

Adjuvant Trastuzumab for Early Stage Breast Cancer: Efficacy Data

**American Society of Breast Disease
30th Anniversary Meeting
April 27, 2006**

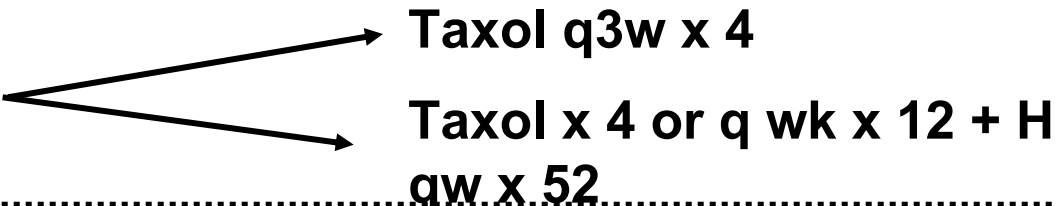


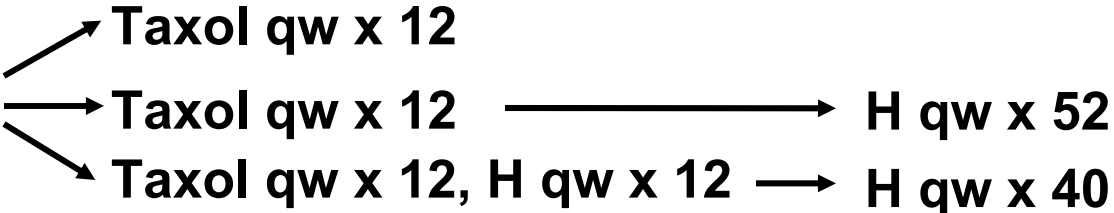
**Debu Tripathy, M.D.
Professor of Medicine**

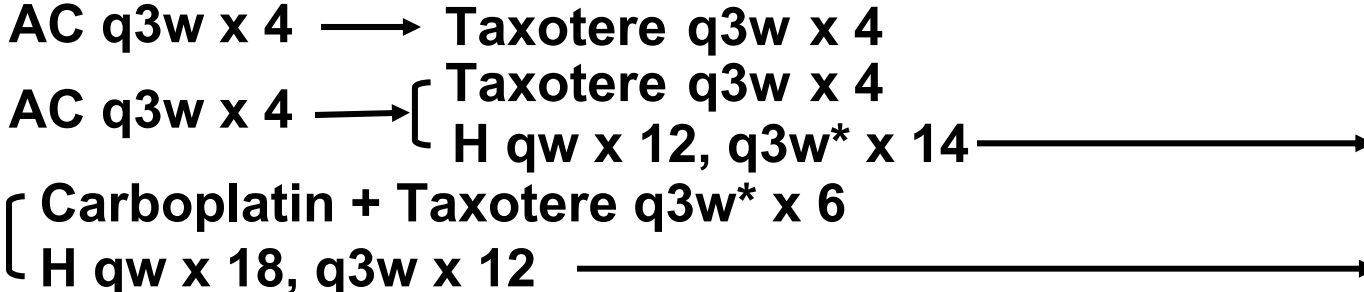
**Director, Komen/UTSW Breast Cancer Research Program
University of Texas Southwestern Medical Center at Dallas**

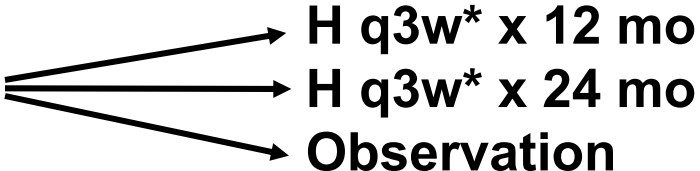


Herceptin Adjuvant Therapy: Summary of Completed Trials

NSABP B-31 AC q3w x 4 

N9831 AC q3w x 4 

BCIRG 006 AC q3w x 4 

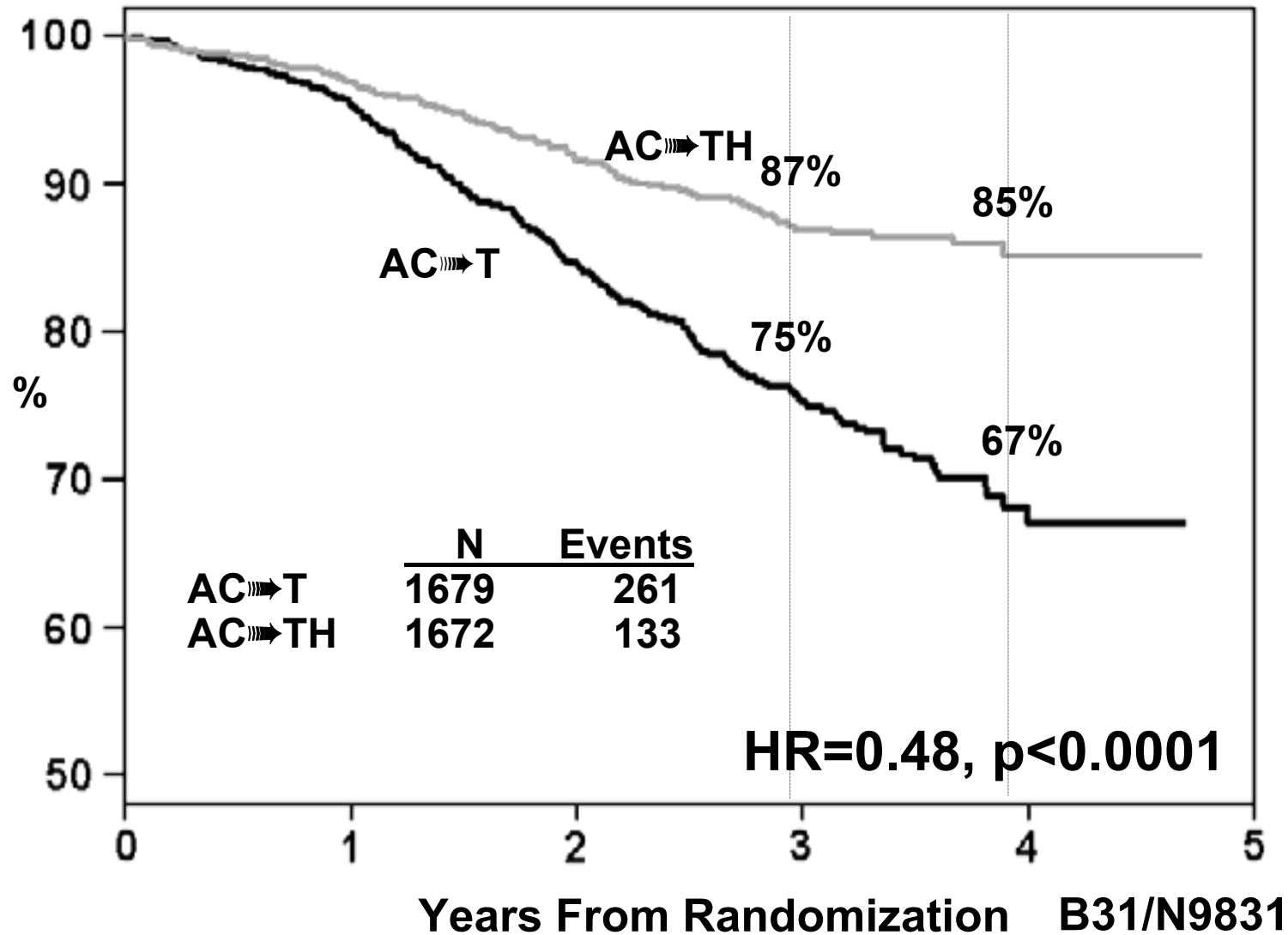
HERA Trial Any CT and/or RT 

*H q3w at 6 mg/kg.

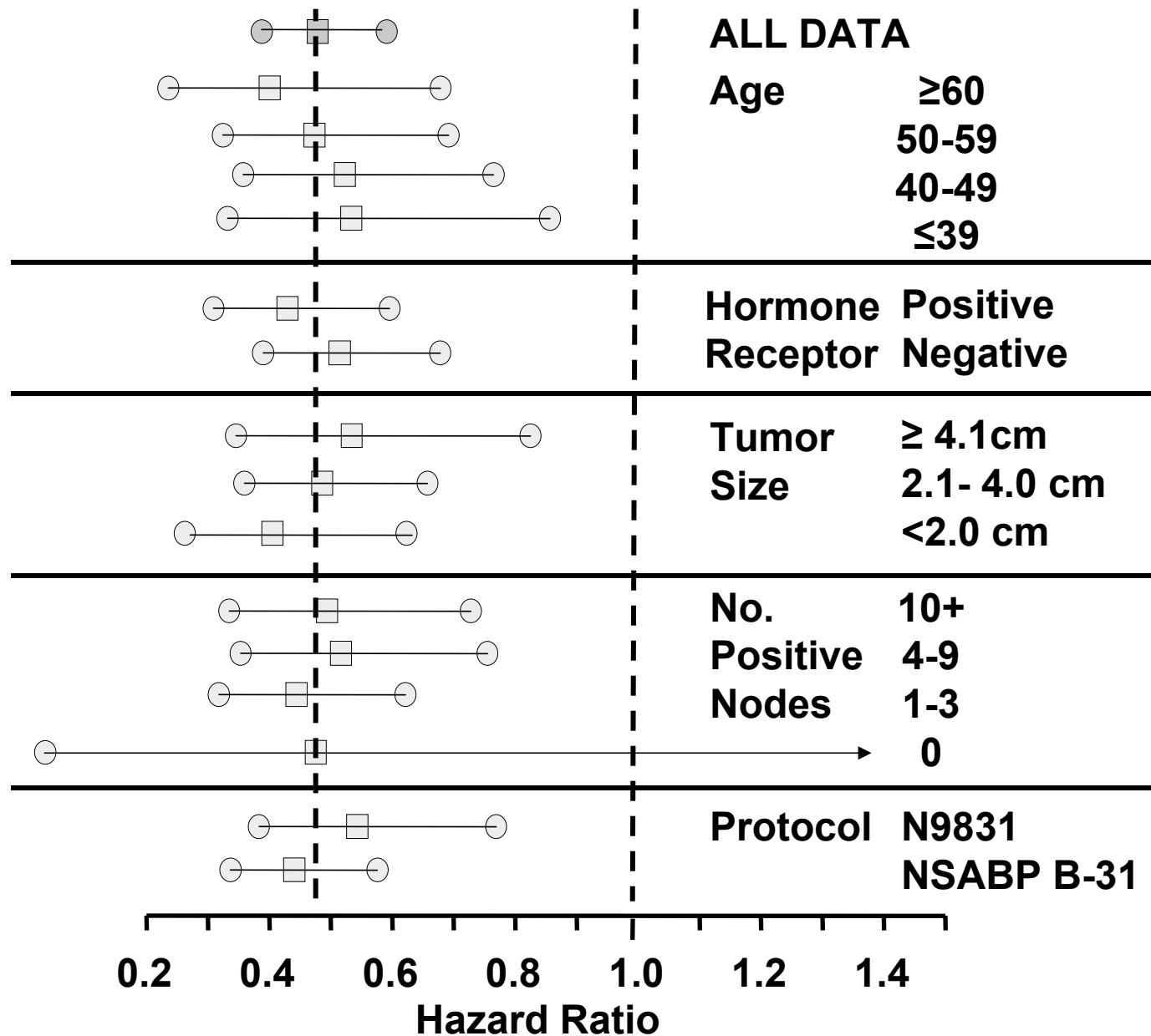
Combined NSABP B-31 and NCCTG 9831 Statistical Analysis

- **Compared AC → TH (concurrent) arms only**
- **Median follow-up: 2.0 years**
 - **2.4 years on B-31**
 - **1.5 years on N9831**
- **Primary endpoint: DFS**
 - **Analyzed by intent-to-treat**
- **Secondary endpoints: OS and Time to 1st Distant Recurrence**
- **Definitive analysis after 710 DFS events**
- **First interim analysis after 355 DFS events**
- **Stop trials only if equivalence is rejected at $p=0.0005$ ($2p=0.001$)**

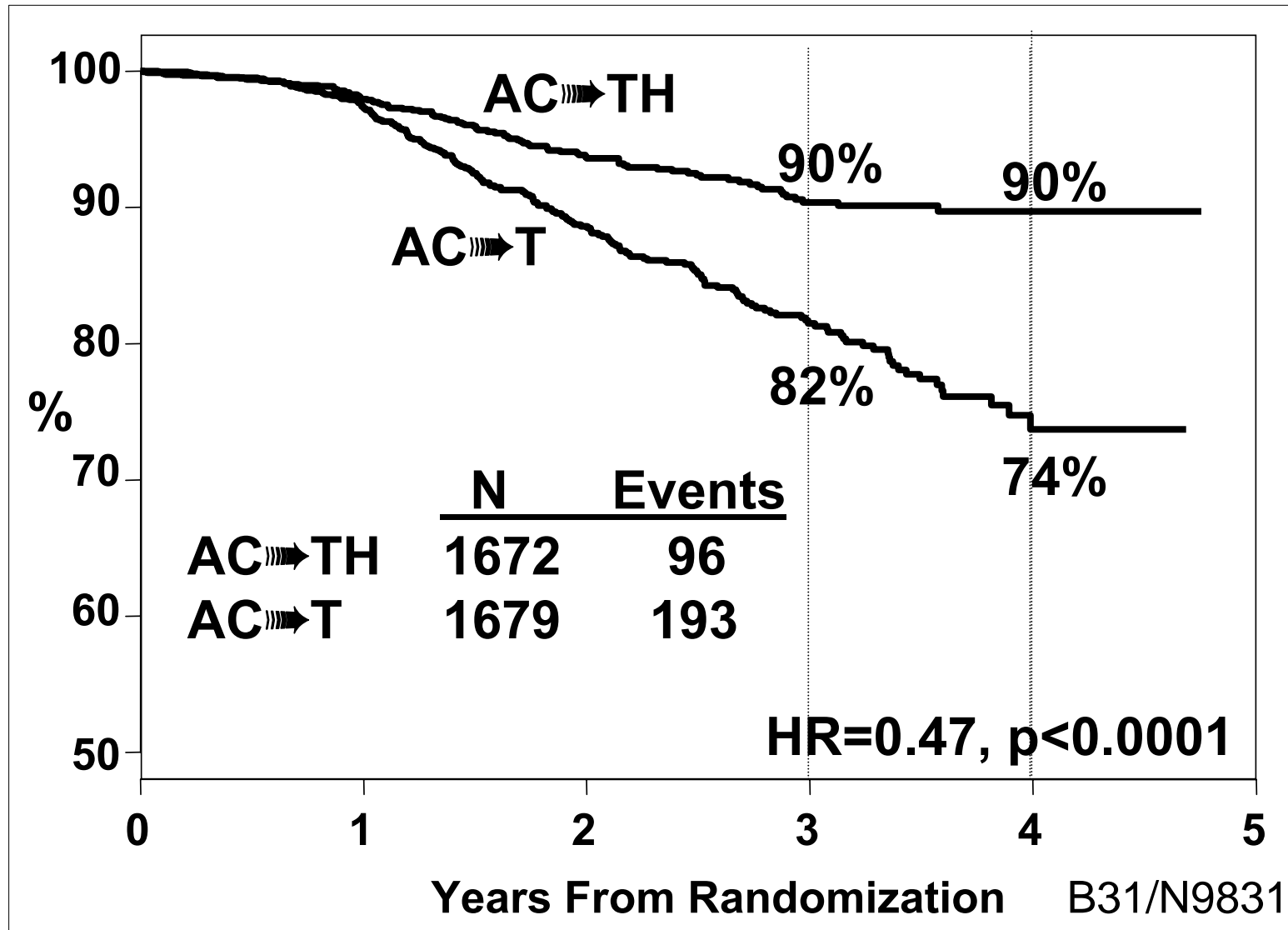
Disease-Free Survival



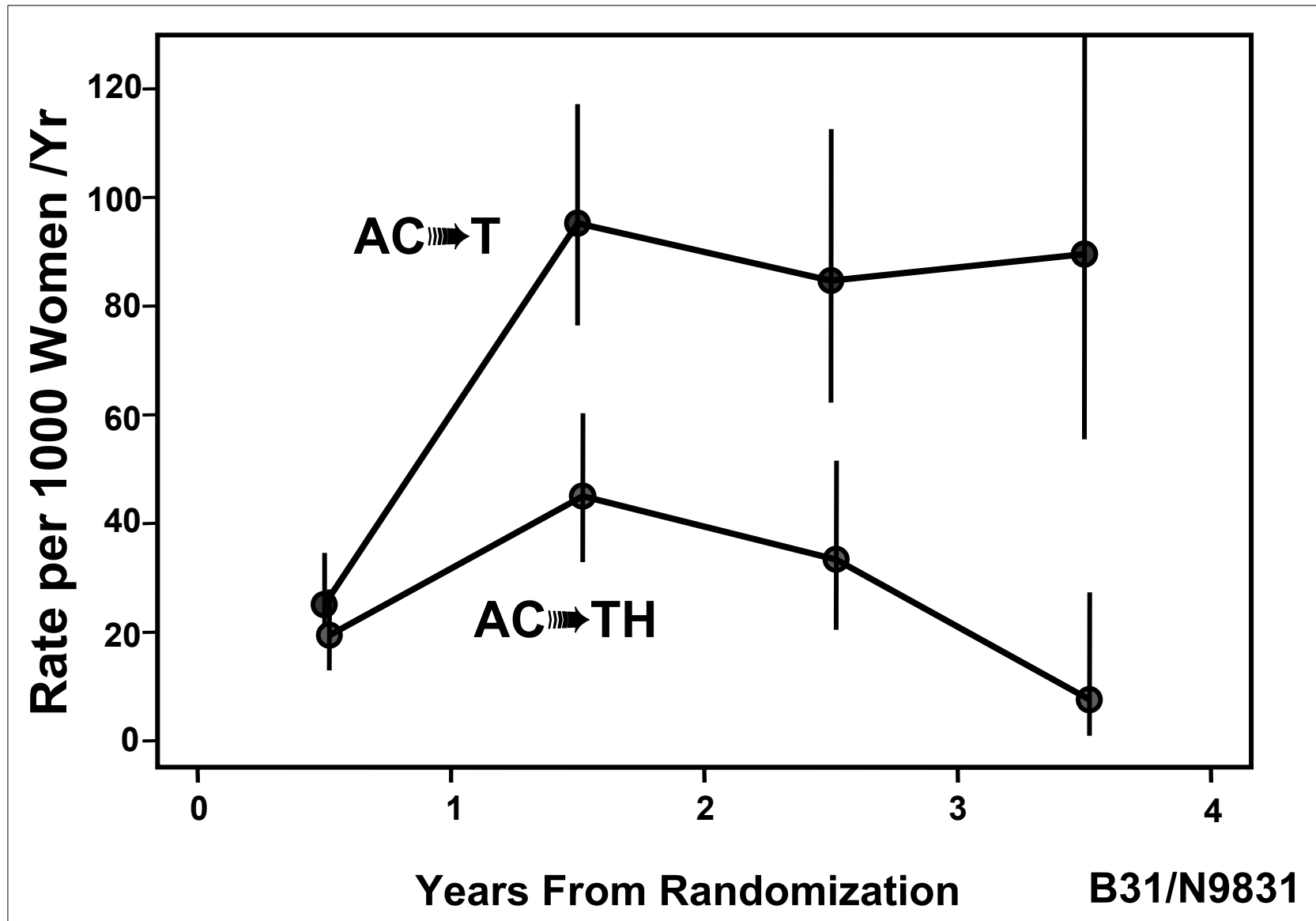
Forest Plot For Disease-Free Survival



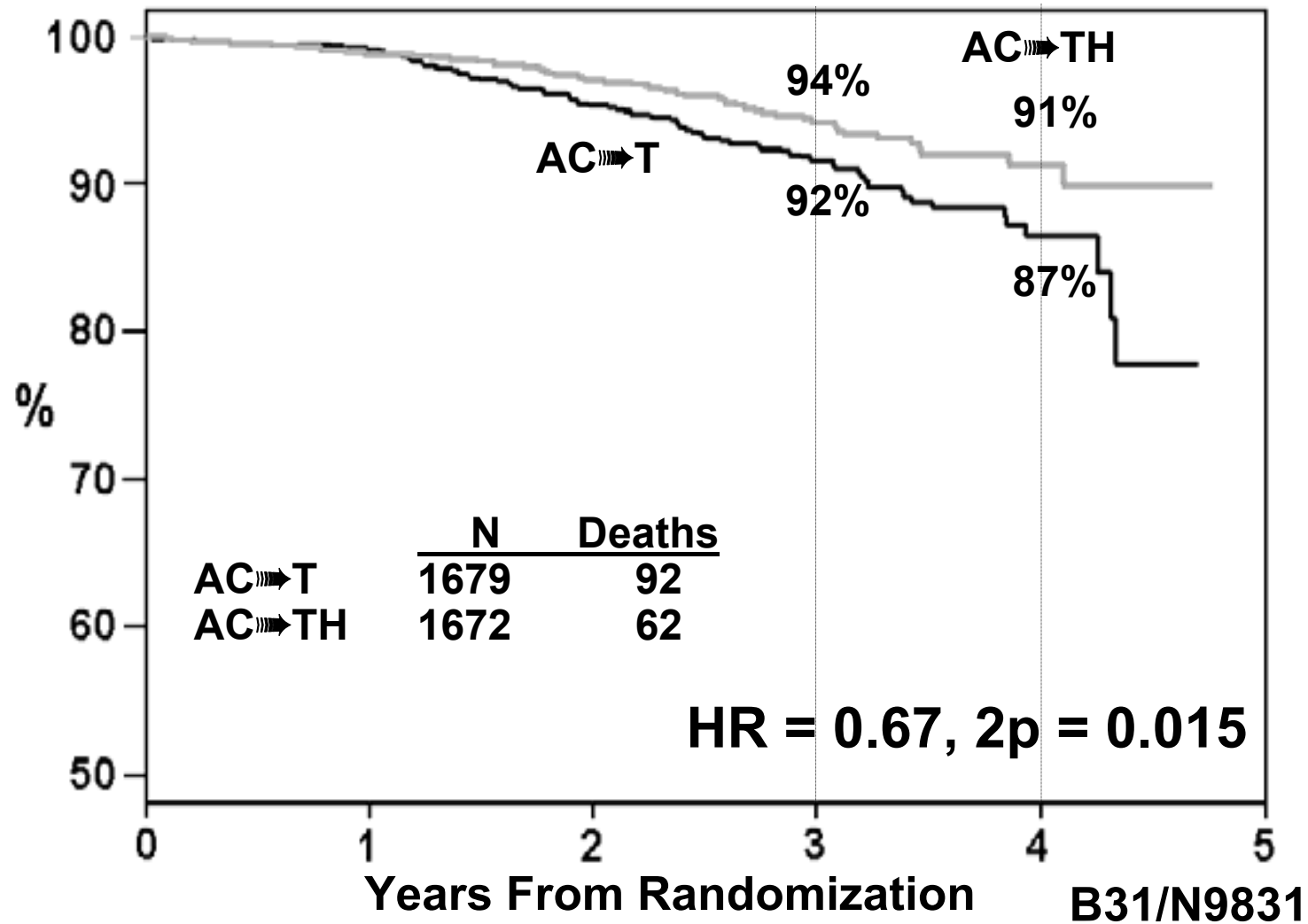
Time to First Distant Recurrence



Hazard of Distant Recurrence

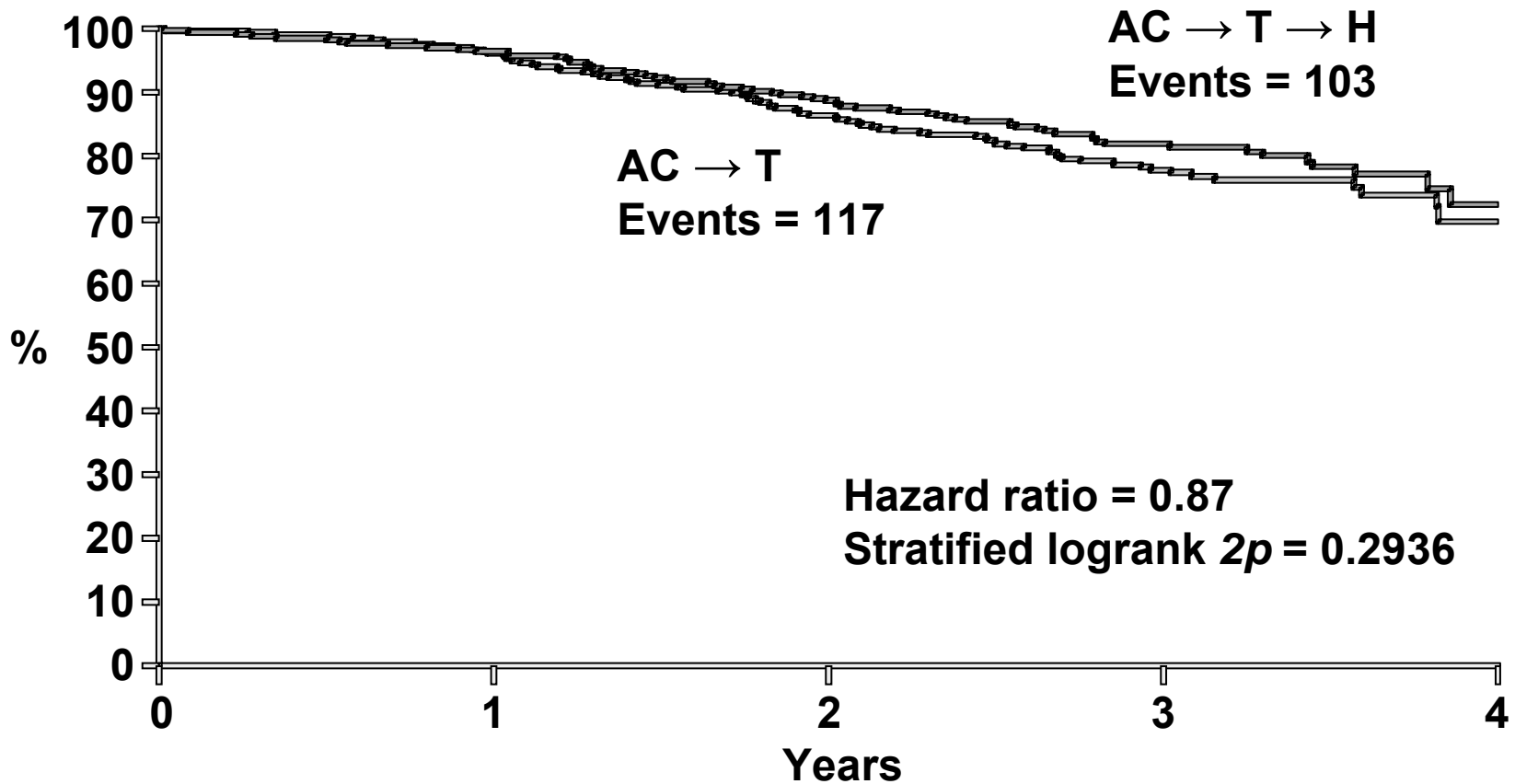


B-31/N9831 Survival



Disease-Free Survival: A vs B

N9831

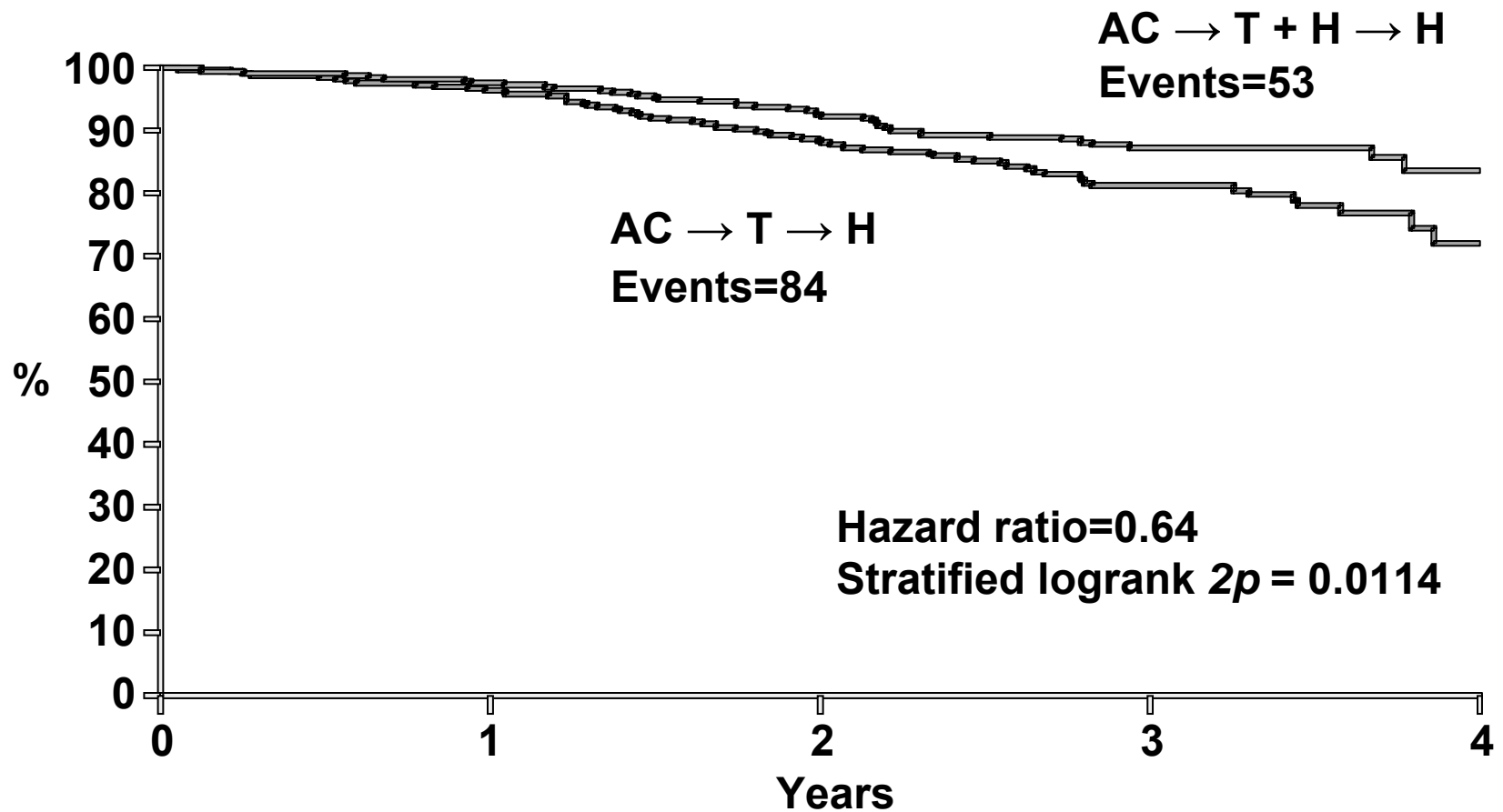


Number of patients followed

A	979	629	353	168	15
B	985	637	403	169	20

Disease-Free Survival: B vs C

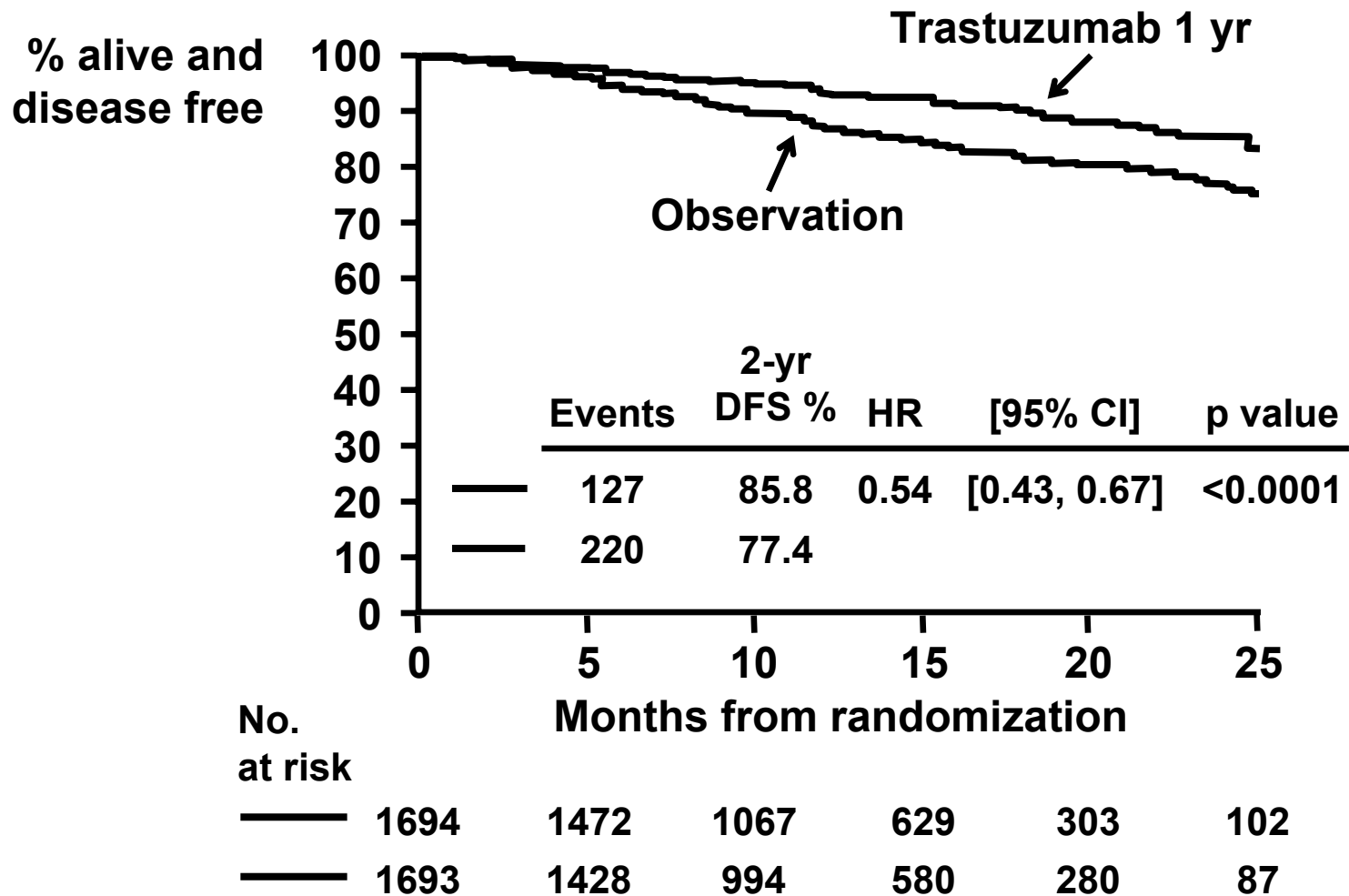
N9831



Number of patients followed

B	842	501	285	162	20
C	840	520	285	178	17

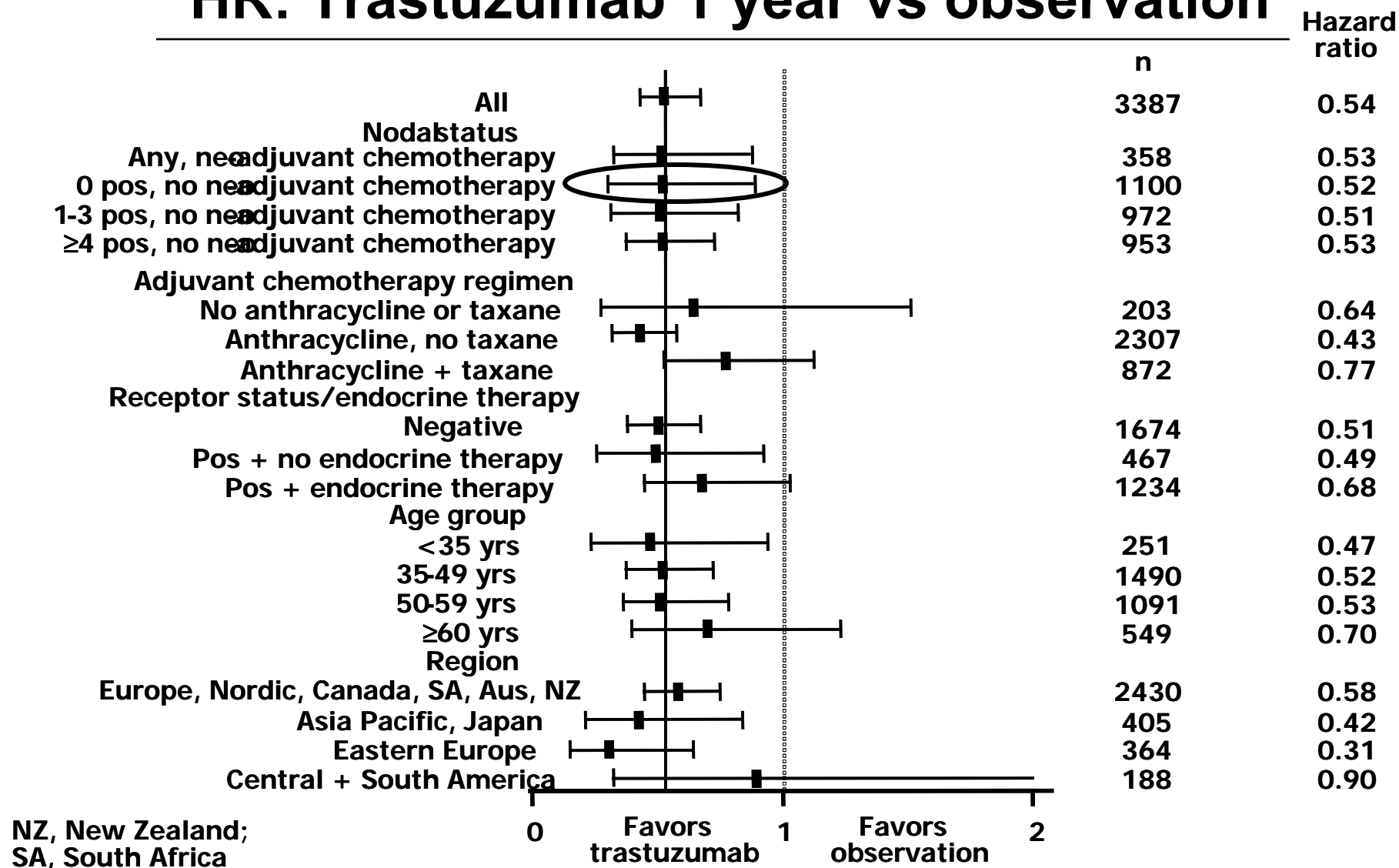
DISEASE-FREE SURVIVAL - HERA



HERA TRIAL

DFS BENEFIT ACCORDING TO SUBGROUPS

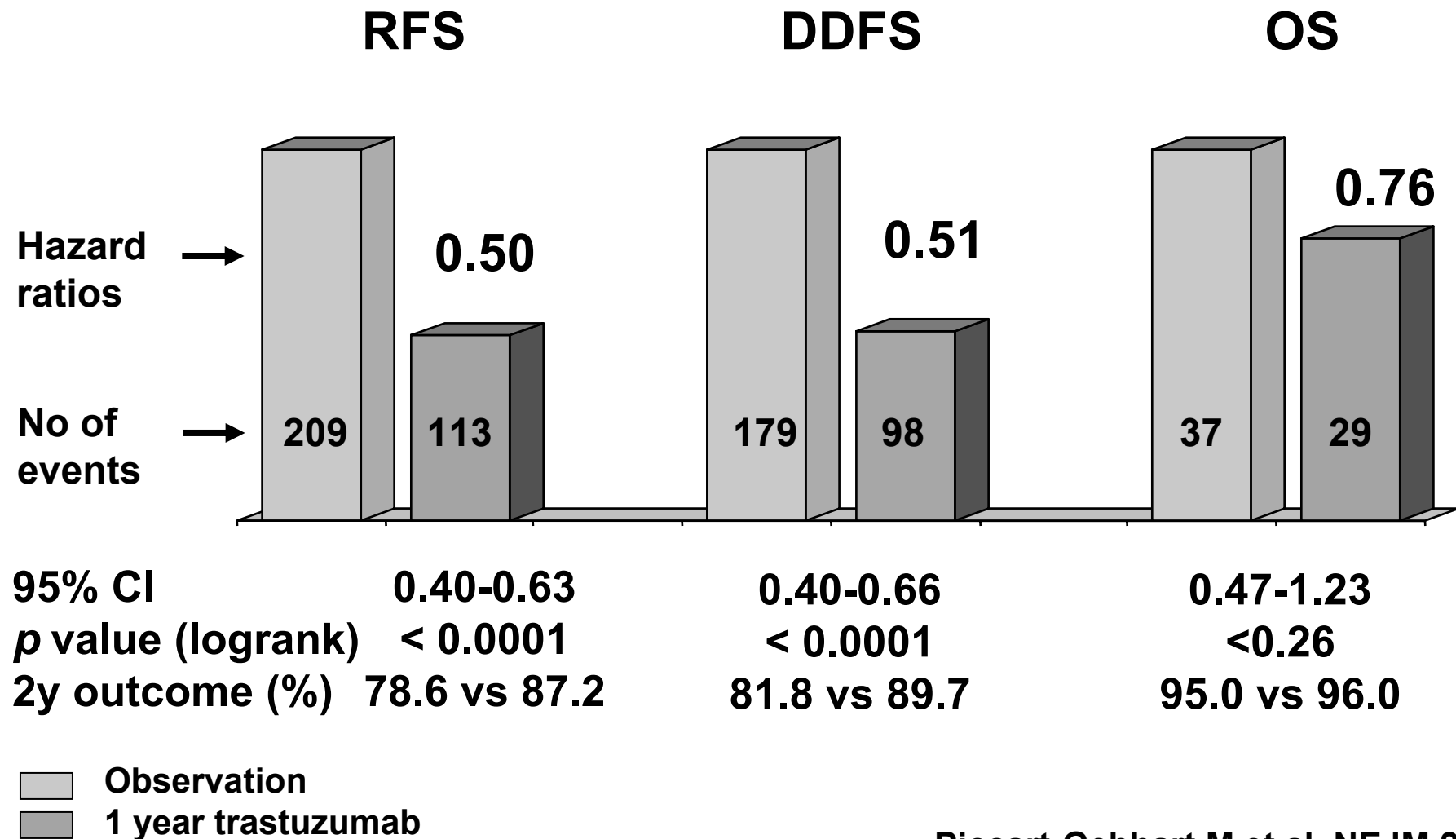
HR: Trastuzumab 1 year vs observation



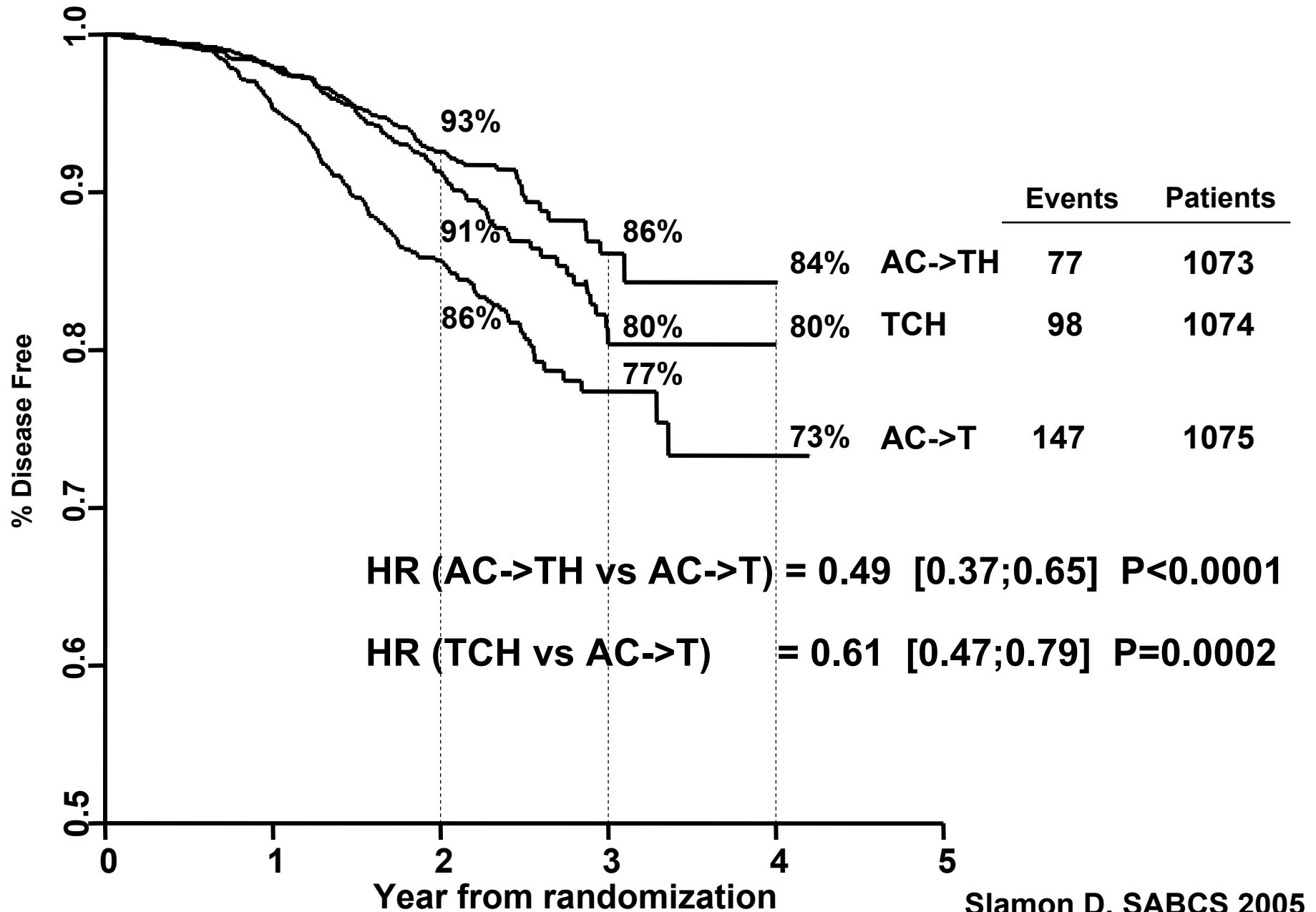
HERA TRIAL

Secondary efficacy endpoints

INTENT-TO-TREAT ANALYSIS



Disease Free Survival BCIRG 006

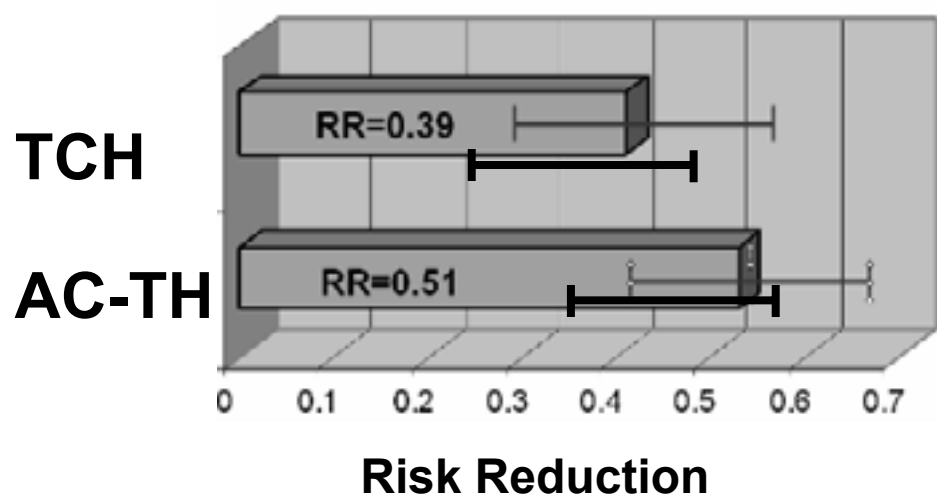


Disease Free Survival BCIRG 006

	AC-T n=1,073	AC-TH n=1,074	TCH n=1,075
Patients with event	147	77	98

Observed p-values

$p = 0.0000005$

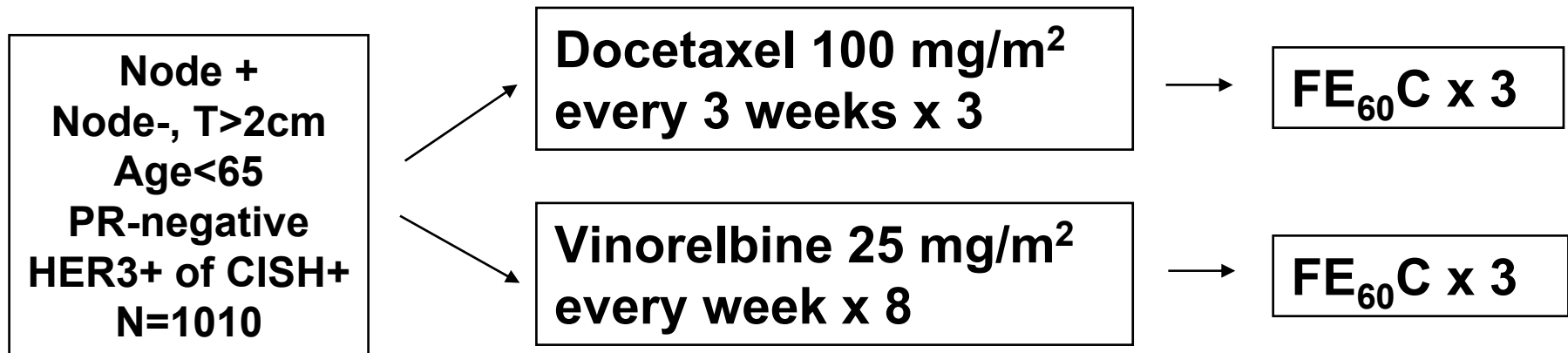


$p = 0.000153$

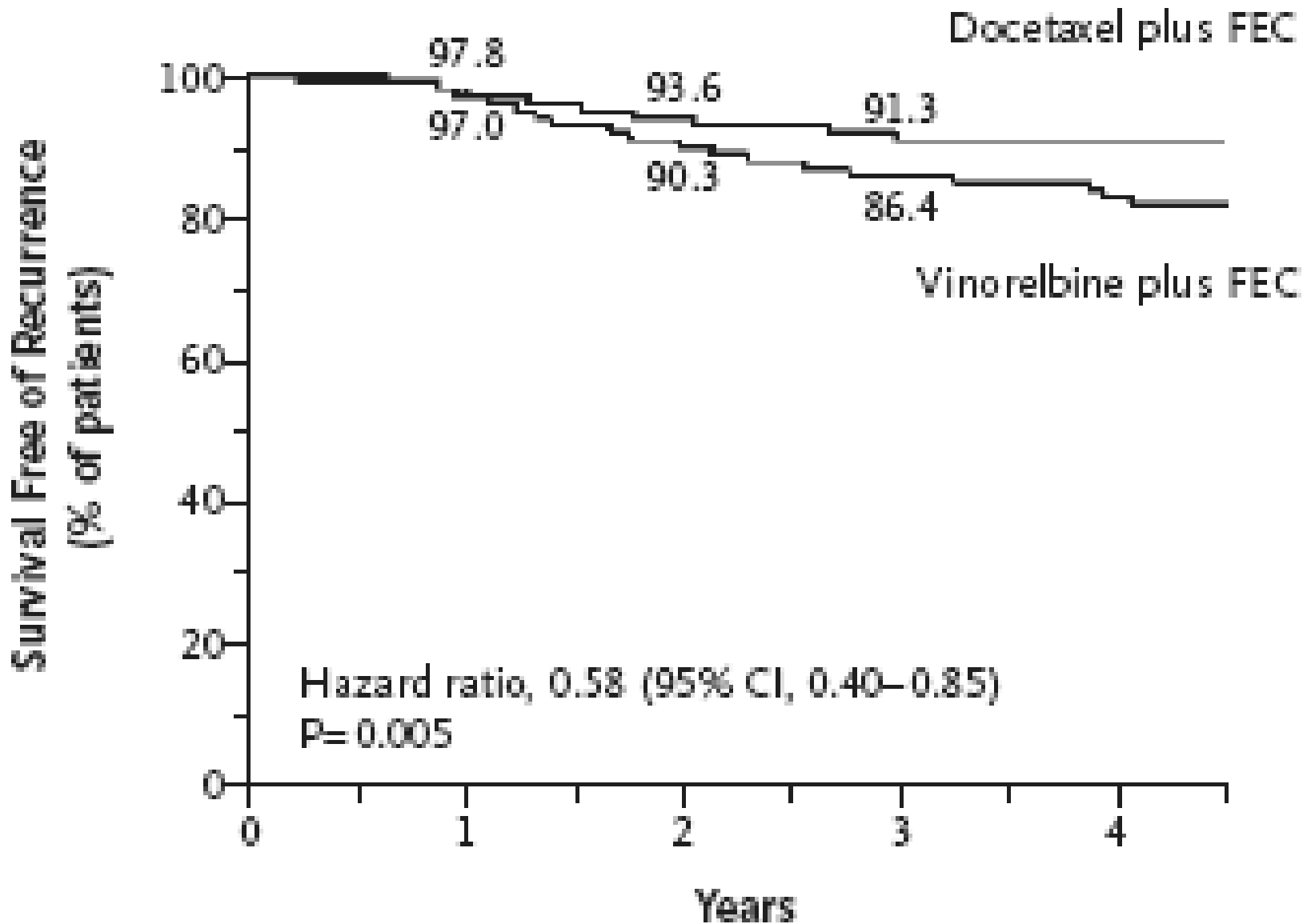
$p = 0.16$

Brief Adjuvant Trastuzumab FIN HER Study

- Two Independent Randomizations (2 x 2 Design)
- Median Follow-up 3 Years

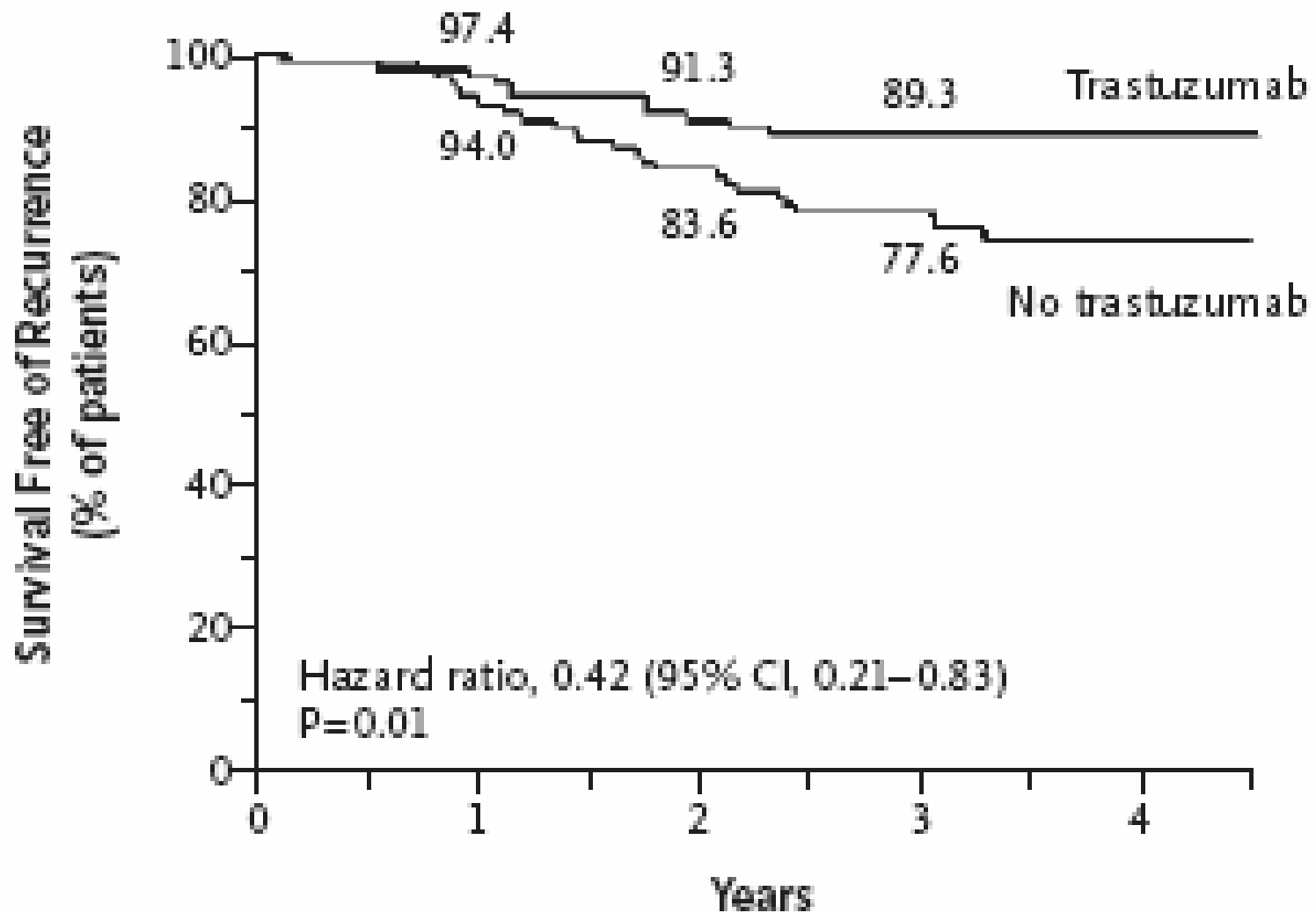


FIN HER Study



FIN HER Study

C Participants with *HER2/neu+* Cancer



Docetaxel vs Vinorelbine → CEF +/- Brief Course of Trastuzumab

Outcome	Docetaxel/CEF (n = 502)	Vinorelbine/CEF (n = 507)	P Value	HR (95% CI)
Recurrence-free 3-year survival, %	91.3	86.4	.005	0.58 (0.40-0.85)
Overall survival, %	96.4	95.4	.15	0.66 (0.38-1.17)

Outcome	Chemotherapy Alone (n = 115)	Chemotherapy + Trastuzumab (n = 116)	P Value	HR (95% CI)
Recurrence-free 3-year survival, %	77.6	89.3	.01	0.42 (0.21-0.83) [0.3 V; 0.6 D]
Overall survival, %	89.7	96.3	.07	0.41 (0.16-1.08)

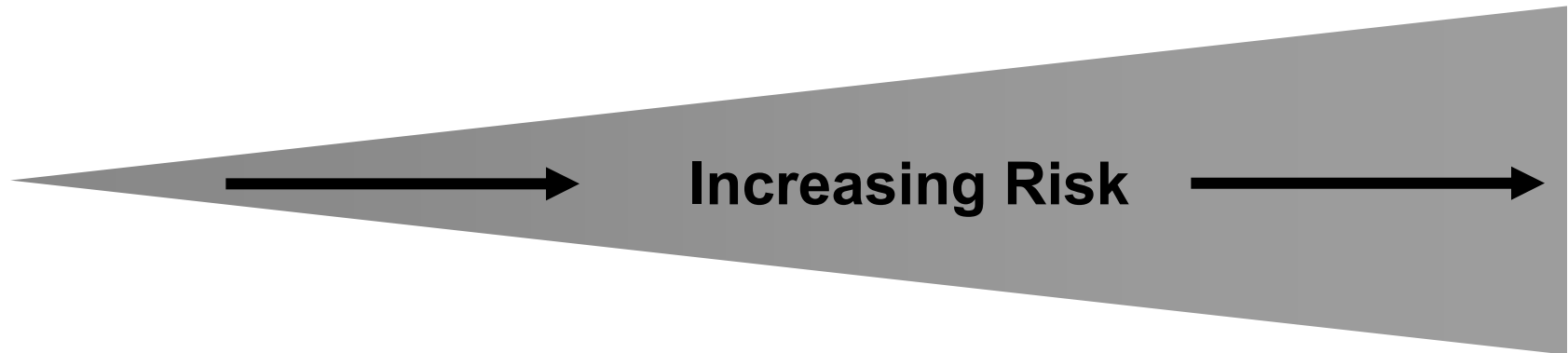
Docetaxel vs Vinorelbine → CEF +/- Brief Course of Trastuzumab

- **More adverse events in docetaxel vs vinorelbine arm**
- **Grade 3/4 toxicity in docetaxel arm**
 - **Neutropenia: 98%**
 - **Neutropenic fever: 24%**
- **Grade 3/4 toxicity in vinorelbine arm**
 - **Neutropenia: 58%**
 - **Neutropenic fever: 3%**
- **Addition of short-term trastuzumab well tolerated**
 - **No reported congestive heart failure**
 - **Decrease in LVEF of < 15% in 3% of patients (6% in control)**

Is a Brief Course of Adjuvant Trastuzumab Appropriate?

- The total N of 230 patients with HER2+ BC is about one-tenth the size of the definitive trials
- The confidence intervals are wide (0.21-0.83)
- However, it does point to the need to consider randomized trials of shorter as well as longer trastuzumab duration
- There is hint of greater efficacy of combining trastuzumab with vinorelbine compared to docetaxel, but better overall results with docetaxel in HER2-neg without trastuzumab
- Best current duration is 1 year

Systemic Adjuvant Therapy Guidelines: 2006



If ER or PR+ :

Tamoxifen (Premeno) or Aromatase Inhibitor (Postmeno)



Chemotherapy:

CMF or AC



Anthracycline plus Taxane



HER2+ :



Trastuzumab x 1 year