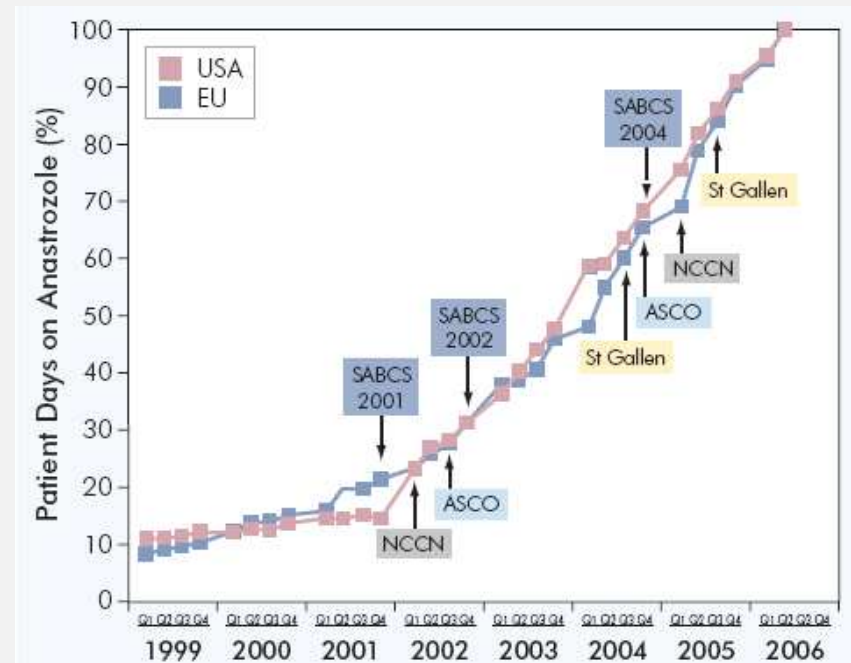
**1. Patients Imbalanced in Number and Characteristics Between Patients on and outside of Clinical Trials.**

**1. Guideline Violations More Prevalent in the Trial-Nonparticipating-Group Corroborating the Assumption of Better Treatment of the Trial Population.**



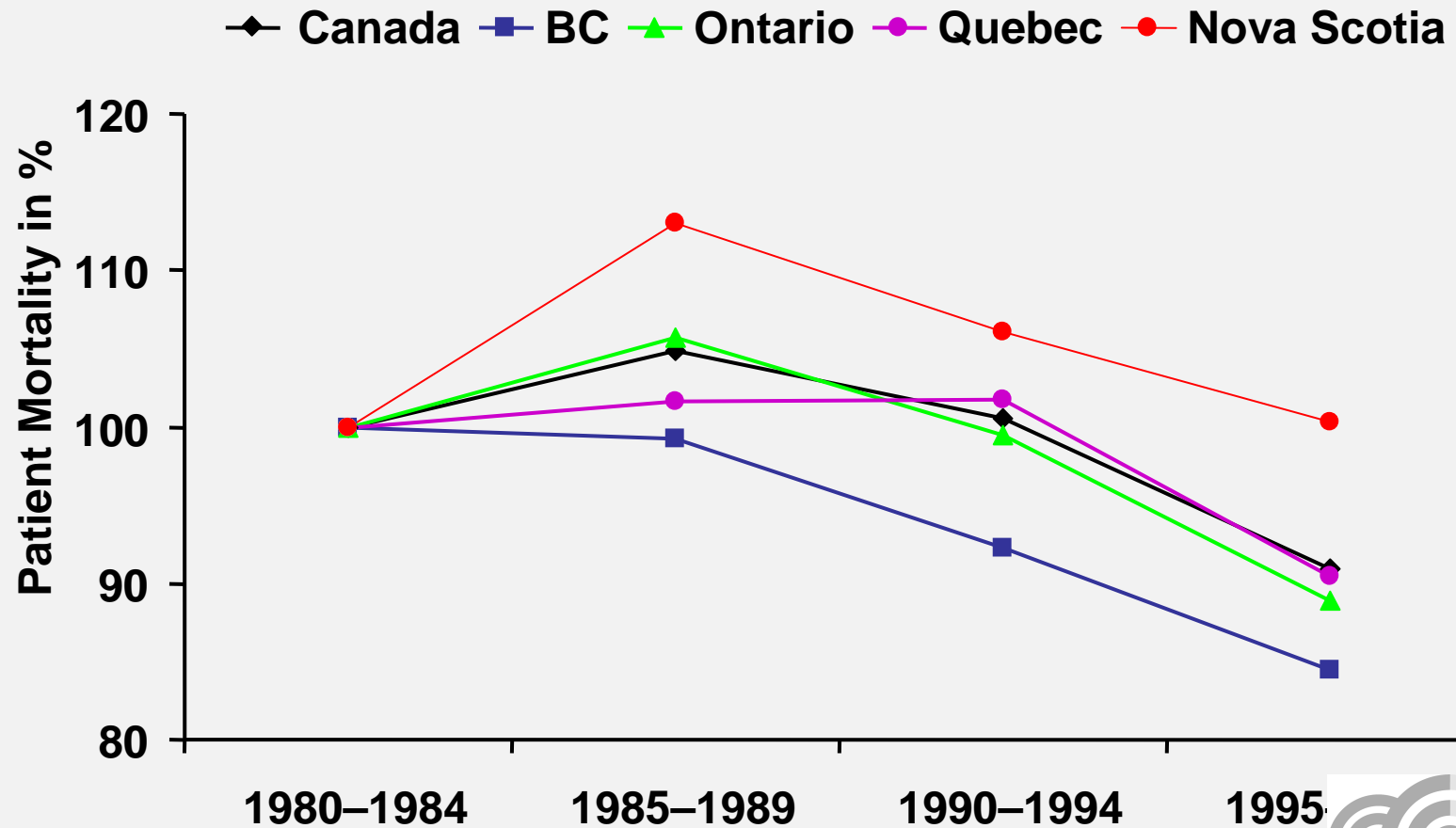
# What Influences Clinical Practice?

- **uptake of anastrozole after the ATAC phase III adjuvant study**
  - anastrozole use in clinical practice increased following oral presentation of data at congresses
  - uptake was not strongly influenced by guidelines
  - findings were consistent in Europe and the USA



- **The authors found that inclusion in guidelines appeared to lag, rather than lead, clinical usage**

# Reduction of Breast Cancer Mortality Through the Implementation of Guidelines.



# What is Sufficient Evidence for Adoption of a New Therapy/New Use of Existing Therapy?

- **Inclusion in national/international guidelines?**

## **For**

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The data have been reviewed by an expert panel in the context of the practice of specific countries or regions

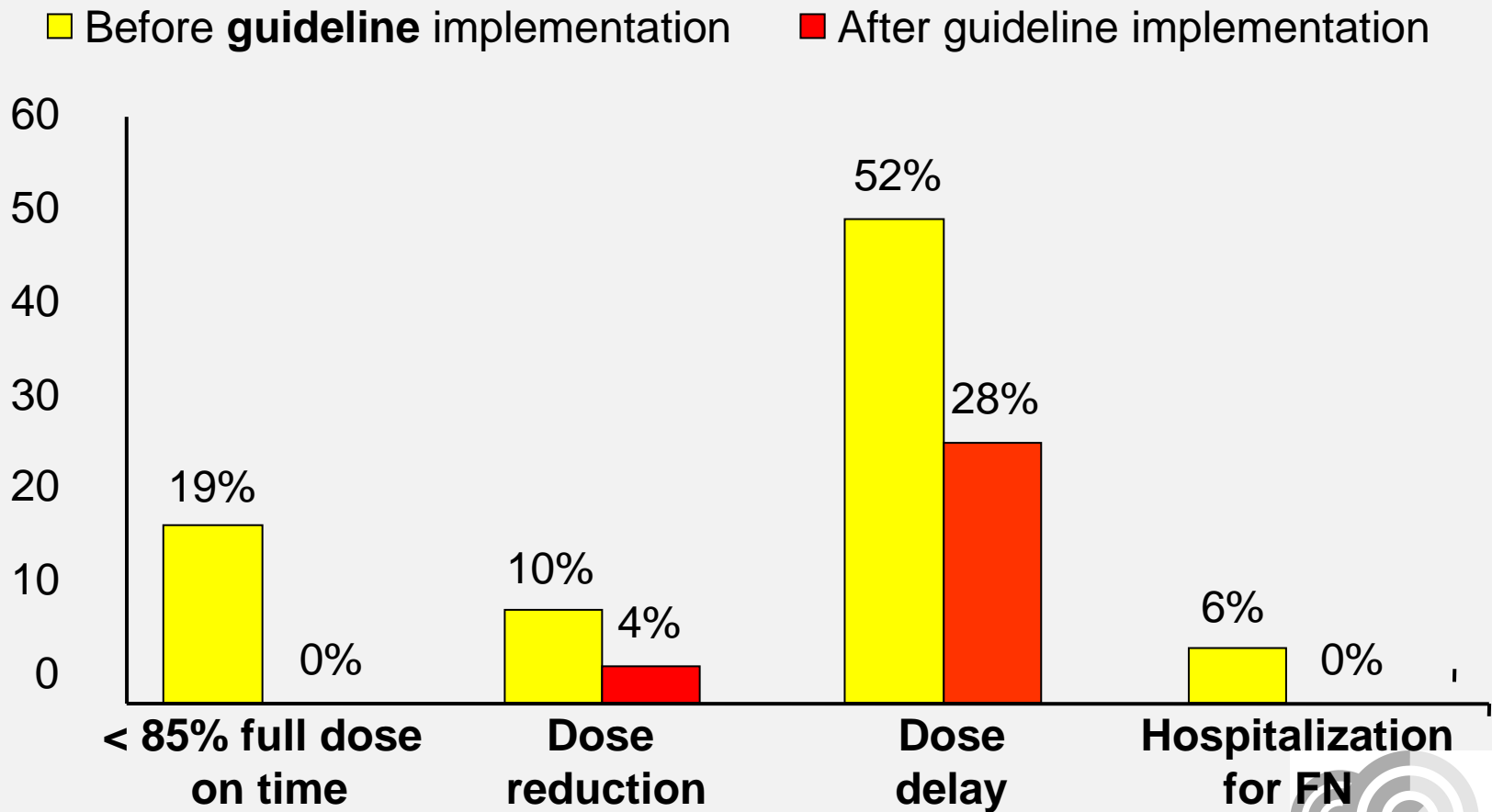
## **Against**

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The process causes, on average, more than 12 months' delay before patients receive benefit



# Implementation of Local G-CSF Guidelines can Reduce the Incidence of FN



Data from the West Michigan Cancer Centre  
White N et al. *Cancer Nurs* 2005;28:62-69

# **Advantages of Treatment within a Randomized Clinical Trial: Conclusions**

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- 1. The Likelihood of Optimal Care is Significantly Higher in a RCT.**
- 1. Even under Good Circumstances, Treatment Guidelines Applying to Patients Outside of the Trial Have to be Defined, Implemented and Followed.**
- 1. Even Then, Treatment Violations Occur Frequently thus Compromising the Delivery of Optimal Care.**

