

# Case #2: Role of Nonanthracycline Regimens in Early Breast Cancer

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# Patient Profile

- **A 68-year-old postmenopausal lawyer**
  - **Myocardial infarction (66 years): Coronary angioplasty**
  - **Hyperlipoproteinemia**
  - **Medication: ACE inhibitor, beta blocker, statin, aspirin**
- **Right breast mass by screening mammogram**
- **Lumpectomy and sentinel node biopsy**
- **Pathology review**
  - **IDC, grade 3, LVI negative**
  - **Tumor size 1.2 cm (clear margins), SN negative**
  - **IHC: ER 20%, PR 15%, HER2 FISH positive**
  - **LVEF: 58%**

# Clinical Decision

- **Radiation therapy**
- **Systemic therapy**
  - **Endocrine therapy**
  - **Chemotherapy**

# Clinical Decision

- **Radiation therapy** **YES**
- **Systemic therapy**
  - **Endocrine therapy** **YES**
  - **Chemotherapy** **?**
  - **Trastuzumab** **?**

# Cytotoxic Therapy

- **Estrogen and progesterone receptors >10%**
  - **Considered as [+]**
- **Specific questions in this case**
  - **True benefits of CT**
  - **Cardiovascular risk**
  - **HER2 [+]** and trastuzumab therapy

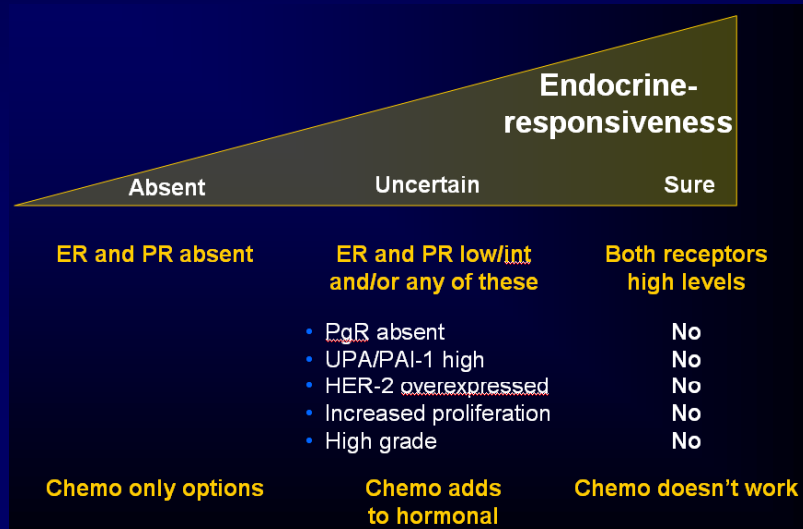
# Does This Patient Need Adjuvant CT?

- Unfavorable factors
  - SBR Grade III
  - HER2[+]

- Favorable factors:
  - Node negative
  - HR positive (low)
  - No LVI

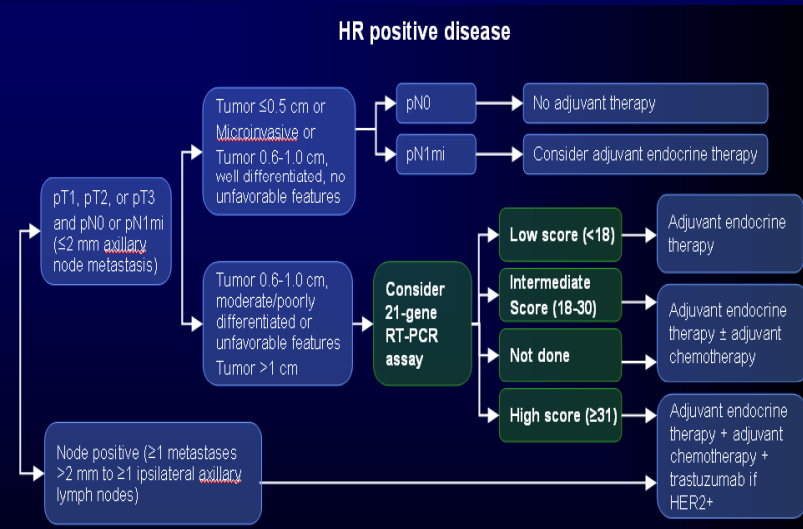
## Breast Cancer Guidelines

### Europe (St Gallen 2007)



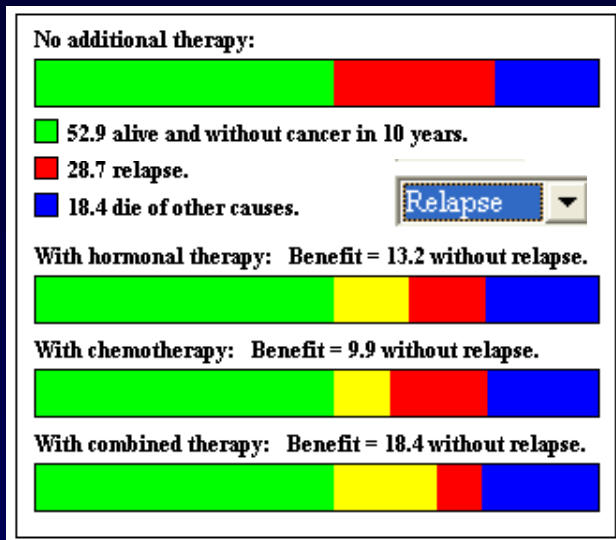
Goldhirsch A, et al. *Ann Oncol.* 2007; 18:1133-1144.

### US (NCCN 2008)



www.nccn.org

# Should We Add CT to Endocrine Therapy for This Patient?



**Patient Information**

Age: 68

Comorbidity: Average for Age

ER Status: Positive

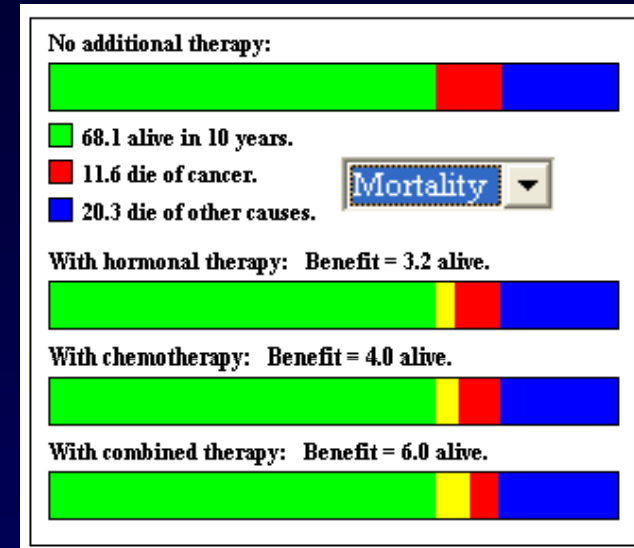
Tumor Grade: Grade 3

Tumor Size: 1.1 - 2.0 cm

Positive Nodes: 0

Calculate For: Relapse

10 Year Risk: 32 Prognostic

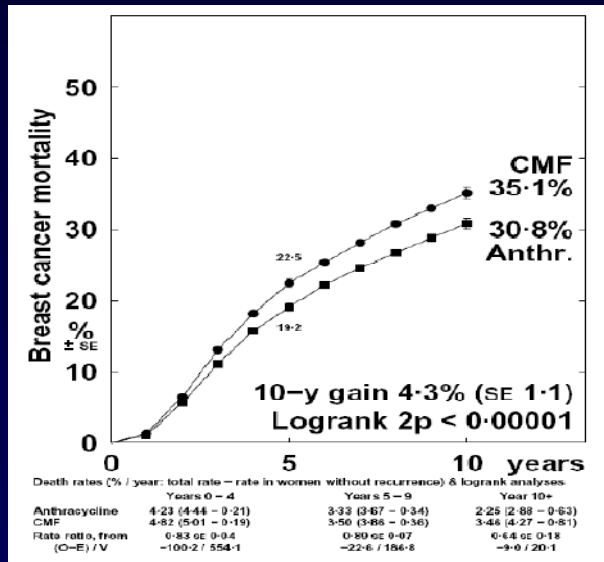


## Benefits from adding CT to an AI x 5 years

10-Year Absolute Gain	CMF x 6	AC x 4	FAC x 6	TAC / TC
Relapse	1.3%	2.9%	3.5%	5.2%
Mortality	0.5%	1.7%	1.9%	2.8%

C, cyclophosphamide; F, 5-fluorouracil; M, methotrexate; A, doxorubicin; P, paclitaxel; T, docetaxel

# Anthracycline-Based CT in Node-Negative Population: EBCTCG Studies

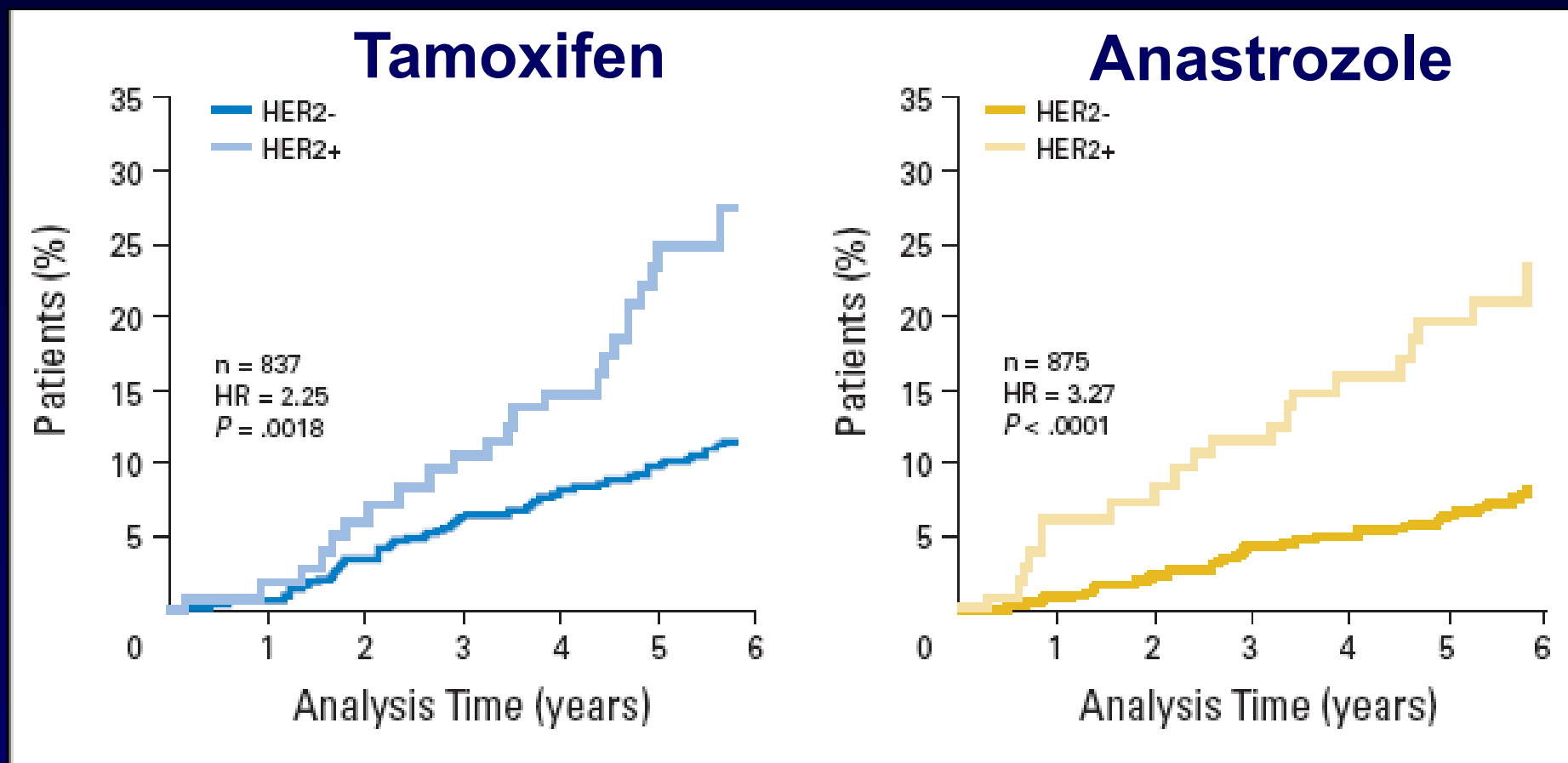


## Breast cancer mortality / Women

Category	Deaths/Women Allocated Anthr.	Adjusted CMF	Anthr. deaths Logrank O-E	Variance of O-E	Ratio of annual death rates Anthr. : CMF
(a) Regimens compared ( $\chi^2_3 = 7.8$ ; $p = 0.05$ )					
6 FAC vs. 6 CMF	217/1721 (12.6%)	277/1738 (15.9%)	-34.3	117.4	0.75 (SE 0.08)
6-9 FEC vs. 6-9 CMF	381/1460 (26.1%)	472/1473 (32.0%)	-58.3	197.7	0.74 (SE 0.06)
A + other vs. 6-12 CMF	958/3132 (30.6%)	1012/3100 (32.6%)	-31.5	344.6	0.91 (SE 0.05)
E ± other vs. 6 CMF	253/915 (27.7%)	276/931 (29.6%)	-7.6	101.4	0.93 (SE 0.10)

Control Arm	Investig. Arm	Population	HR DFS	P	HR OS	P
CMF	AC x 4	N[+]/N[-]	0.94	ns	0.91	ns
CMF	FAC/FEC	N[+]/N[-]	0.83	<.05	0.75	<.05

# Hormonotherapy Alone Is Not an Appropriate Treatment in HER2-Positive Patients<sup>1</sup>



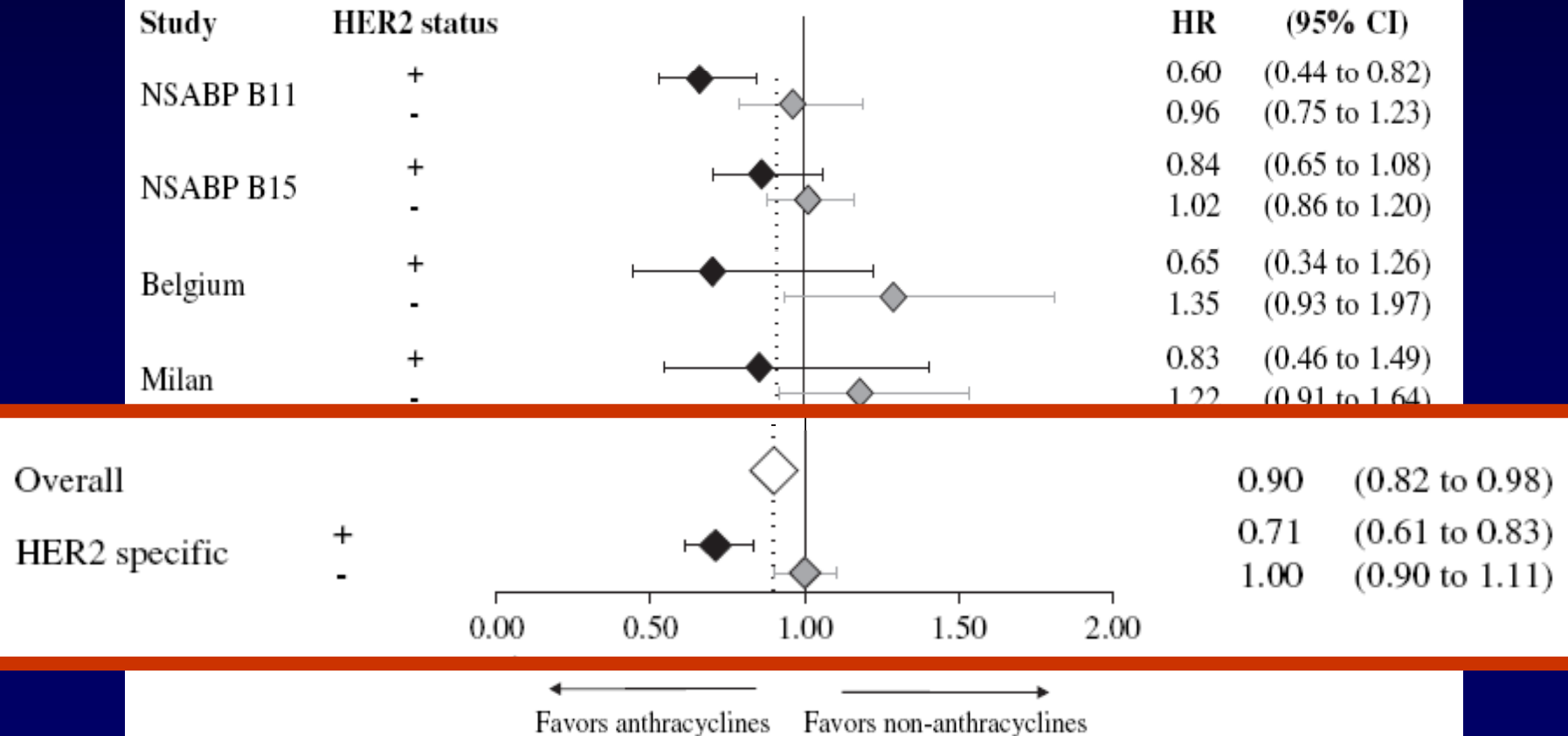
Similar results reported also in the context of the BIG 1-98 trial<sup>2</sup>

1. Dowsett M, et al. *J Clin Oncol*. 2008;26(7):1059-1065. 2. Rasmussen BB, et al. *Lancet Oncol*. 2008;9(1):23-28.

# HER2 Status and Efficacy of Adjuvant Anthracyclines in Early Breast Cancer: A Pooled Analysis of Randomized Trials

Alessandra Gennari, Maria Pia Sormani, Paolo Pronzato, Matteo Puntoni, Mariantonietta Colozza, Ulrich Pfeffer, Paolo Bruzzi

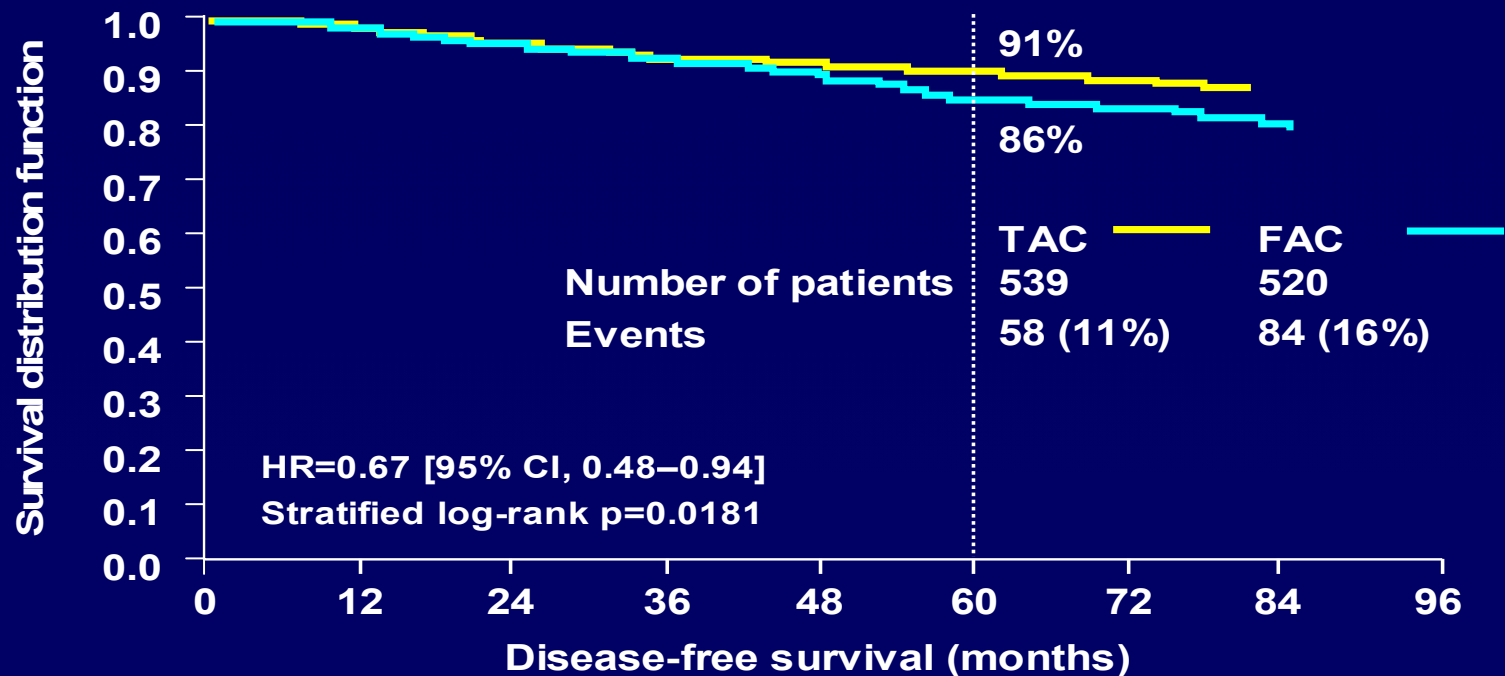
J Natl Cancer Inst 2008;100:14-20



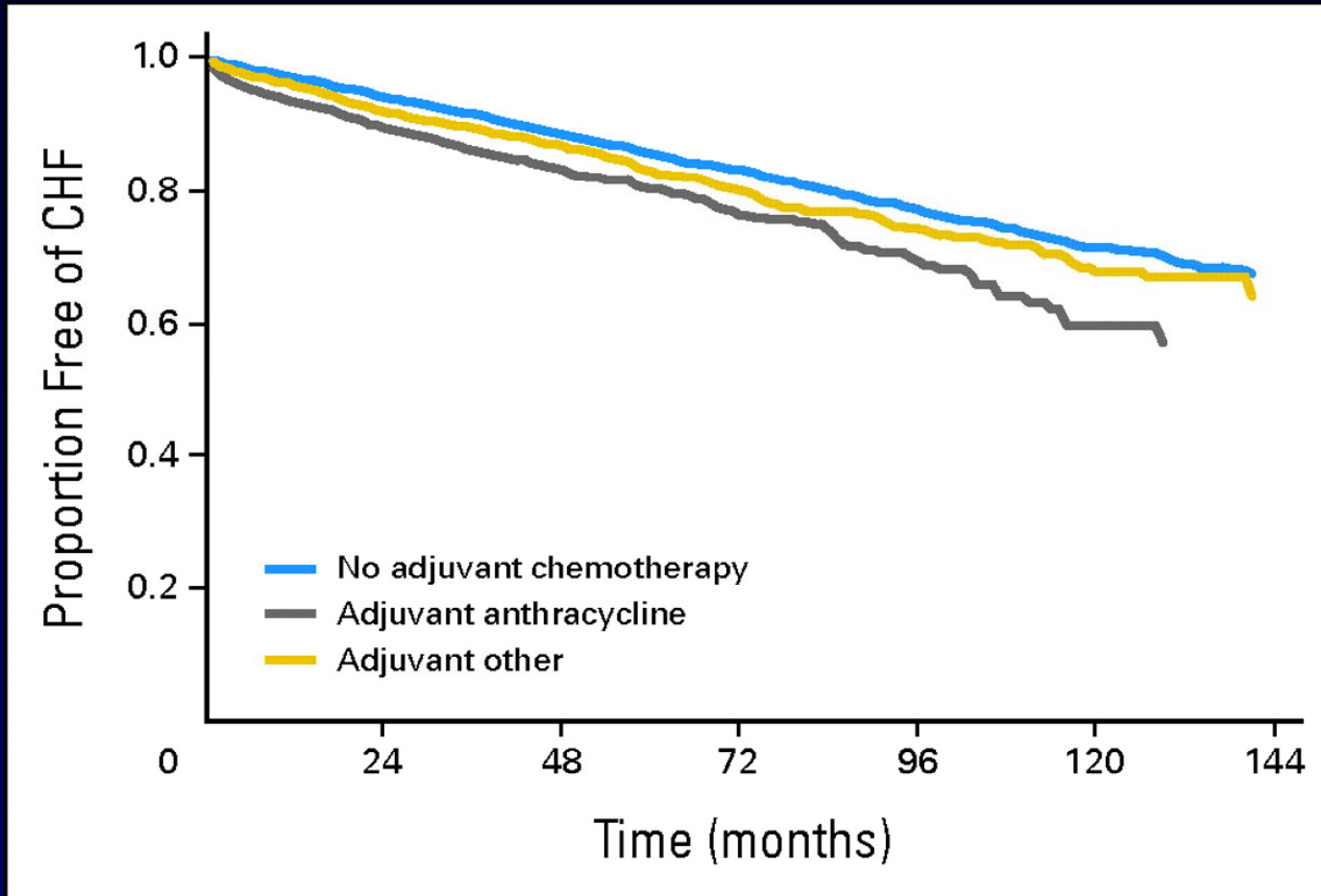
# GEICAM 9805: TAC vs FAC in Node-Negative Population

## DFS

Median follow up: 67 months



# Anthracycline-Related Cardiac Toxicity



**Freedom from congestive heart failure (CHF) by adjuvant chemotherapy type. Women aged 66 to 70 years.**

# Is Chemotherapy-Related Cardiac Risk Relevant to This Patient?

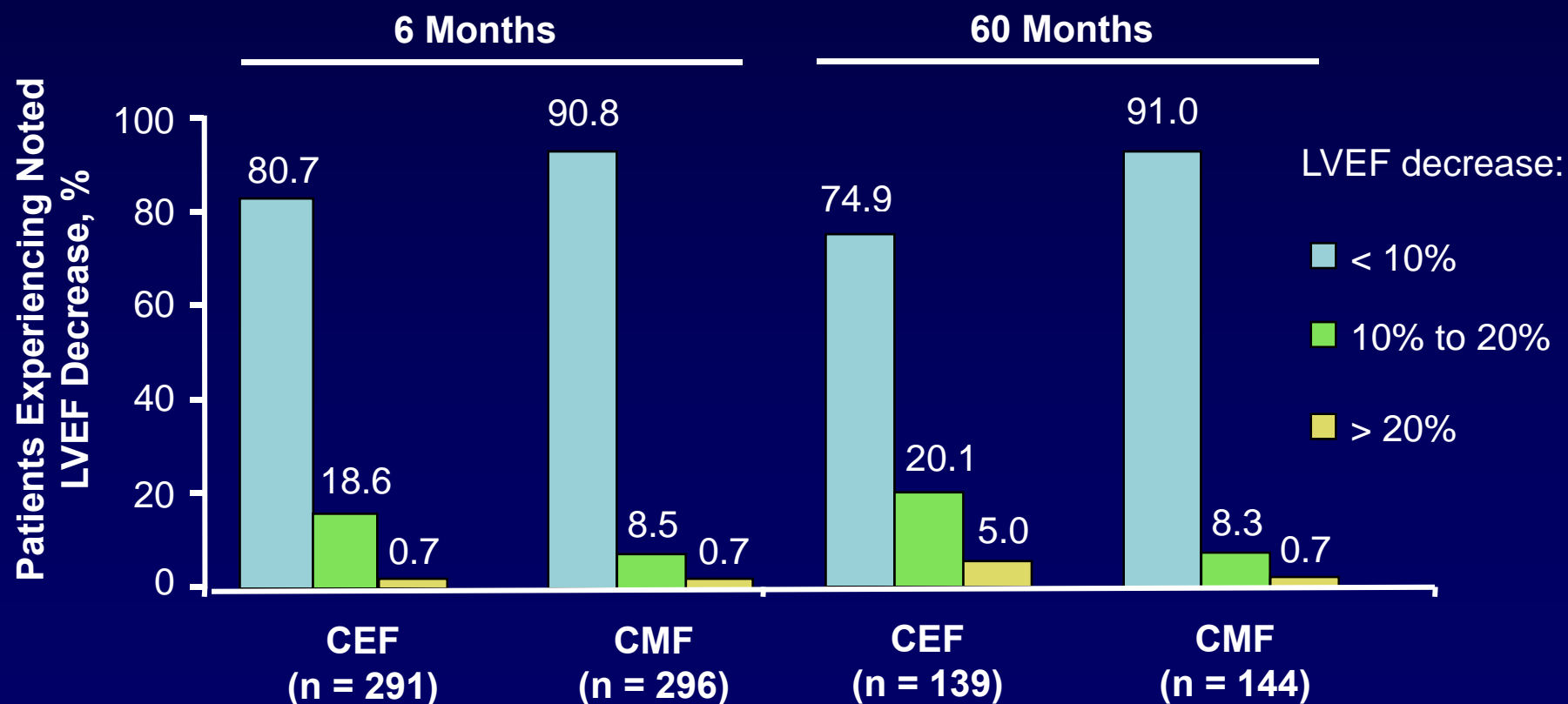
- Risk factors:

- Hypertension

- Hyperlipoproteinemia

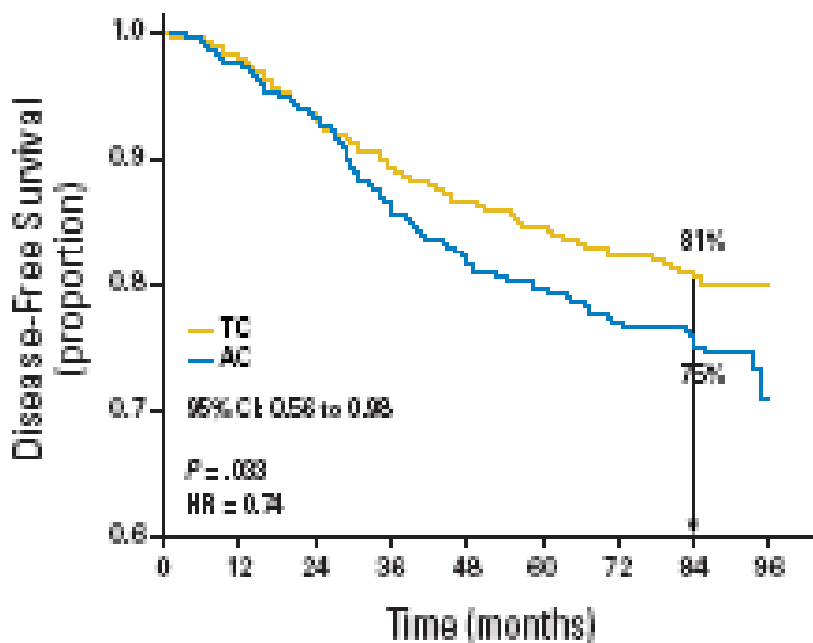
- Myocardial Infarction

- LVEF (58%)

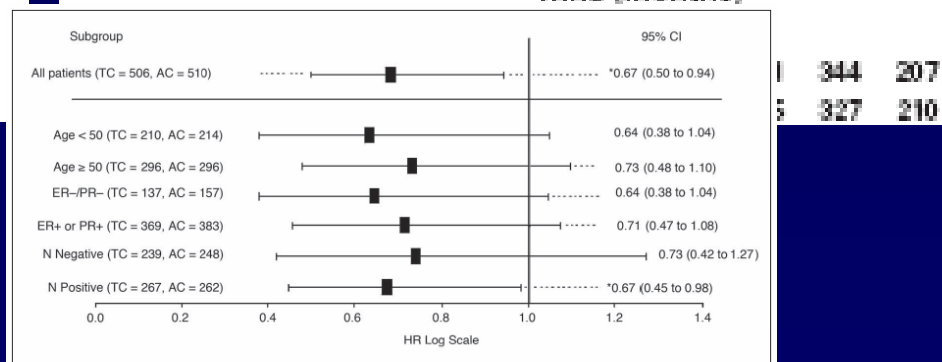
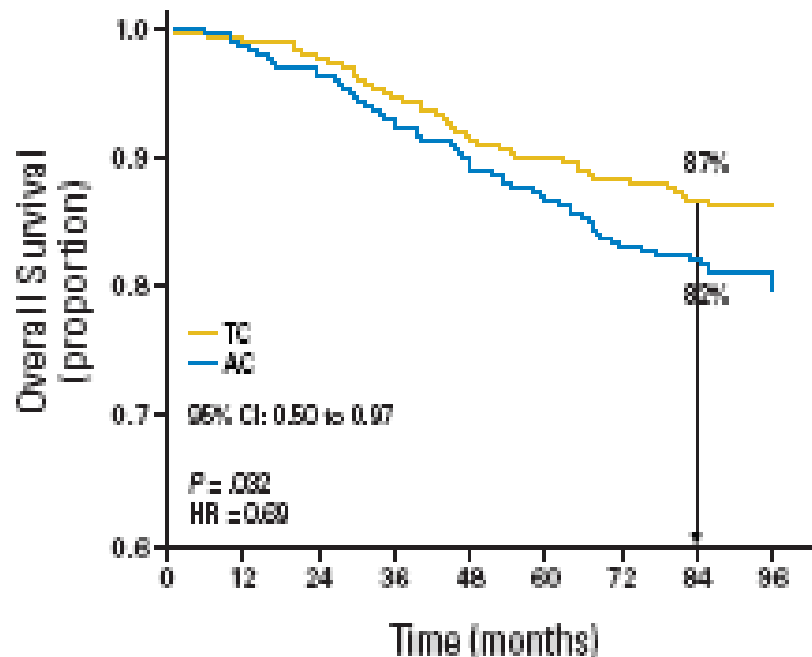


# Docetaxel as an Alternative Option to Anthracycline Regimens

7-year results of the TC (Docetaxel-Cyclophosphamide) vs AC (Doxorubicin-Cyclophosphamide)



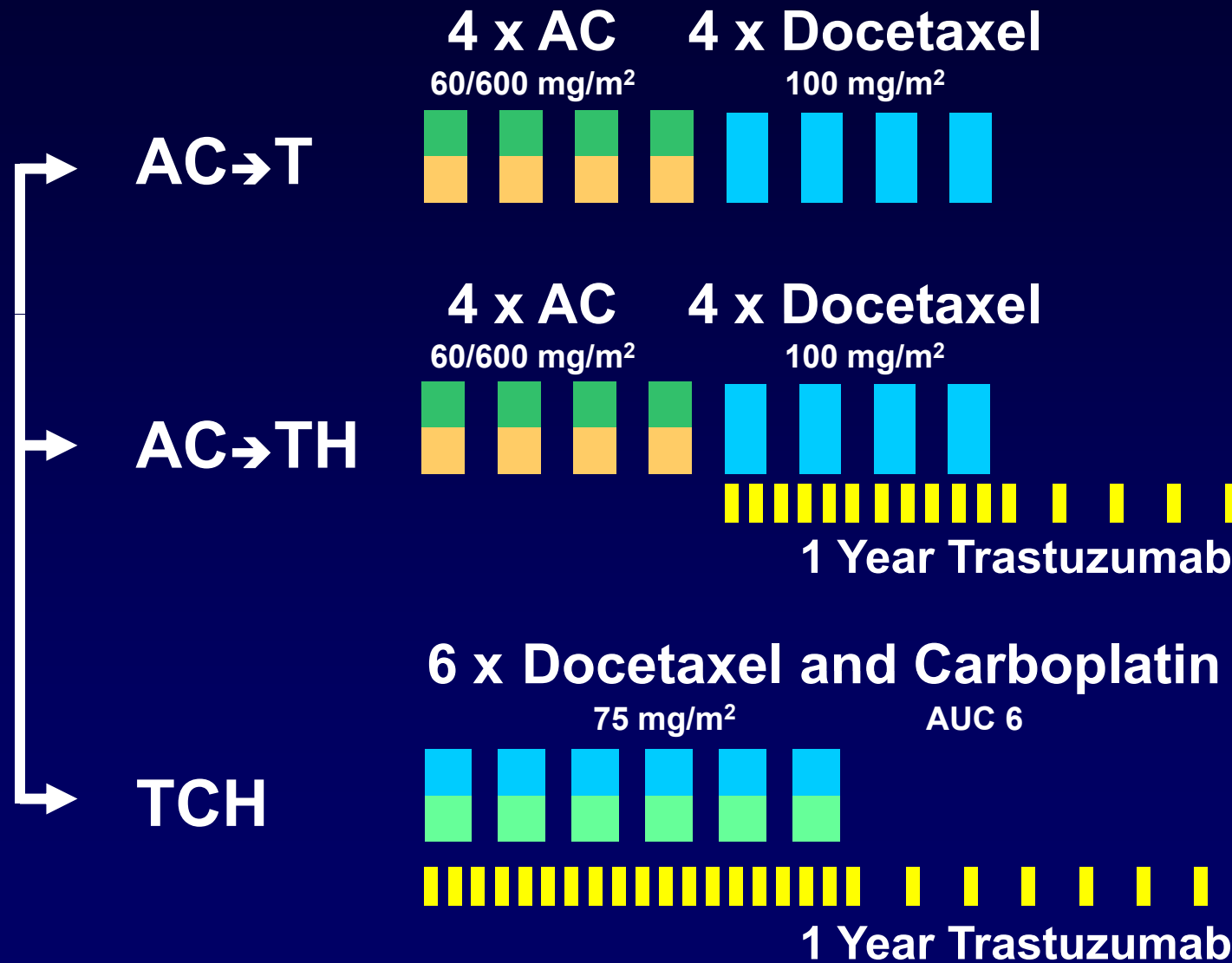
No. at risk	0	12	24	36	48	60	72	84	96
TC	506	481	442	410	378	349	320	195	
AC	510	483	449	405	372	343	303	194	



# Anti-HER2 Therapy

- **Early-stage and HER2 [+] by FISH**
  - Indication for trastuzumab therapy
- **Specific questions in this case**
  - Benefit and risk combining with CT
  - Cardiovascular risk
  - Is possible to give without CT

# Use of Trastuzumab-Based Regimens Without Anthracyclines: the BCIRG 006 Trial

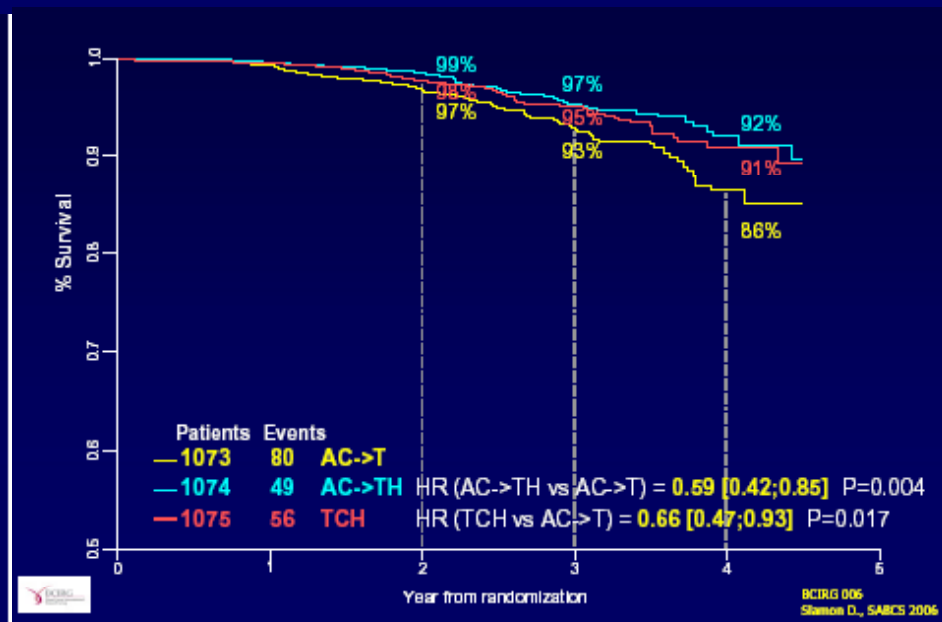
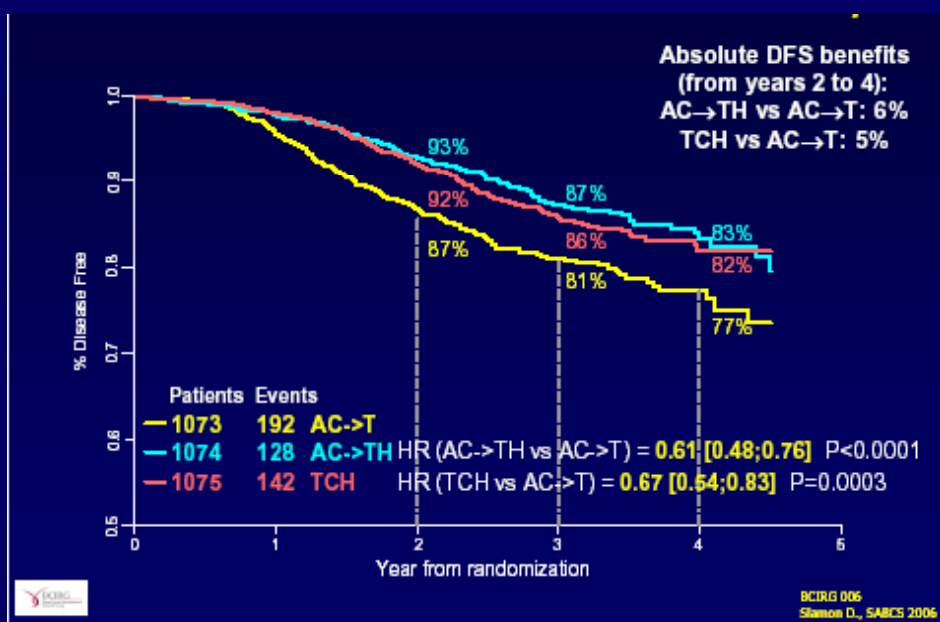


Slamon D, et al. *Breast Cancer Res Treat.* 2006;100(Suppl 1): Abstract 52.

# Efficacy Data

## Disease-Free Survival

## Overall Survival

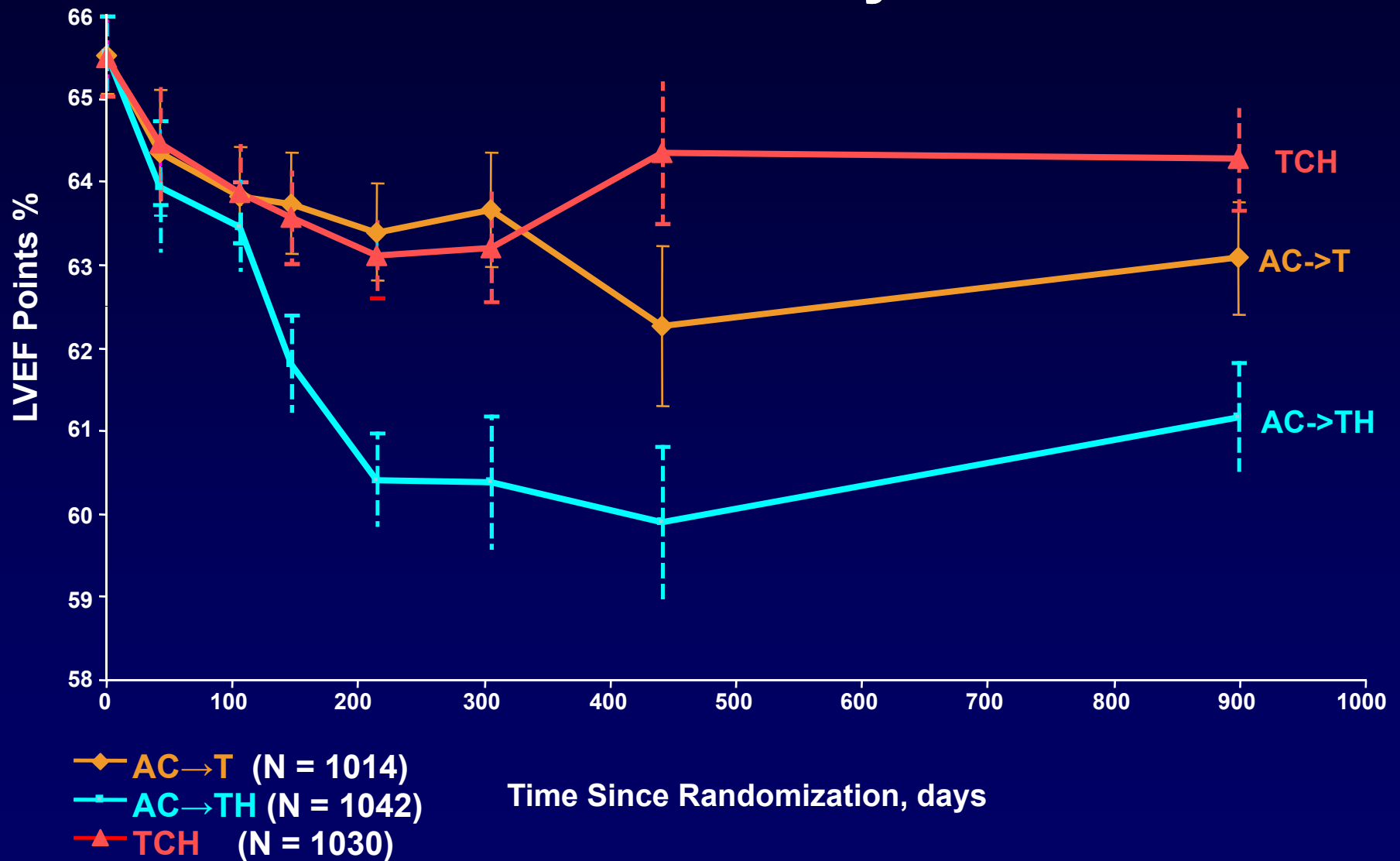


Median follow-up 36 months

# BCIRG 006 Cardiac Safety Data 36-Months Median Follow-Up

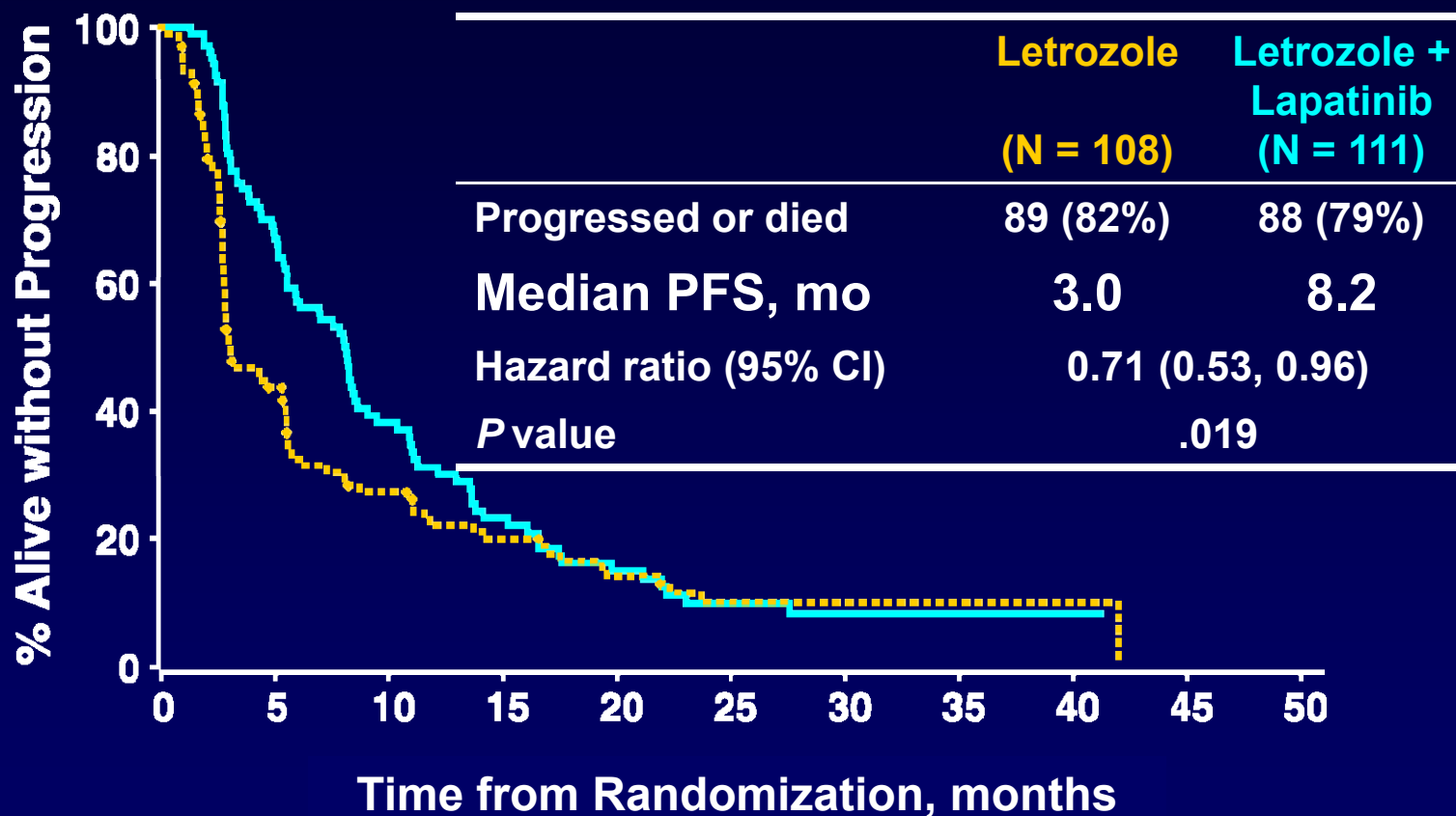
Events	AC-T n = 1050	AC-TH n = 1068	TCH n = 1056
Cardiac-related death	0	0	0
Cardiac left ventricular function (CHF) grade 3/4	4	20	4
Absolute difference between non-H and H arms		1.5%	0
Absolute difference between non-H and H arms at 23 months		1.31%	0.18%

# Mean LVEF—All Observations 2<sup>nd</sup> Interim Analysis



Slamon D, et al. *Breast Cancer Res Treat.* 2006;100(Suppl 1): Abstract 52.

# AI + Lapatinib vs AI in HER2+ MBC 30008 Study



Pts at risk:

Let + Lap	111	69	33	20	12	8	4	1	1
Let	108	43	26	18	12	7	5	2	2

# My Personal Decision About This Patient

**This patient has a high-risk node-negative breast cancer**

- I. Endocrine therapy is mandatory (AI > TAM)**
- II. The administration of a last generation chemotherapy regimen (TC or TAC) increases modestly her chances to survive (absolute benefits at 10 years 2.8%)**
  - An anthracycline regimen does not seem reasonable**
  - The DCarboplatin (or DCycloph) is more appropriate**
- III. There is no clinical trial justifying trastuzumab without CT in the adjuvant setting, but.....**
- IV. The cardiac risk and the PS (1) merits a long discussion with the patient about benefits and risks**