

PREOPERATIVE THERAPY IN INVASIVE BREAST CANCER

Reviewing the State of the Science and Exploring New Research Directions

Preoperative Chemotherapy, NSABP Protocols B-18 and B-27: an update

Norman Wolmark

NSABP





Adjuvant Therapy

B-18

Duration: 88-93

ACCRUAL: 1,523

B-27

Duration: 95-00

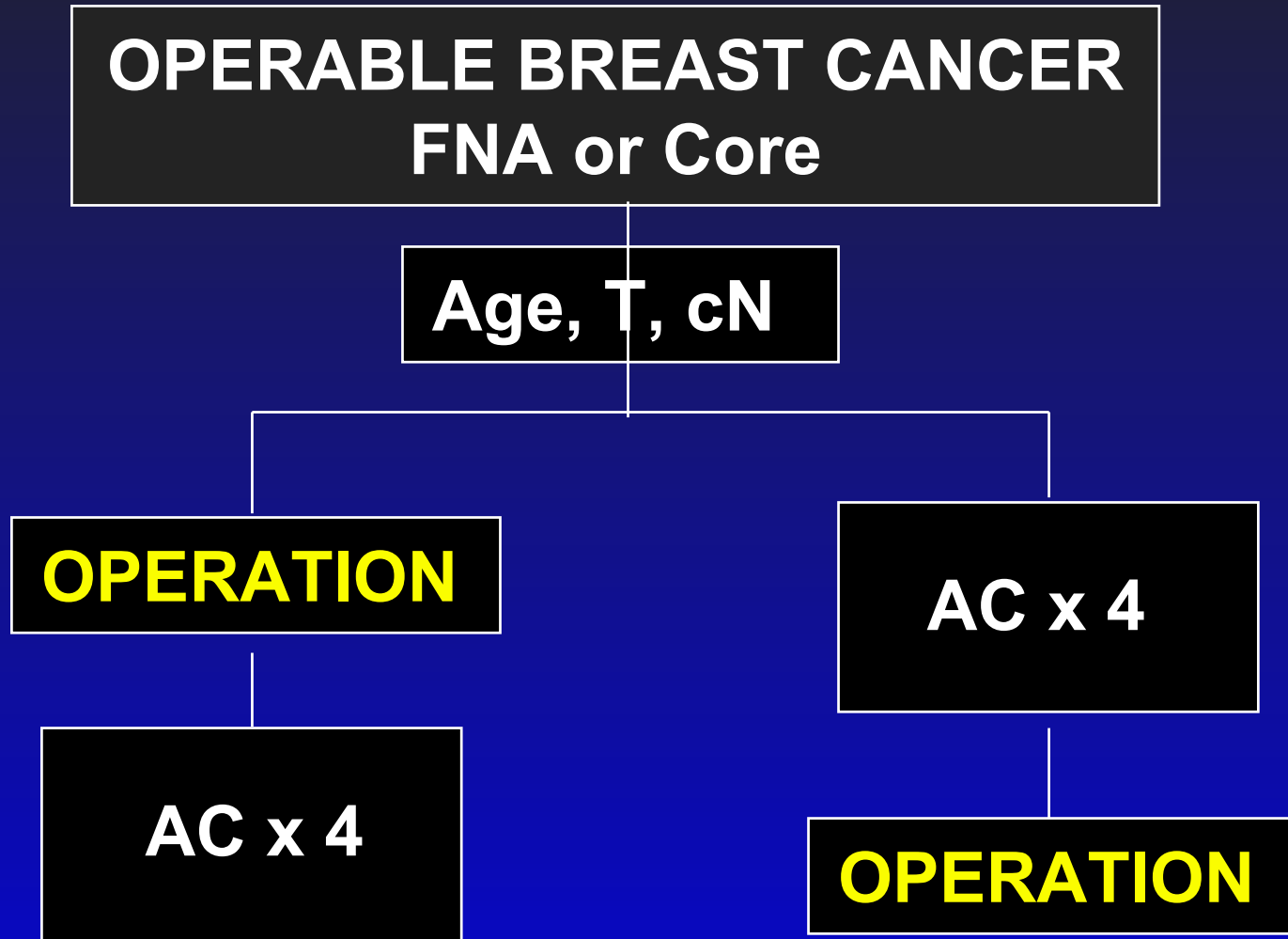
ACCRUAL: 2,411

B-40

pCR endpoint

Started 11-06

B-18



Tam for women ≥ 50 yrs. only

NSABP B-18

OPENED: Oct. 1988

CLOSED: Apr. 1993

ACCRUAL: 1,523

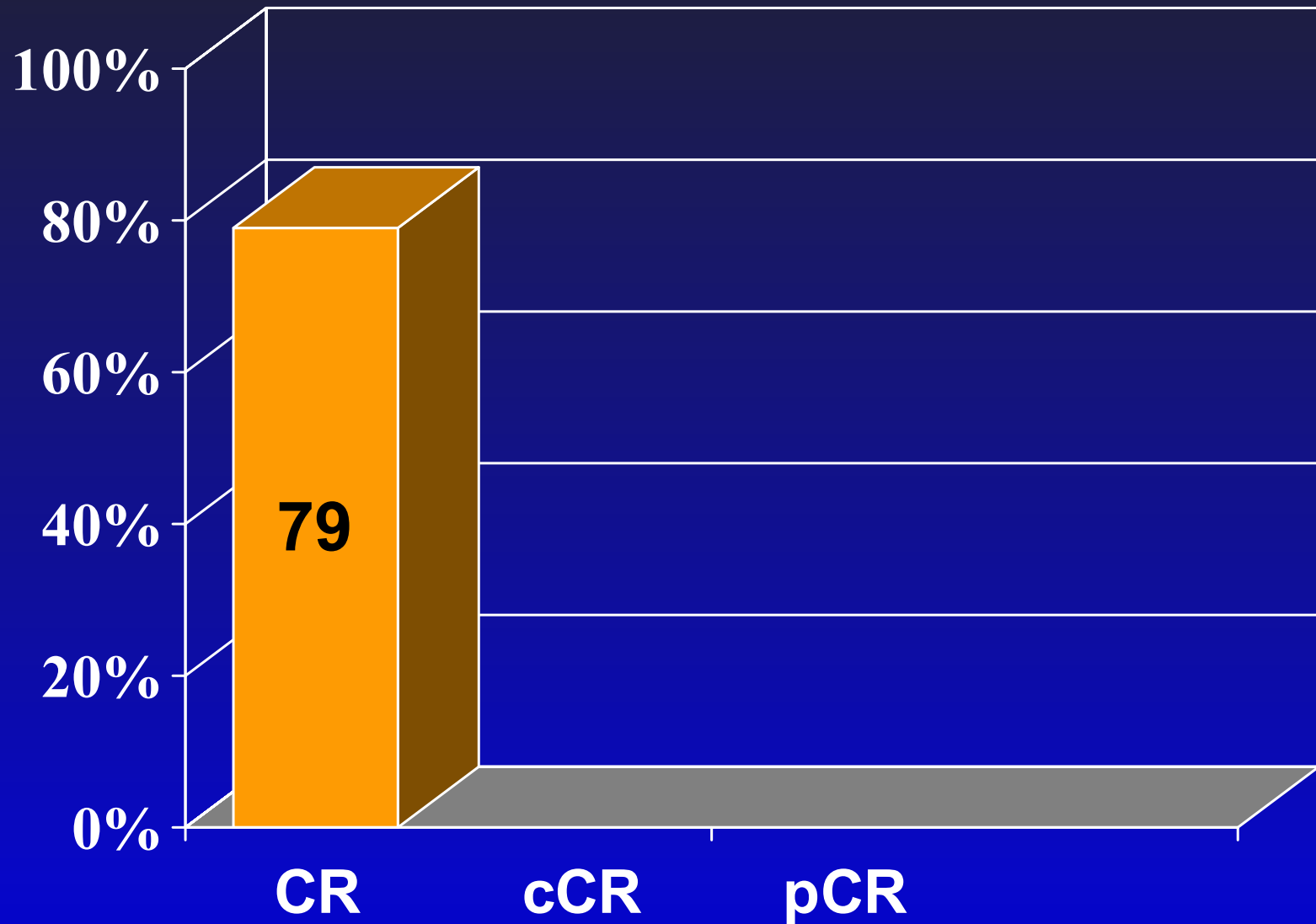
MTS: 9.5 years (2001)
16 years (present)

B-18 Clin.Tumor/Node Status

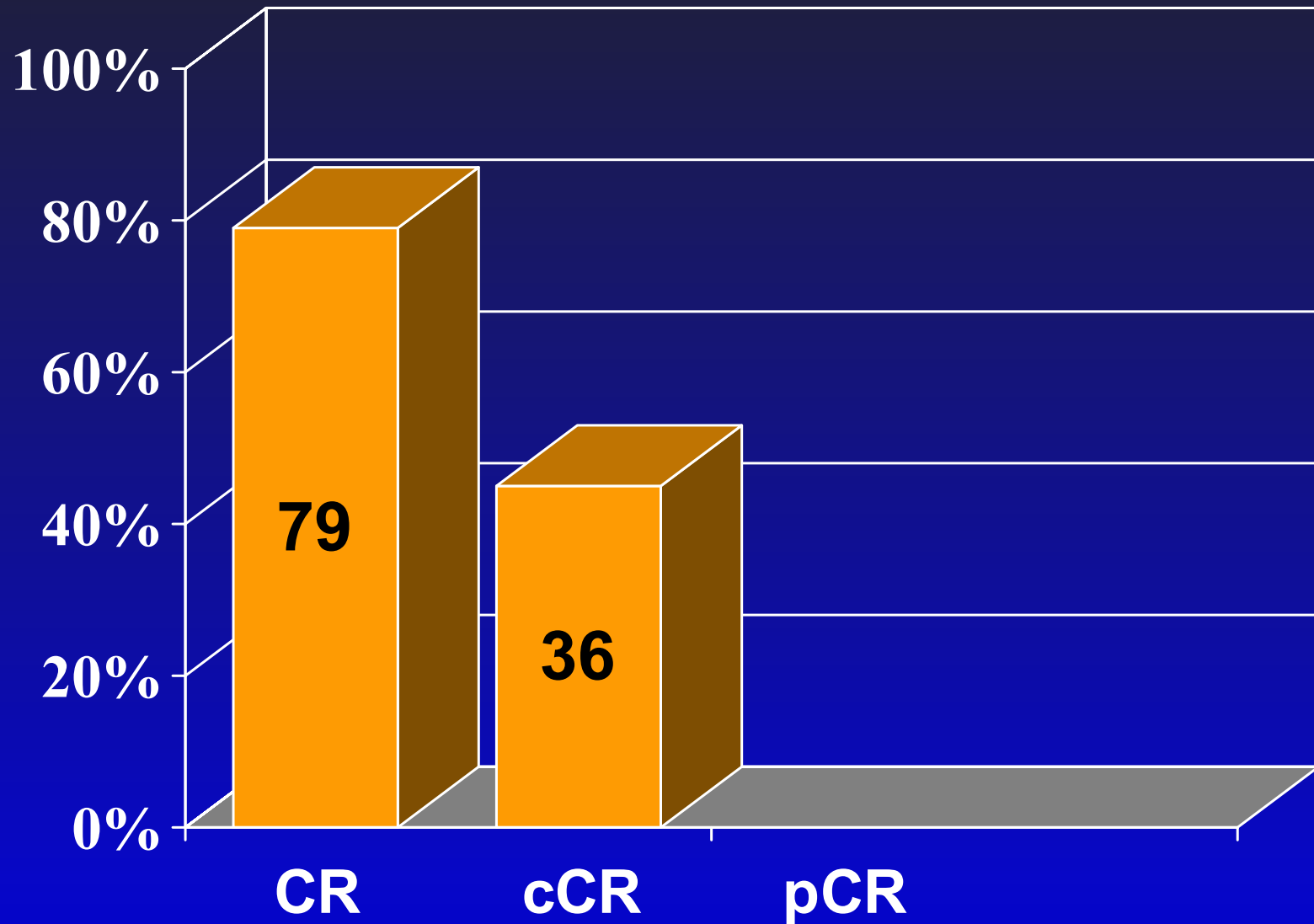
<u>cm</u>	<u>%</u>
< 2.0	28
2.1 - 4.0	59
> 4.1	13
<u>Node neg.</u>	<u>74</u>

Tumor Response

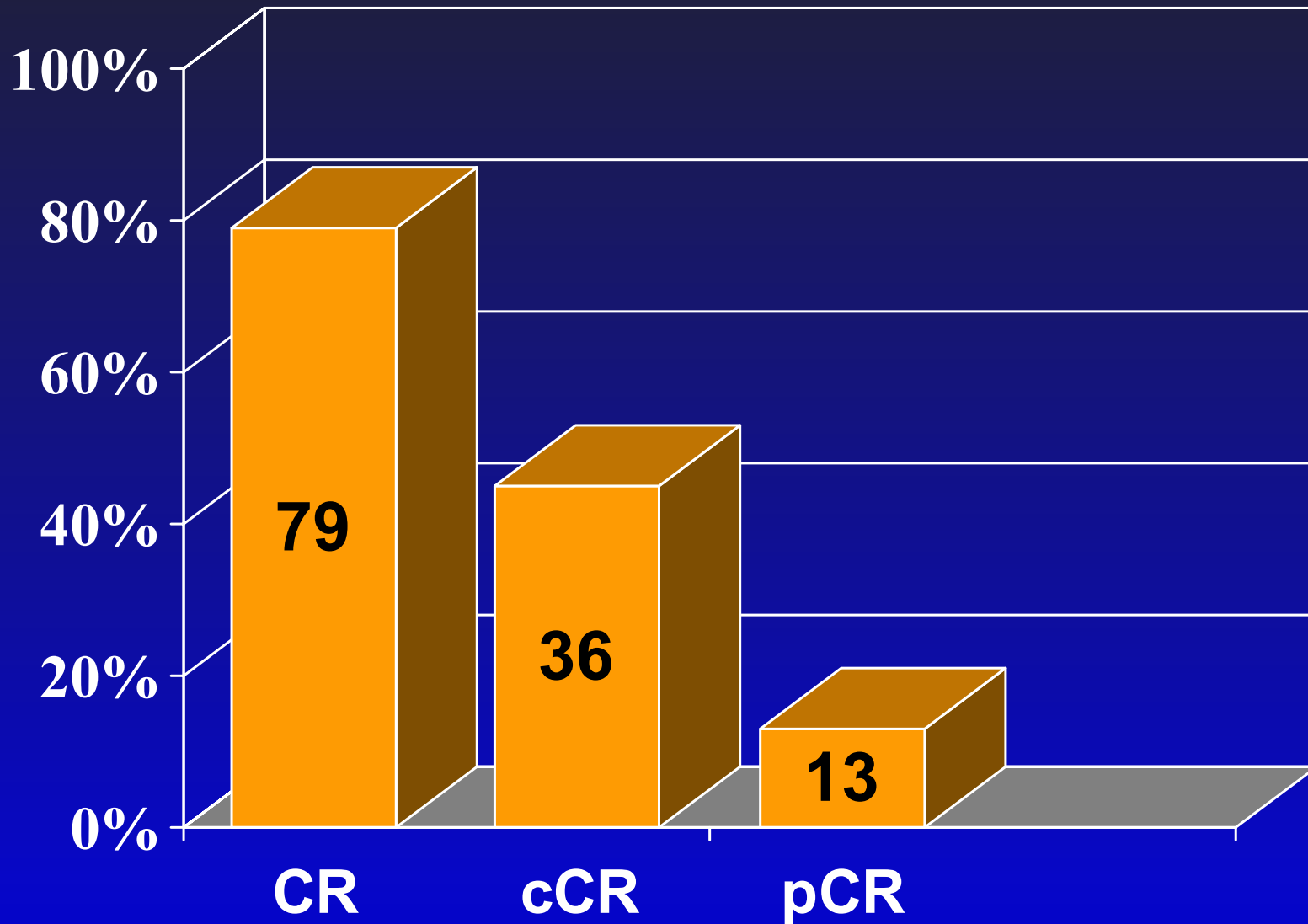
Tumor Response (685pts.)



Tumor Response (685pts.)

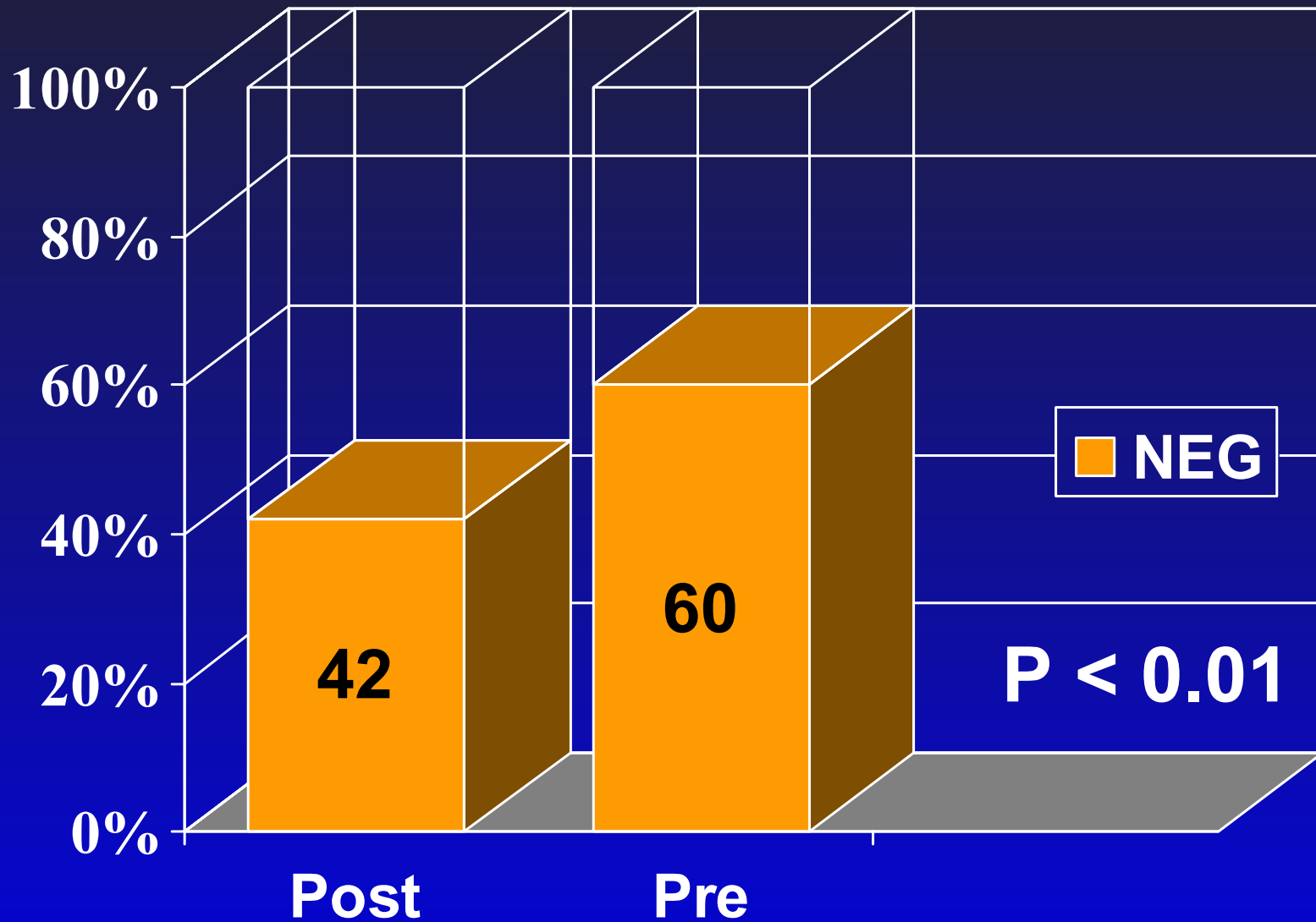


Tumor Response (685pts.)

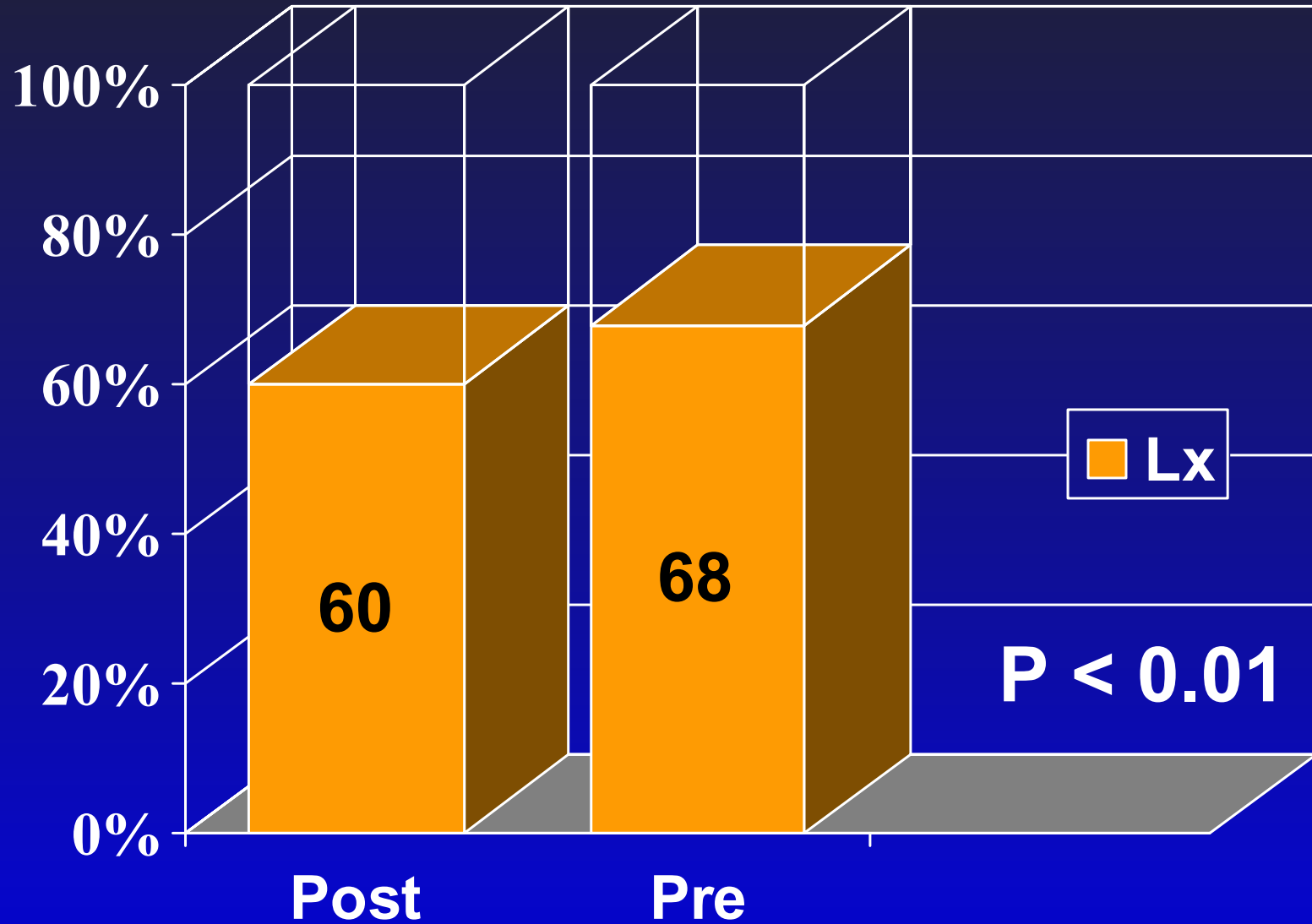


*25% pCR w DCIS

Nodal Response

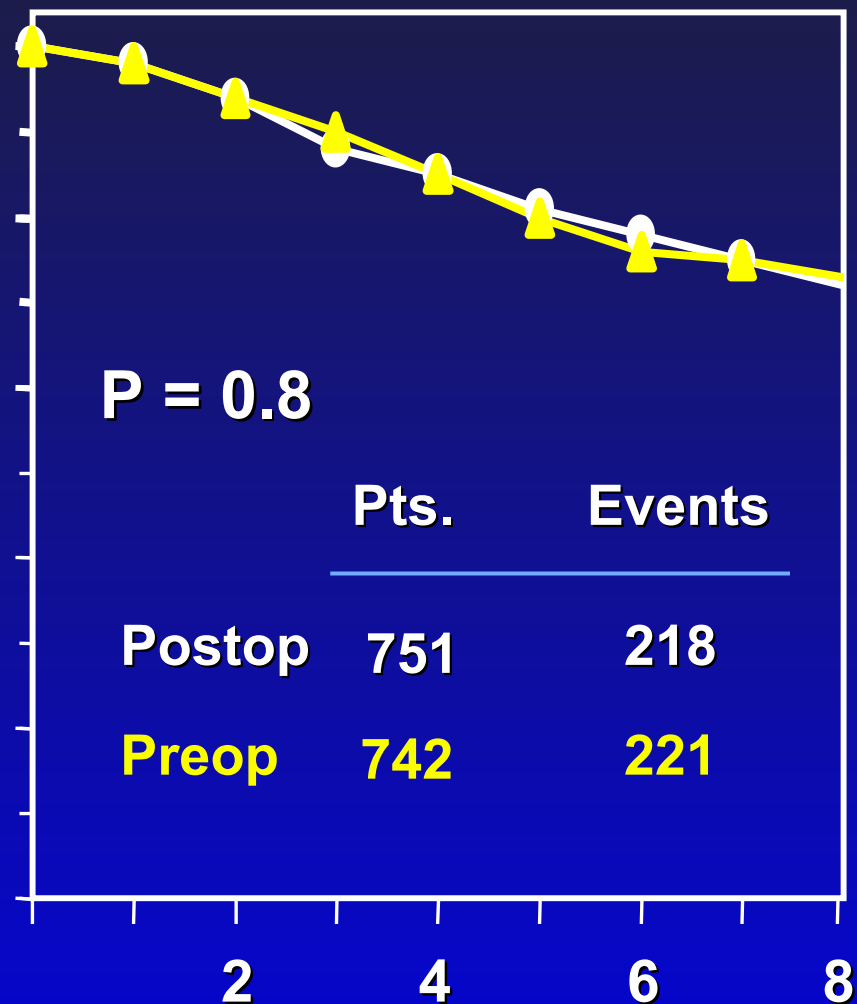
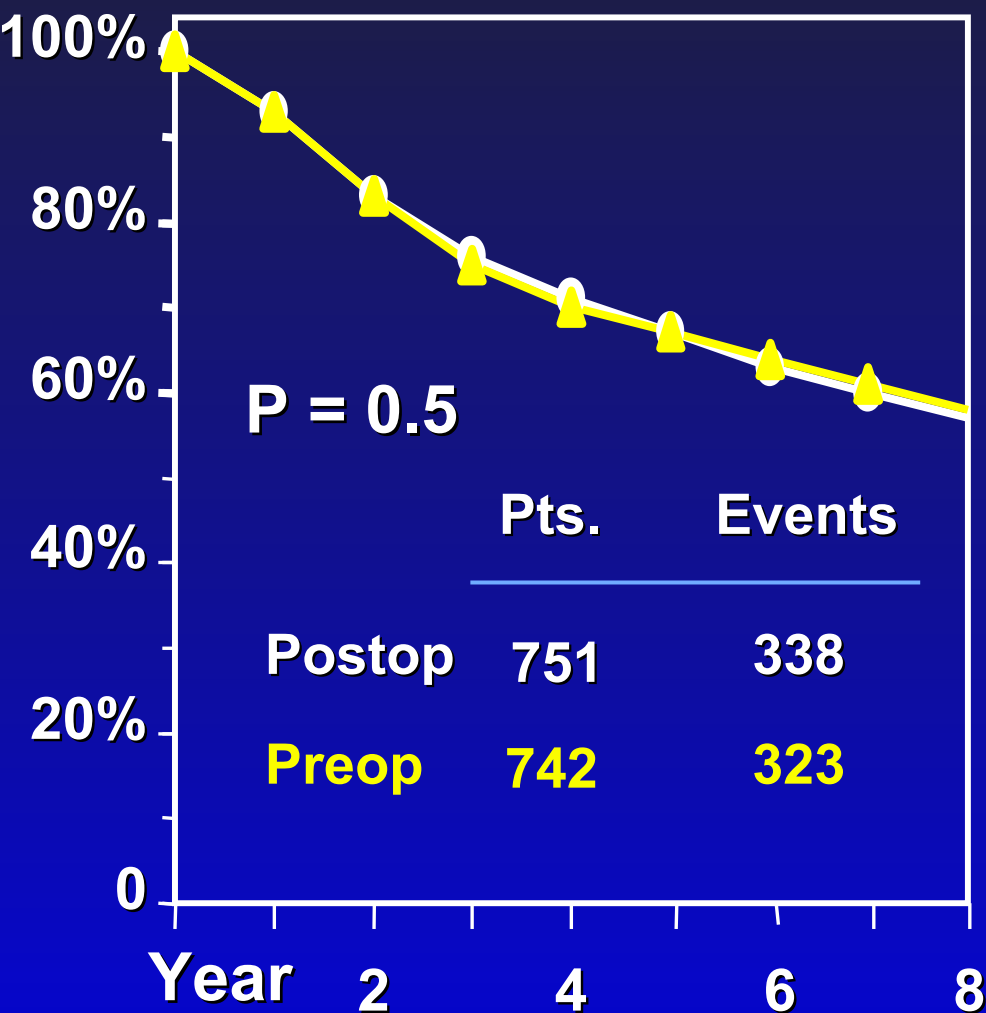


Operation

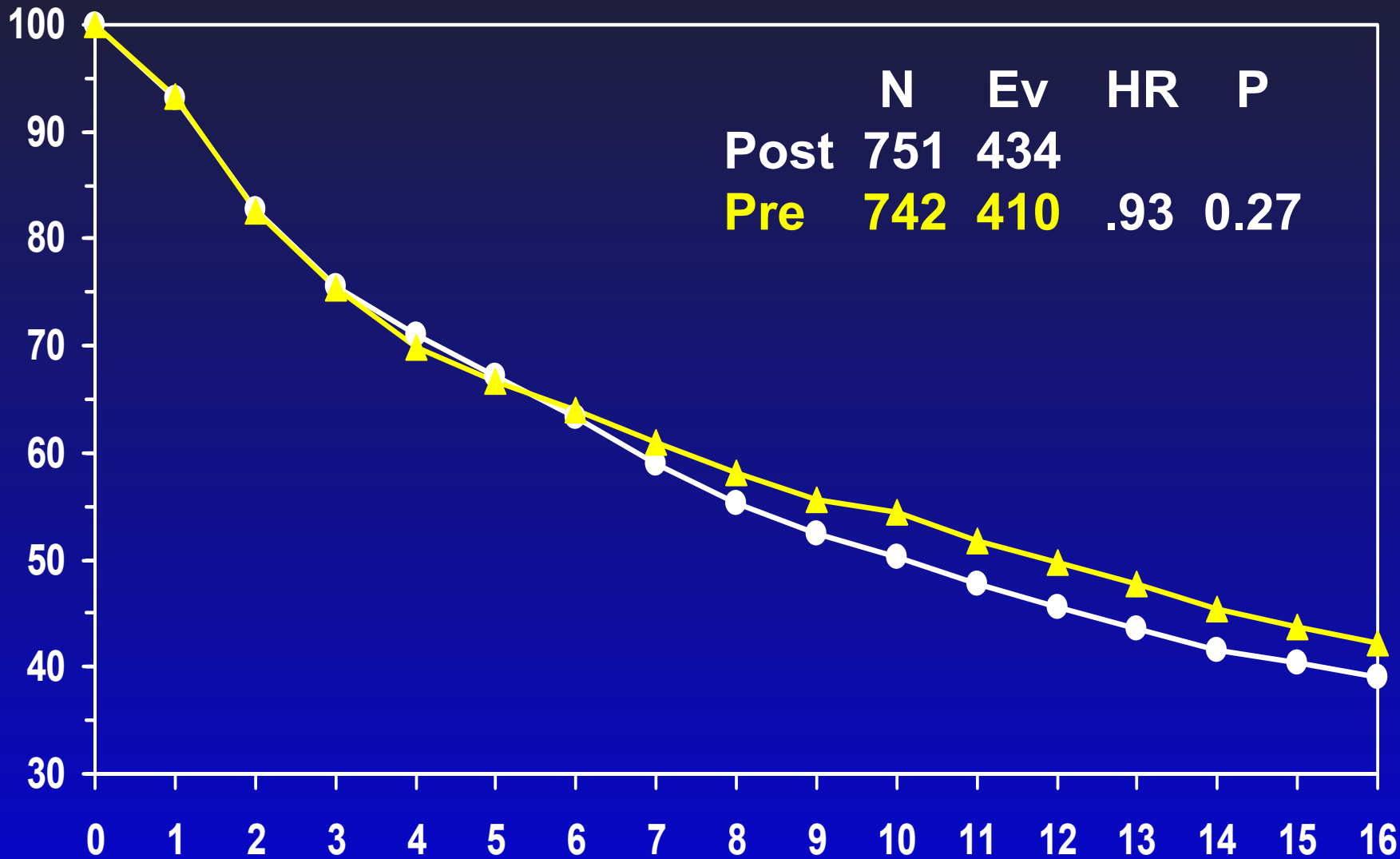


Outcome

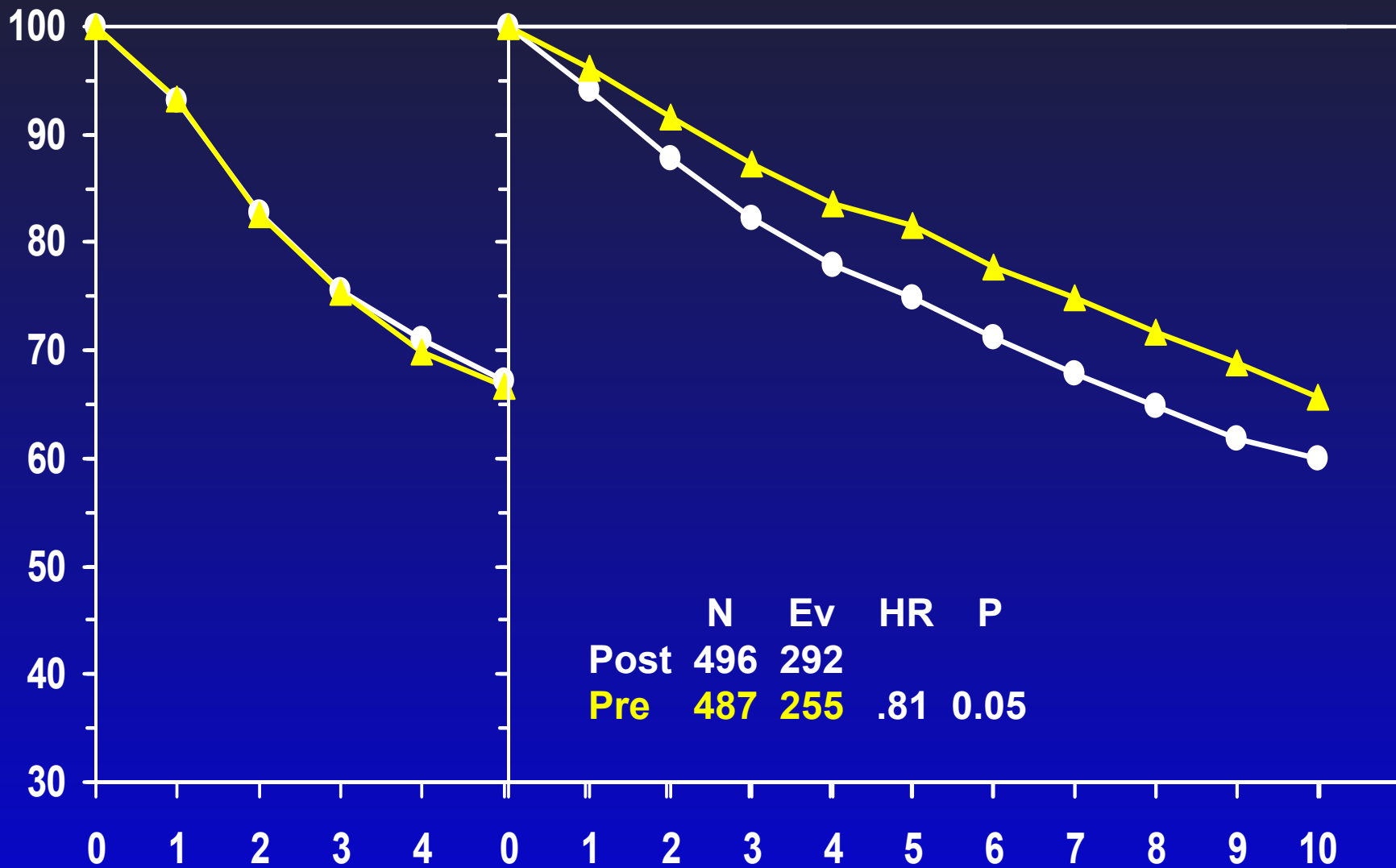
B-18 DFS and Survival



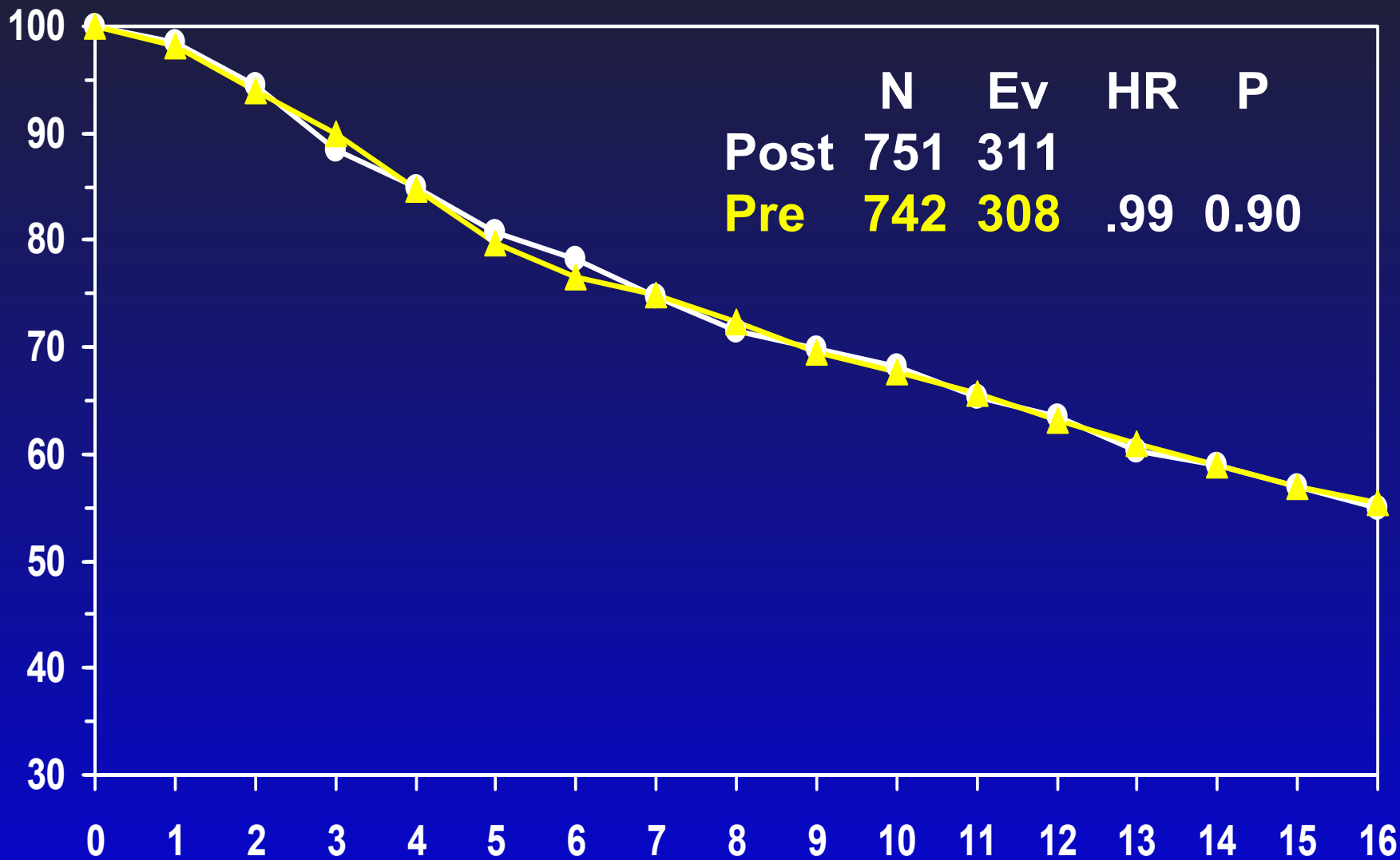
DFS



DFS



Survival

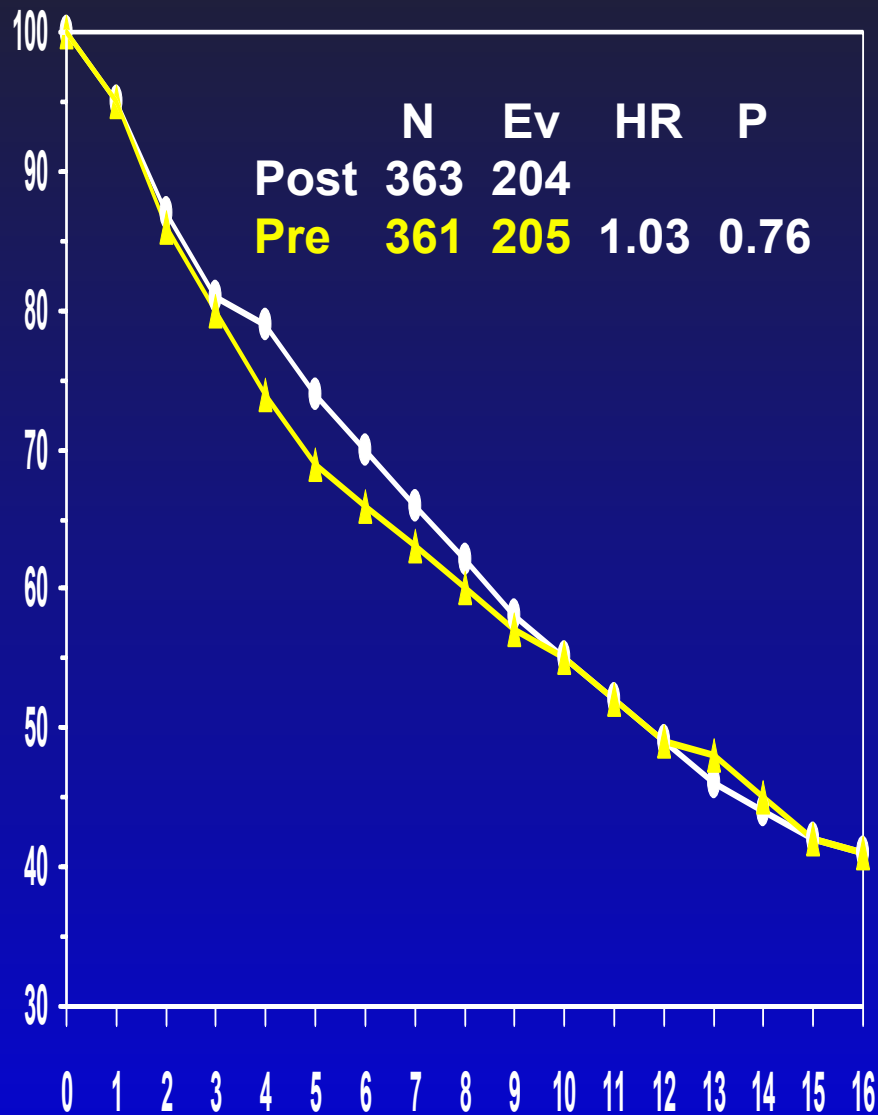
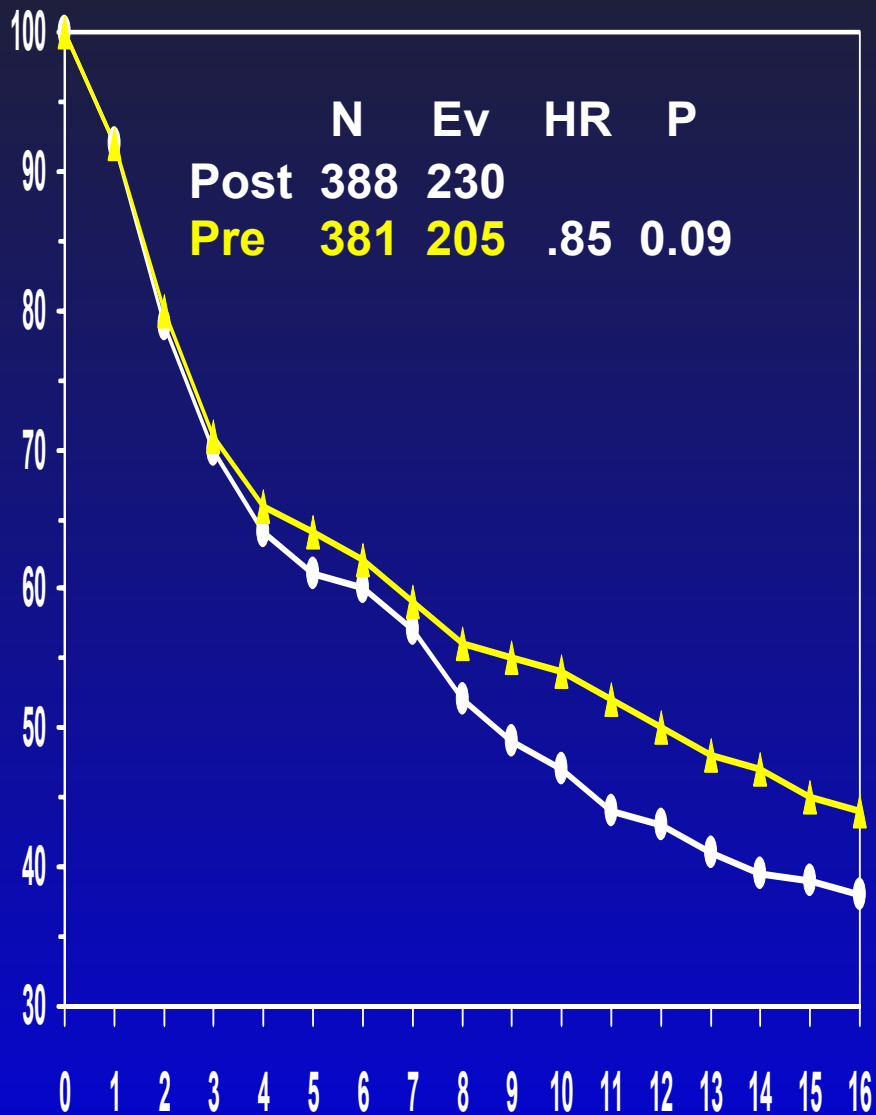


Treatment by Age Interaction

<50yrs

DFS

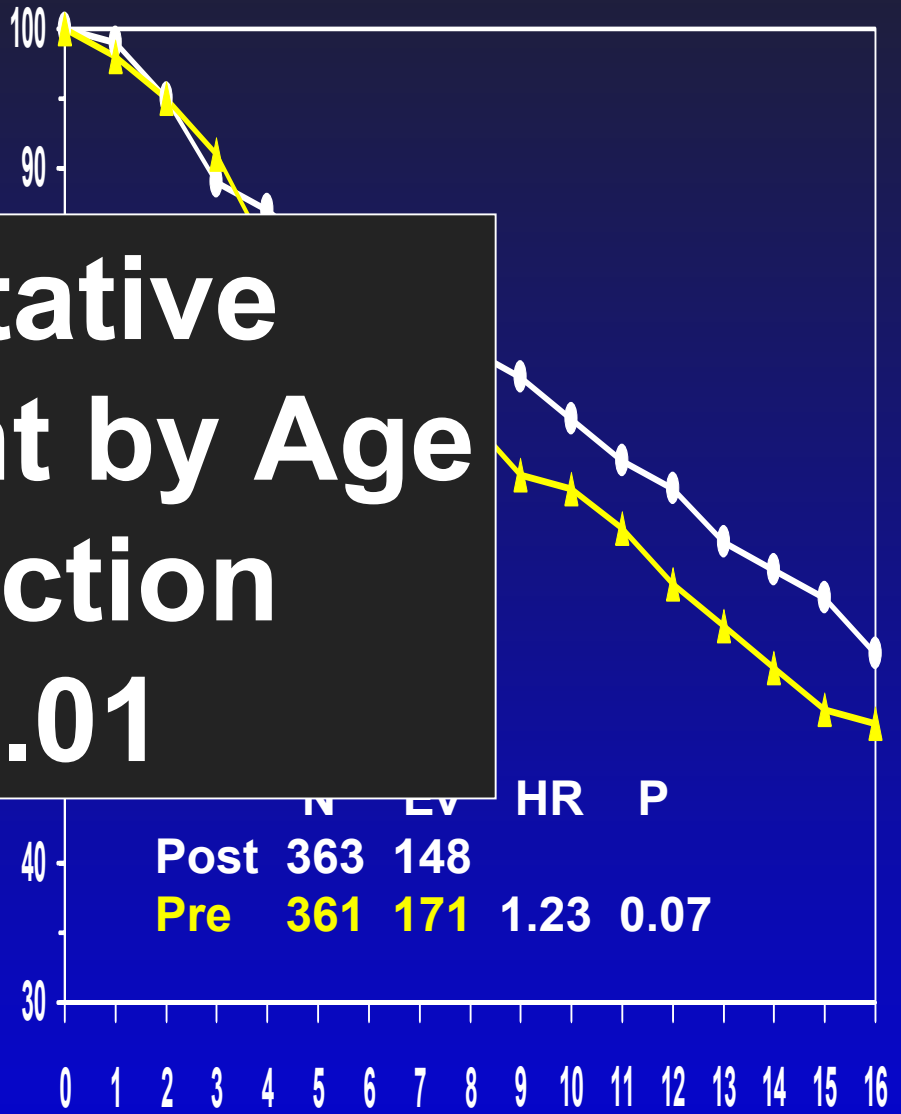
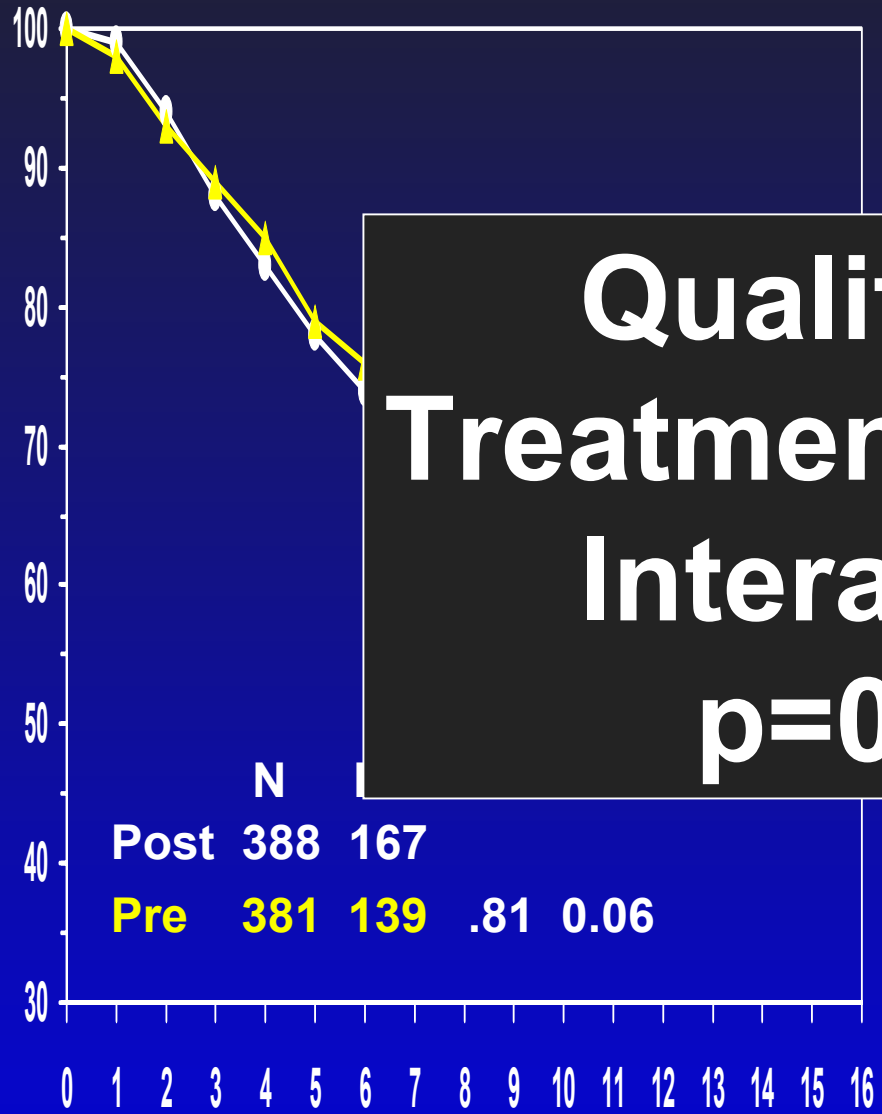
≥50yrs



<50yrs

S

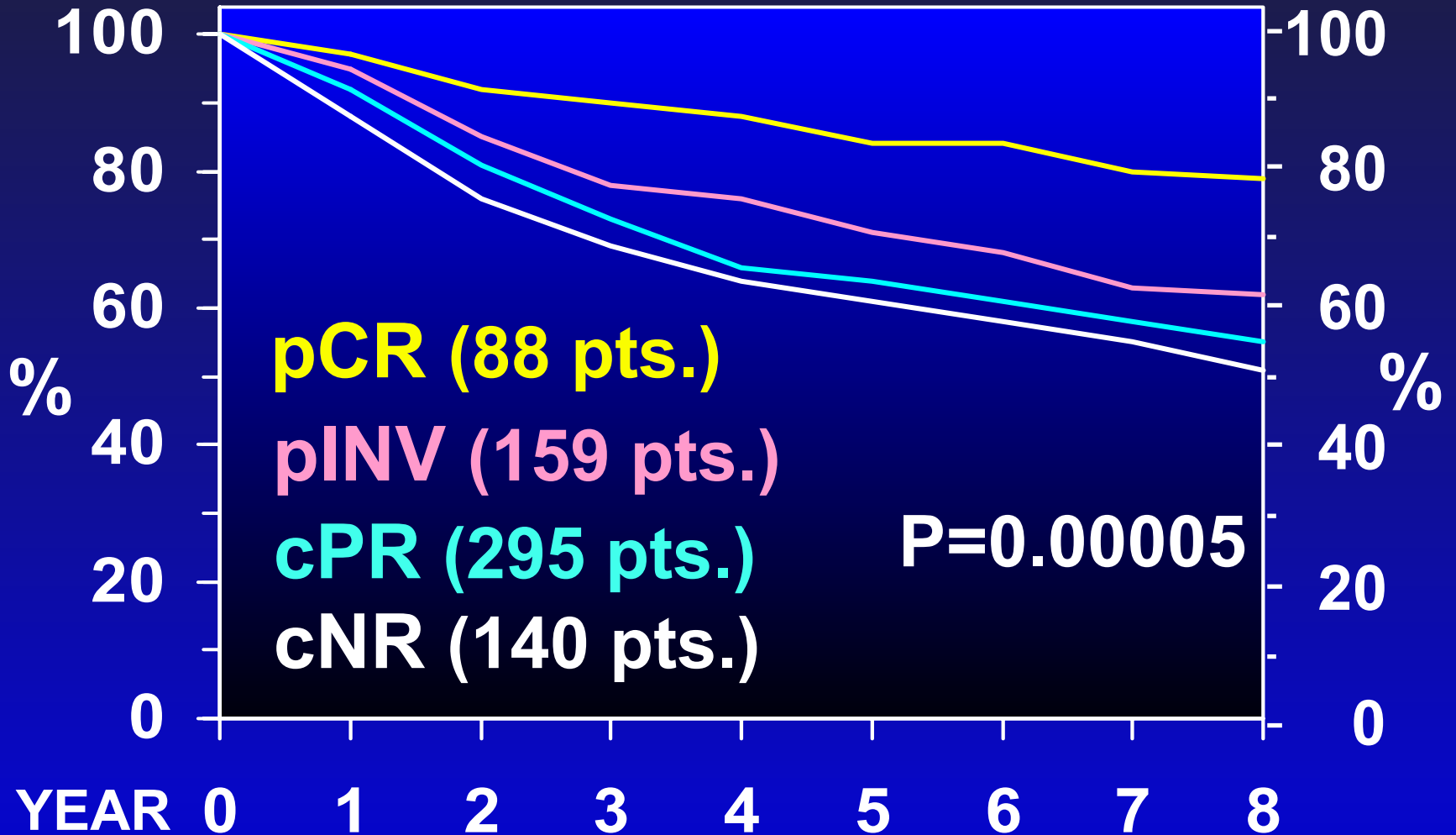
≥50yrs



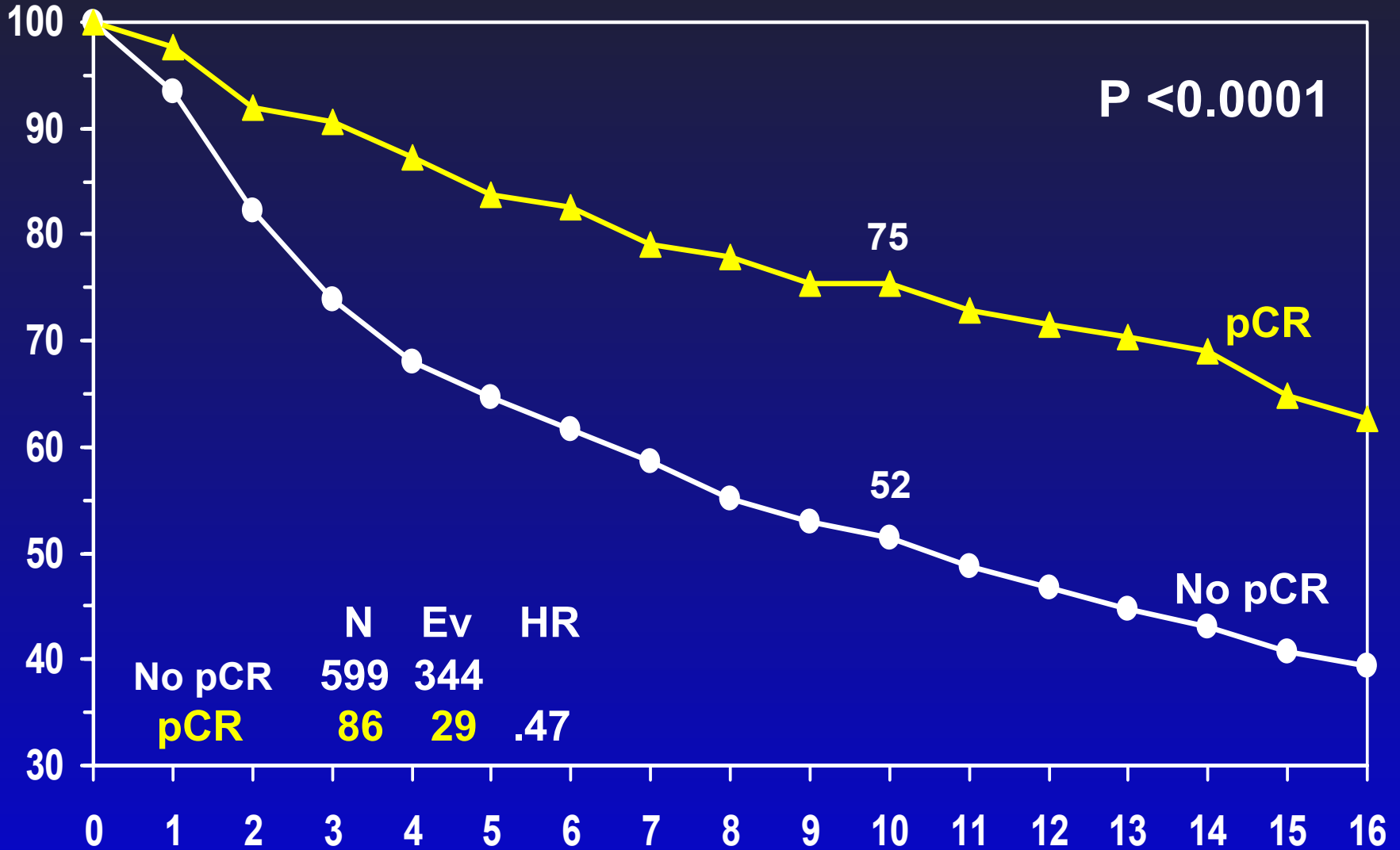
Qualitative Treatment by Age Interaction
p=0.01

pCR and Outcome

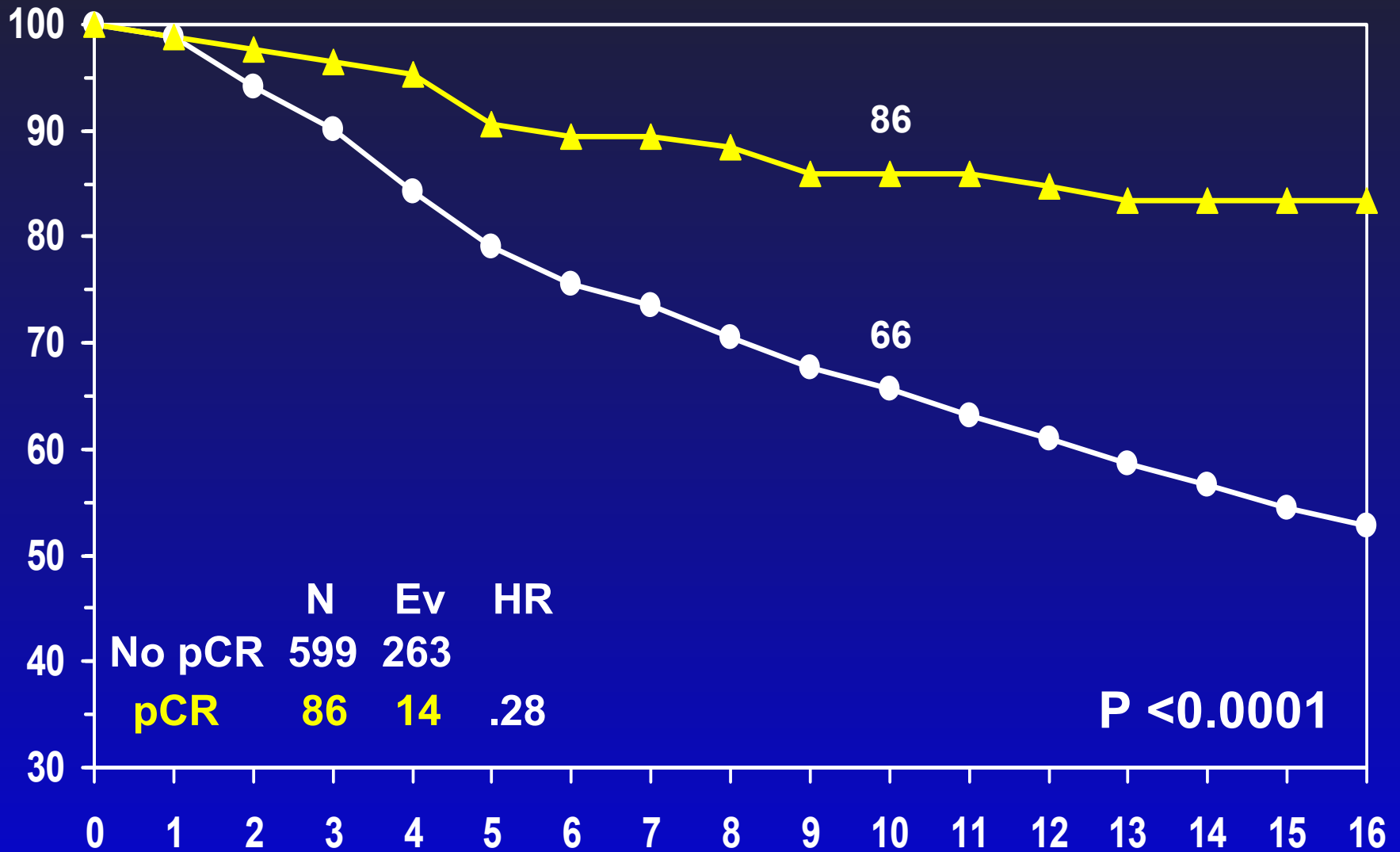
DFS



DFS and pCR

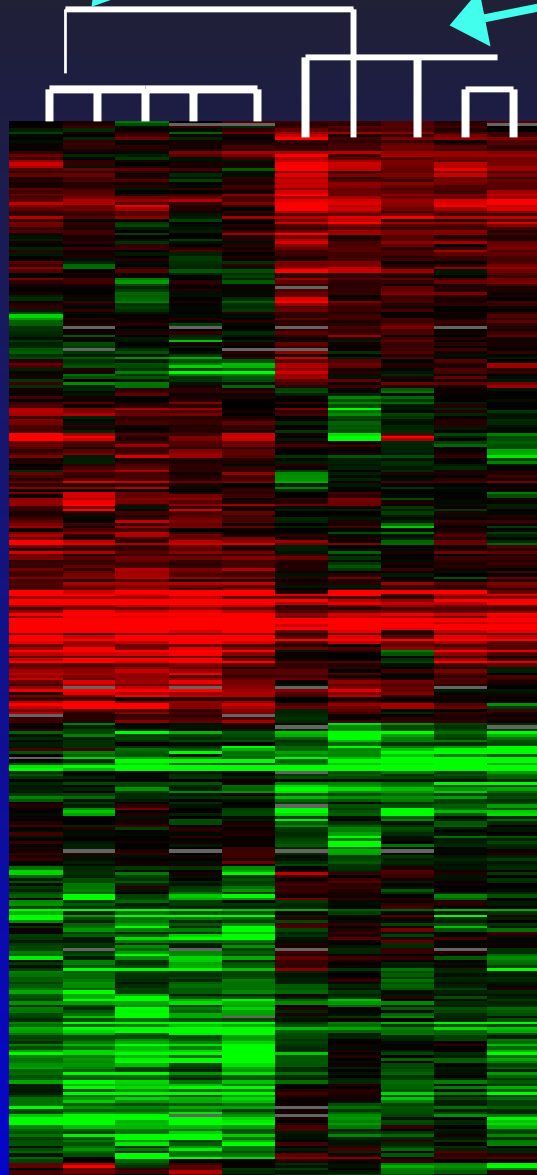


Survival and pCR



RESPONDERS

**NON
RESPONDERS**



**AC
chemotherapy**

B-27

OPERABLE BREAST CANCER

Age, T, cN

AC

AC → Txt*

AC

OPERATION

OPERATION

OPERATION

***100mg/m² x 4; Tam for all**

Txt

NSABP B-27

OPENED: Dec. 1995

CLOSED: Dec. 2000

ACCRUAL: 2,411

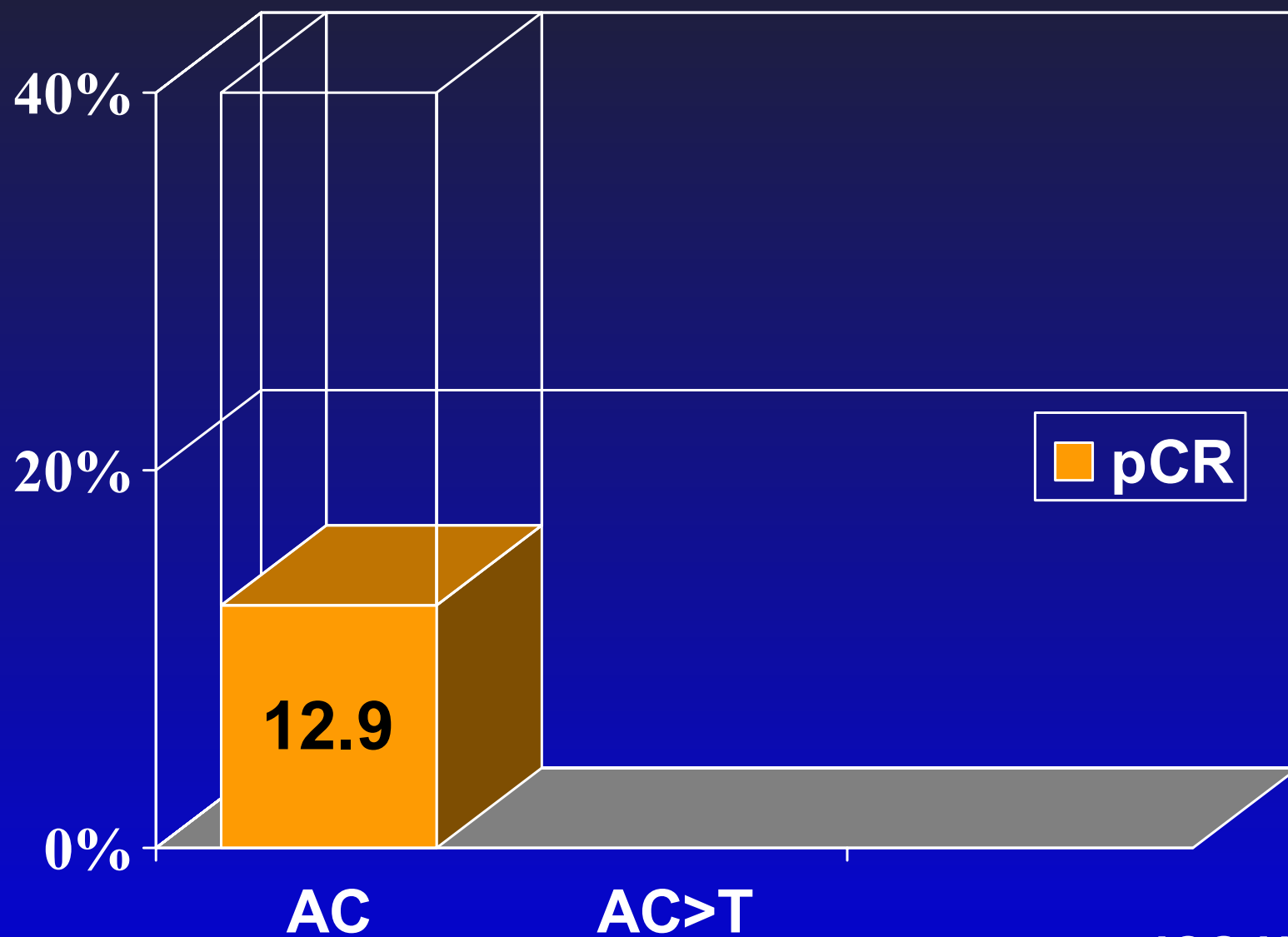
MTS: 6.5 years (2006 JCO)
8.5 years (present)

B-27/18 Clin.Tumor/Node Status

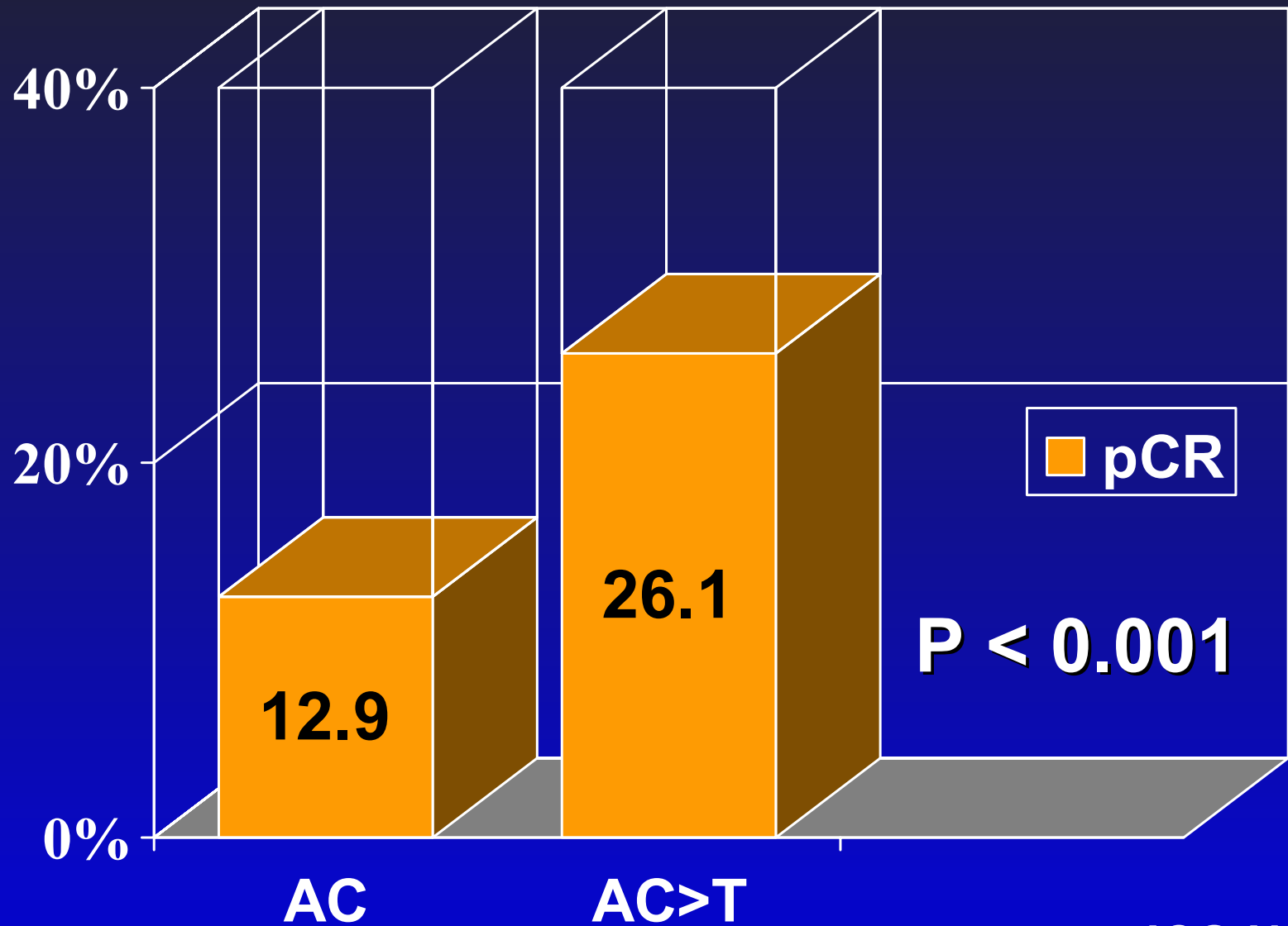
cm	B27	B18
< 2.0	15	28
2.1 - 4.0	41	59
> 4.0	45	13
Node neg.	70	74

Tumor Response

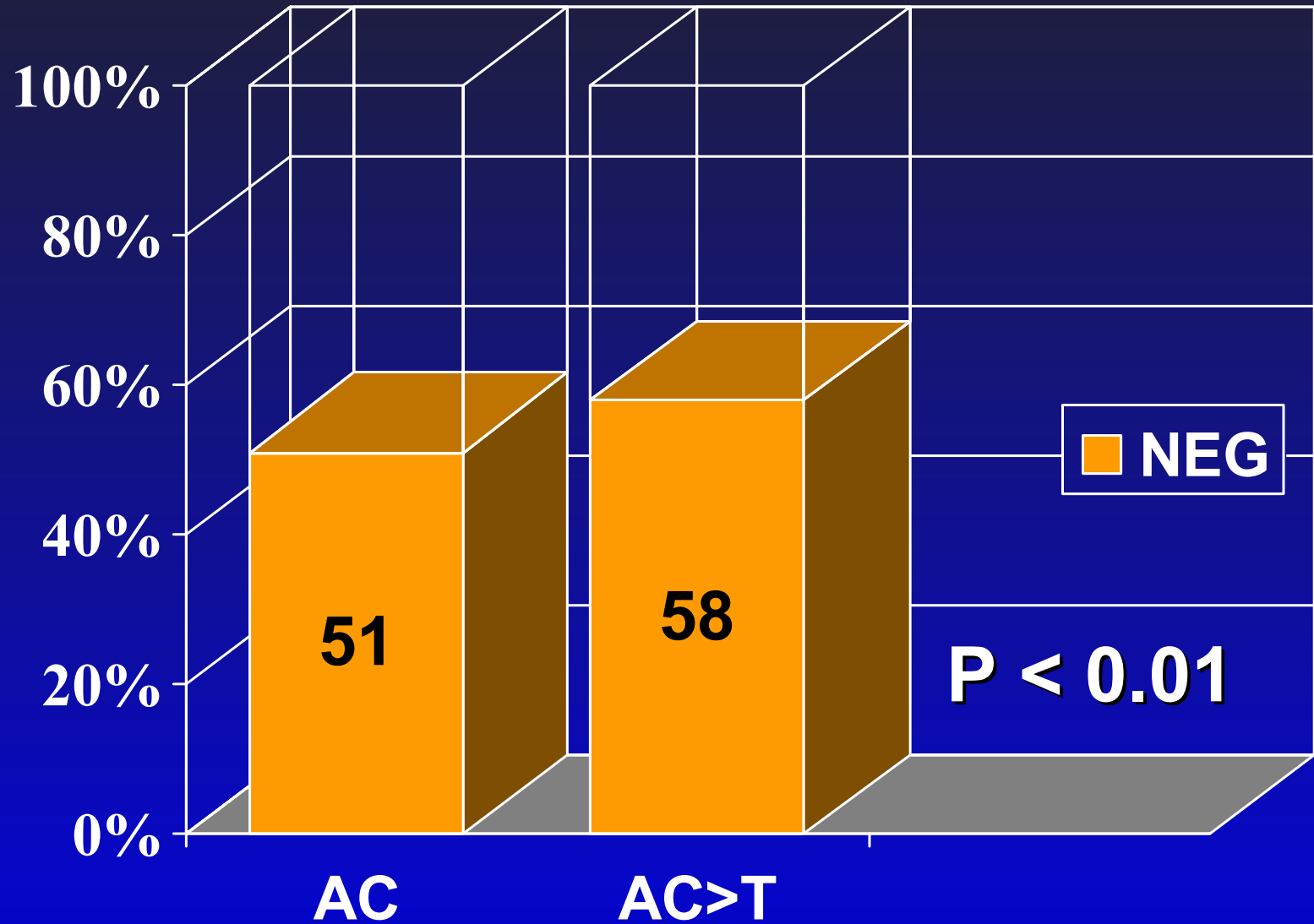
Path Complete Response



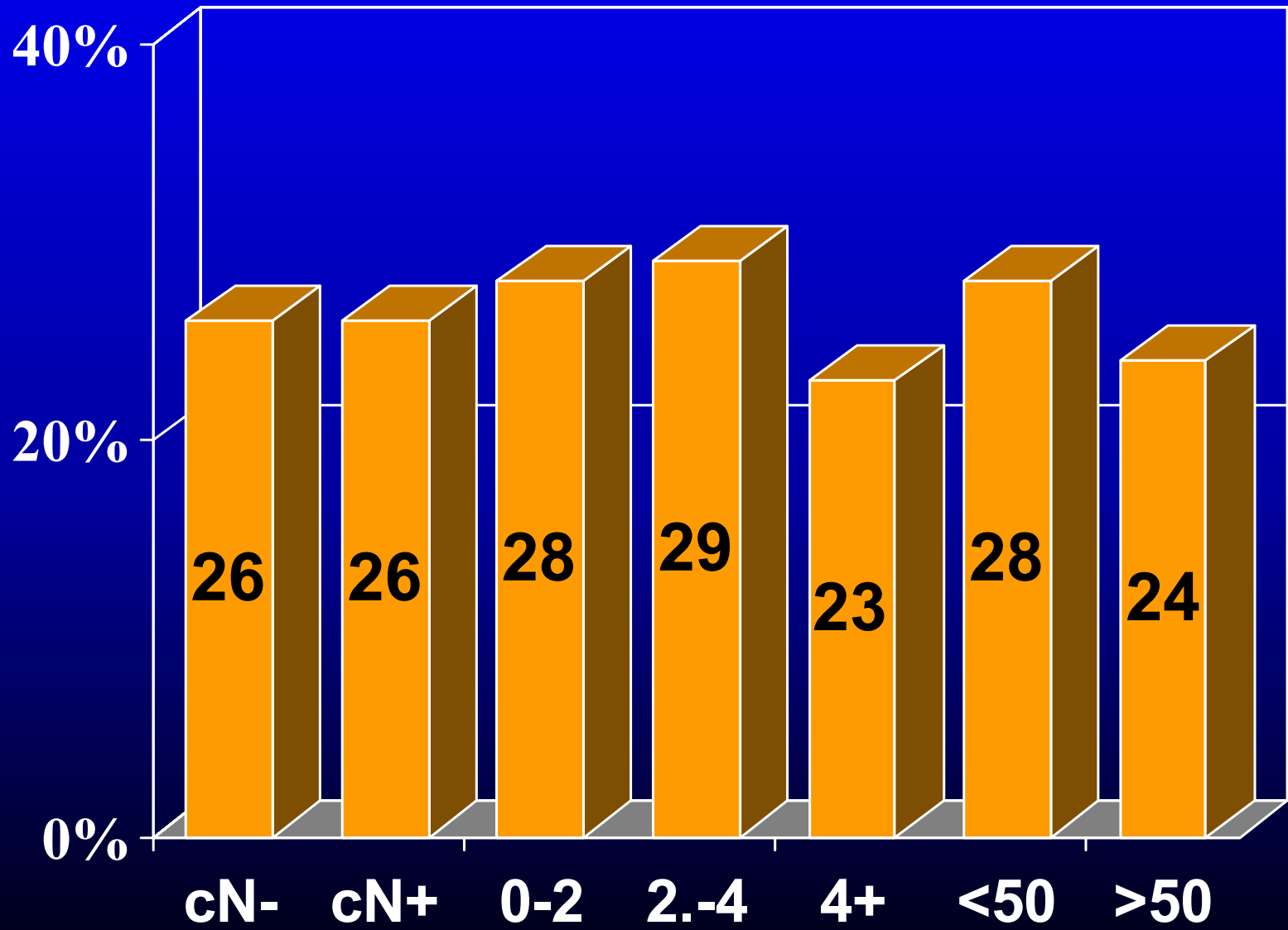
Path Complete Response



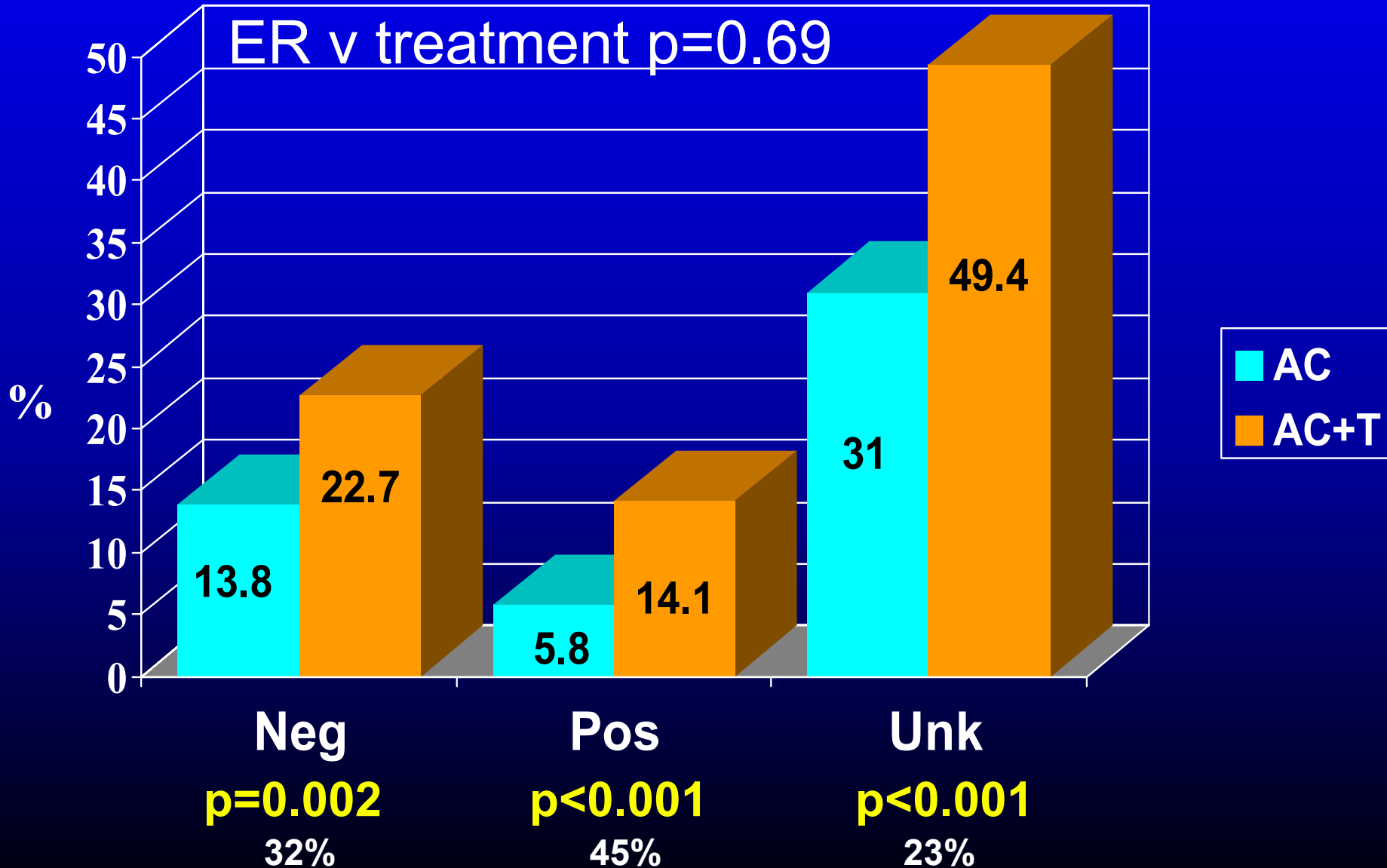
Nodal Response



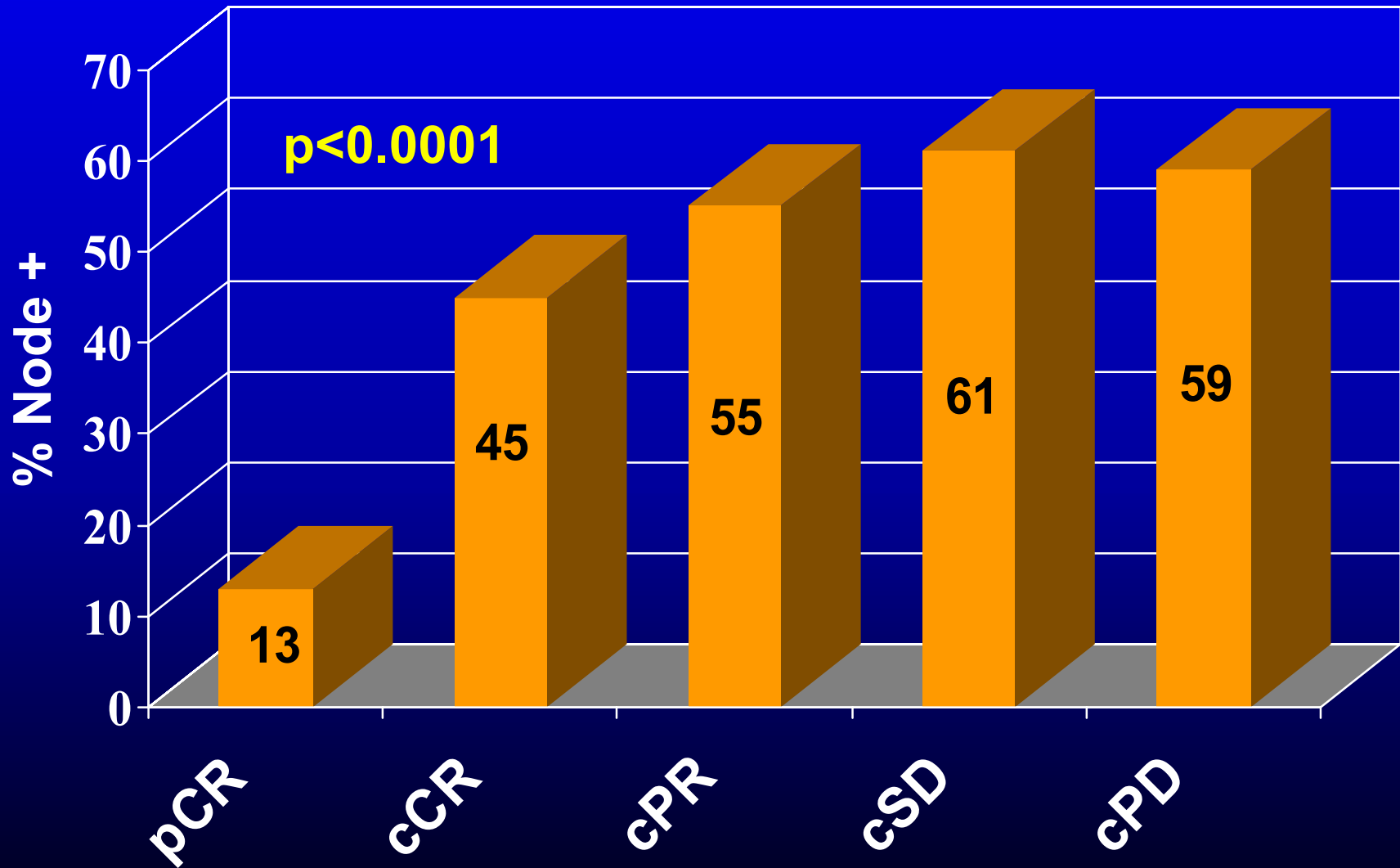
pCR: AC→T



pCR and ER Status

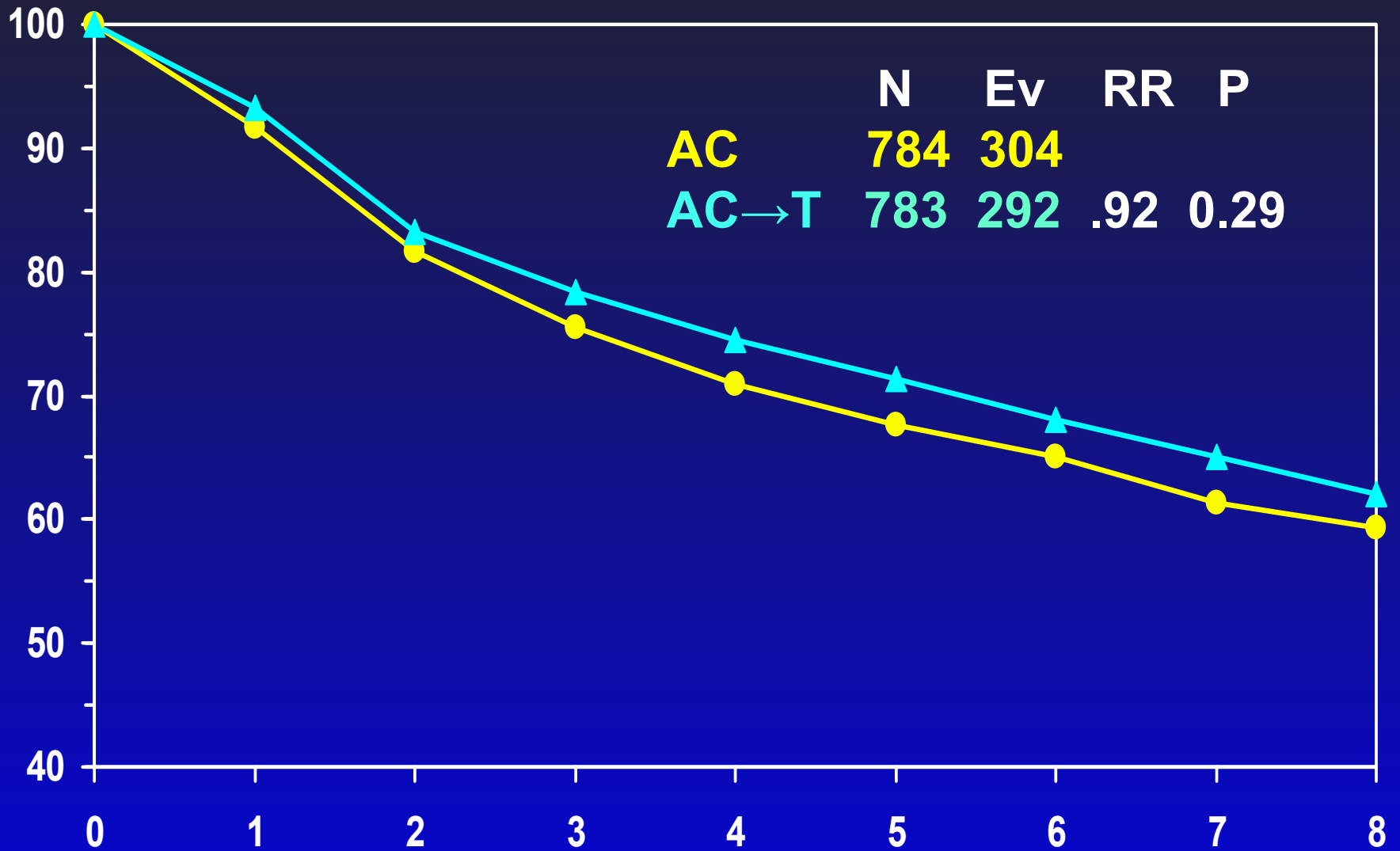


Nodes and Tumor Response

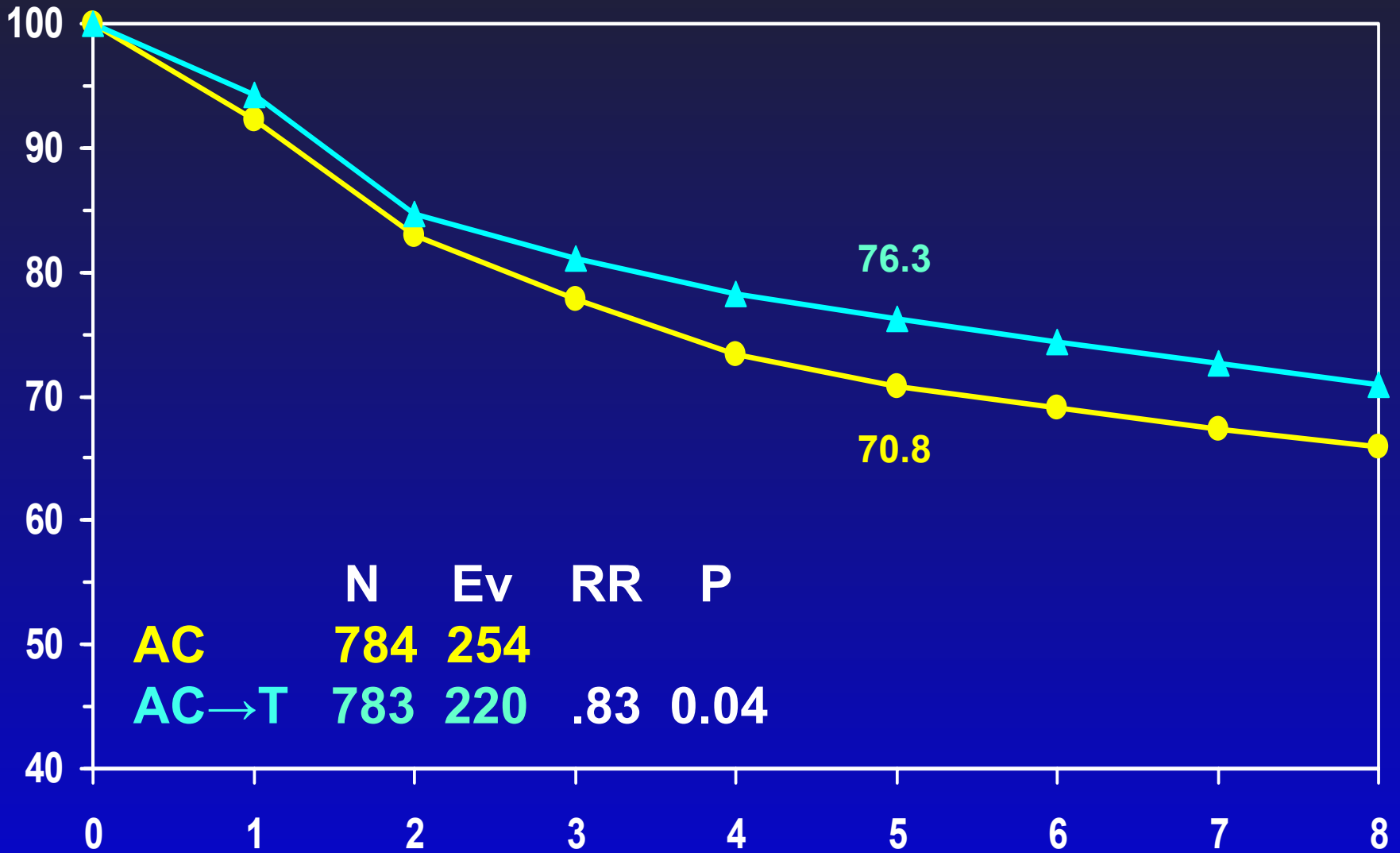


Outcome

DFS

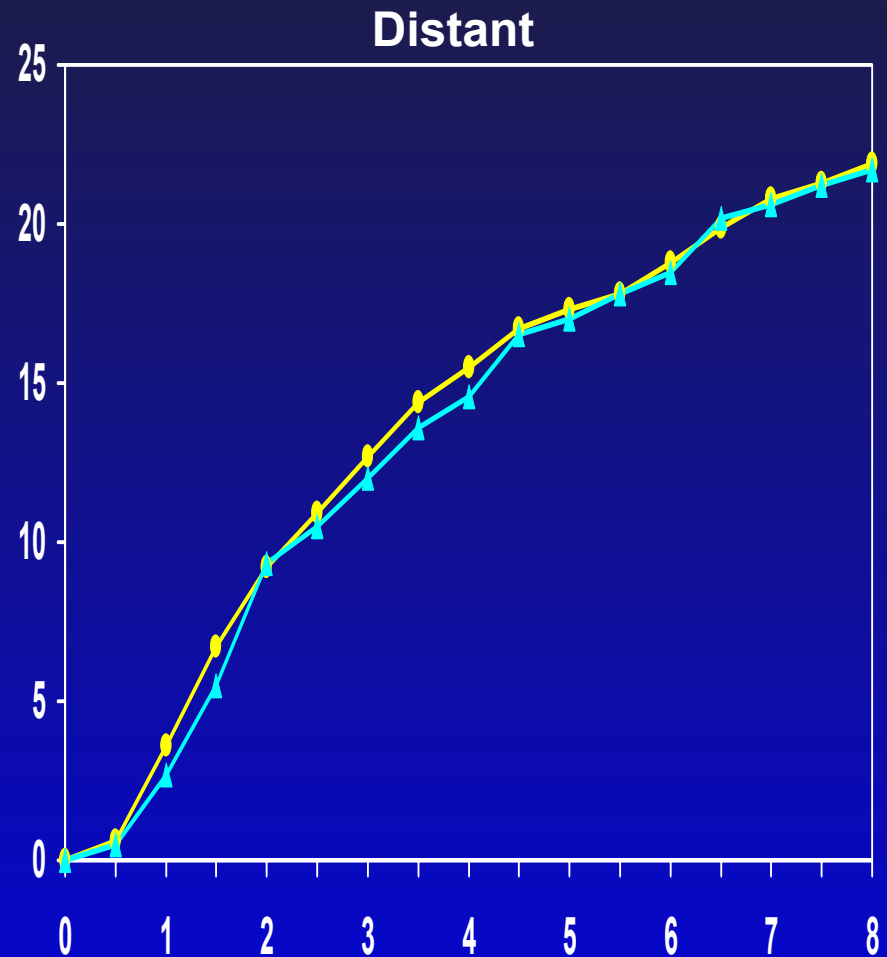
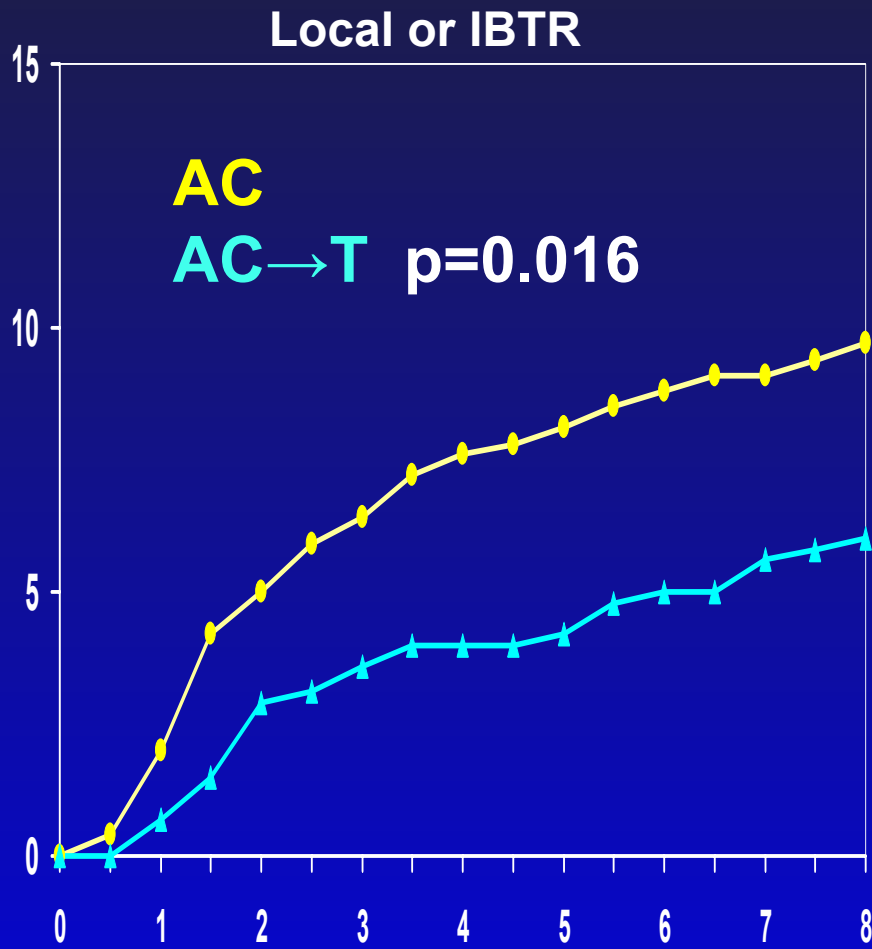


RFS*

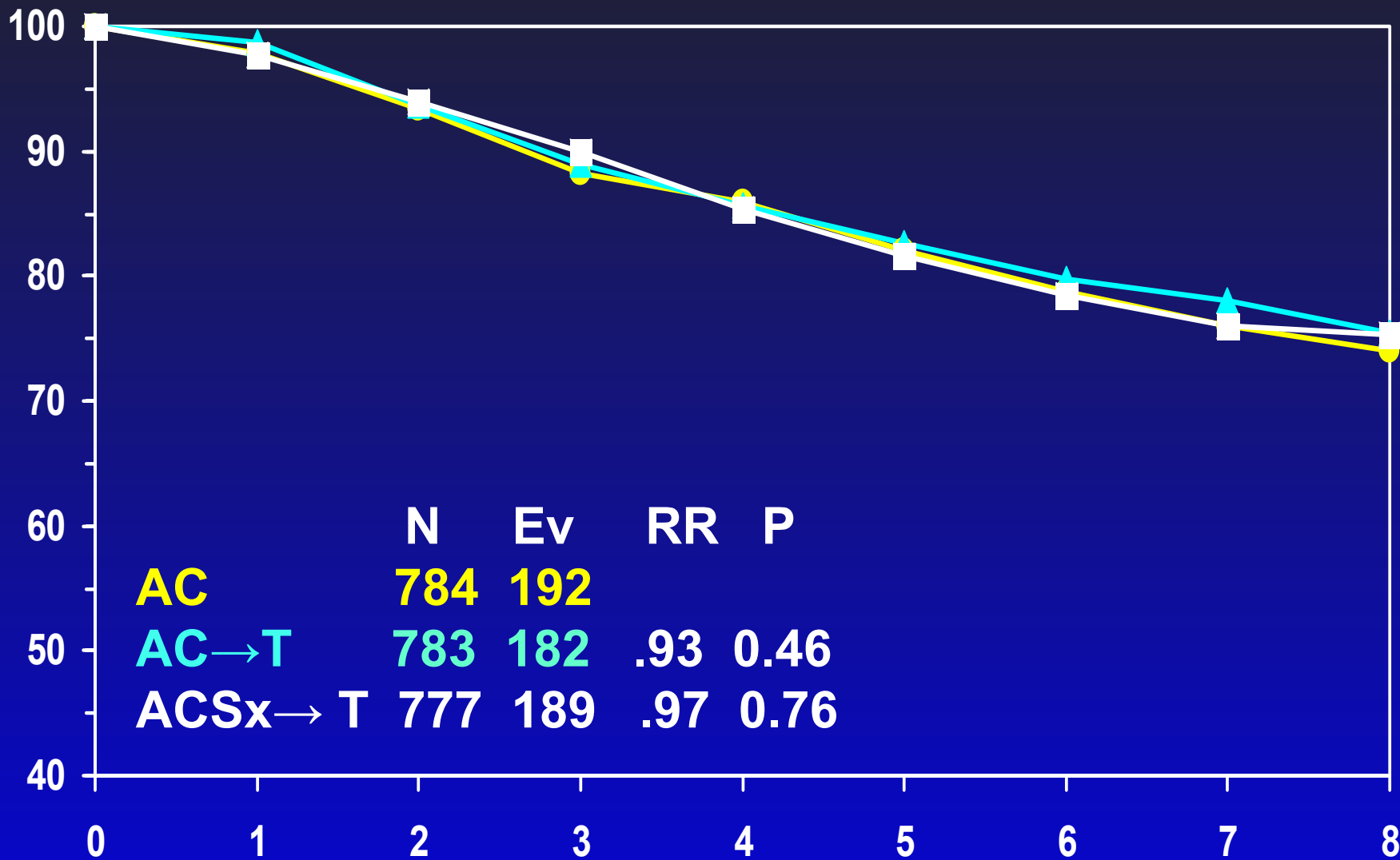


*X Second Primary; X CBC

Recurrence

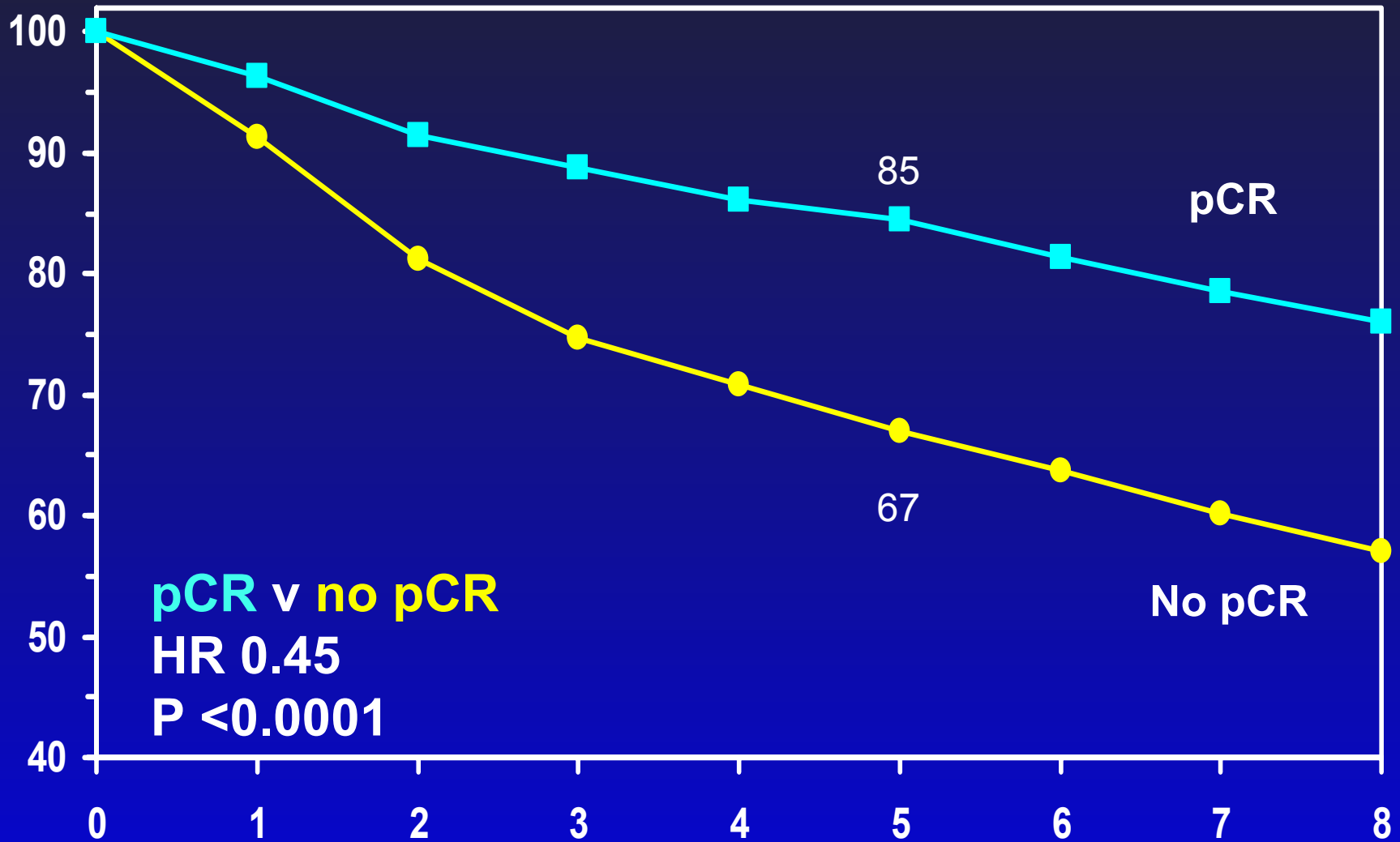


Survival

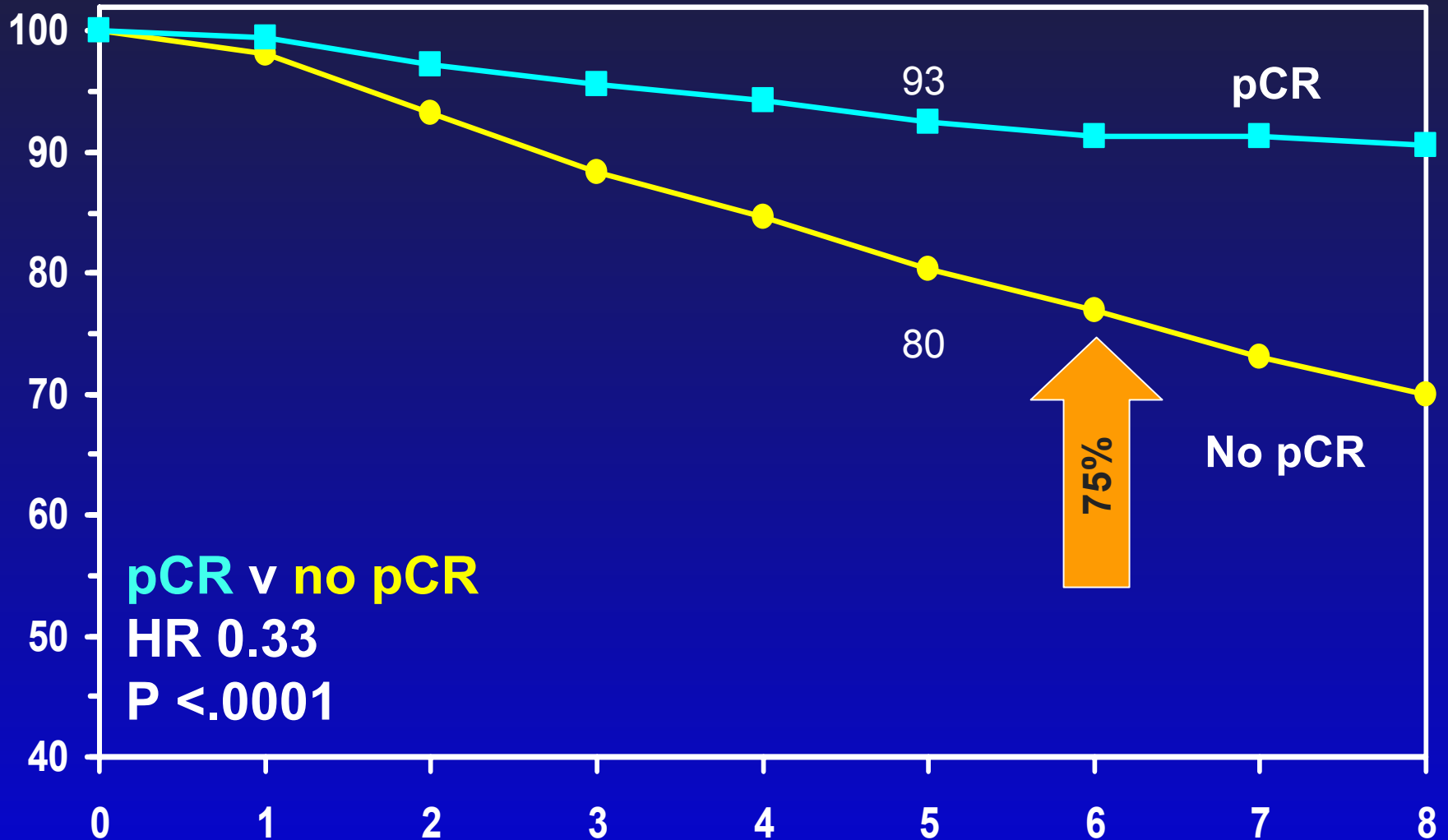


pCR and Outcome

DFS and pCR

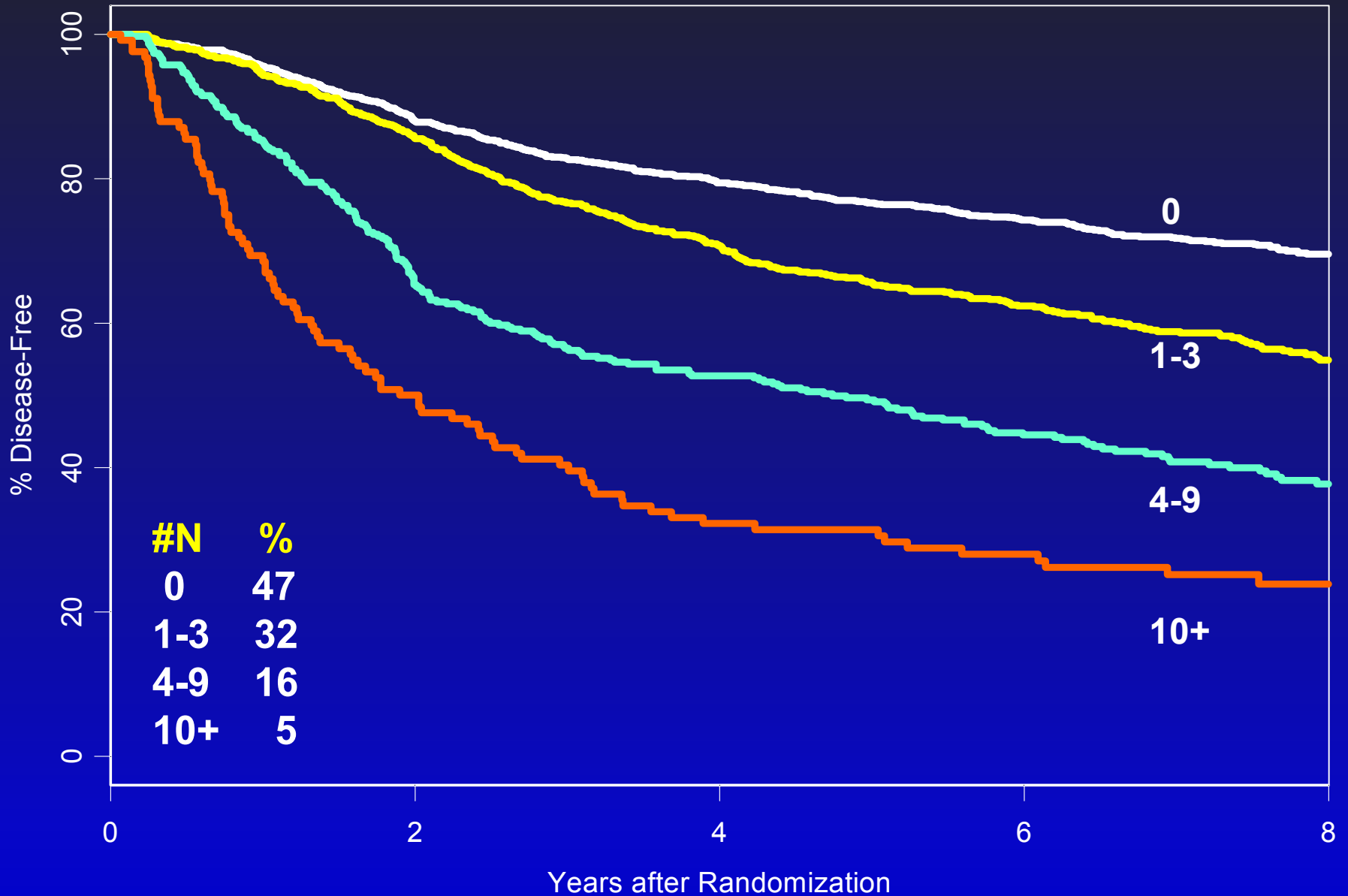


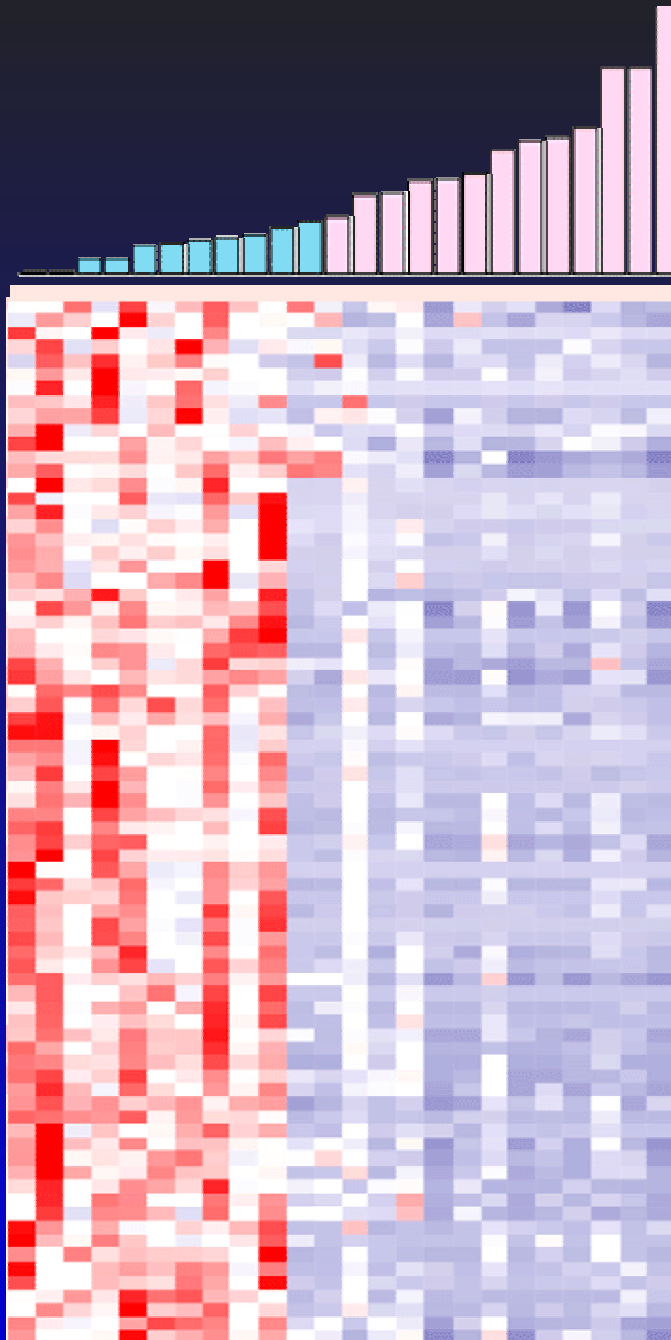
Survival and pCR



B-27 DFS

no pCR and Nodes (1881)





Txt Resp
Txt Non-R

N=24
Txt 100mg/m² q3w x 4
92 genes correlated
with Txt response
(p=0.001)

Jenny Chang
Lancet 362 '03

NSABP B-40

Her2 Neg $\geq 2\text{cm}$

Tissue for Biomarkers



R
a
n
d
o
m
i
z
e

T x 4



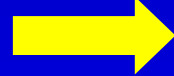
AC x 4

TX x 4



AC x 4

TG x 4



AC x 4

\pm Bevacizumab x 6

Tissue for Biomarkers

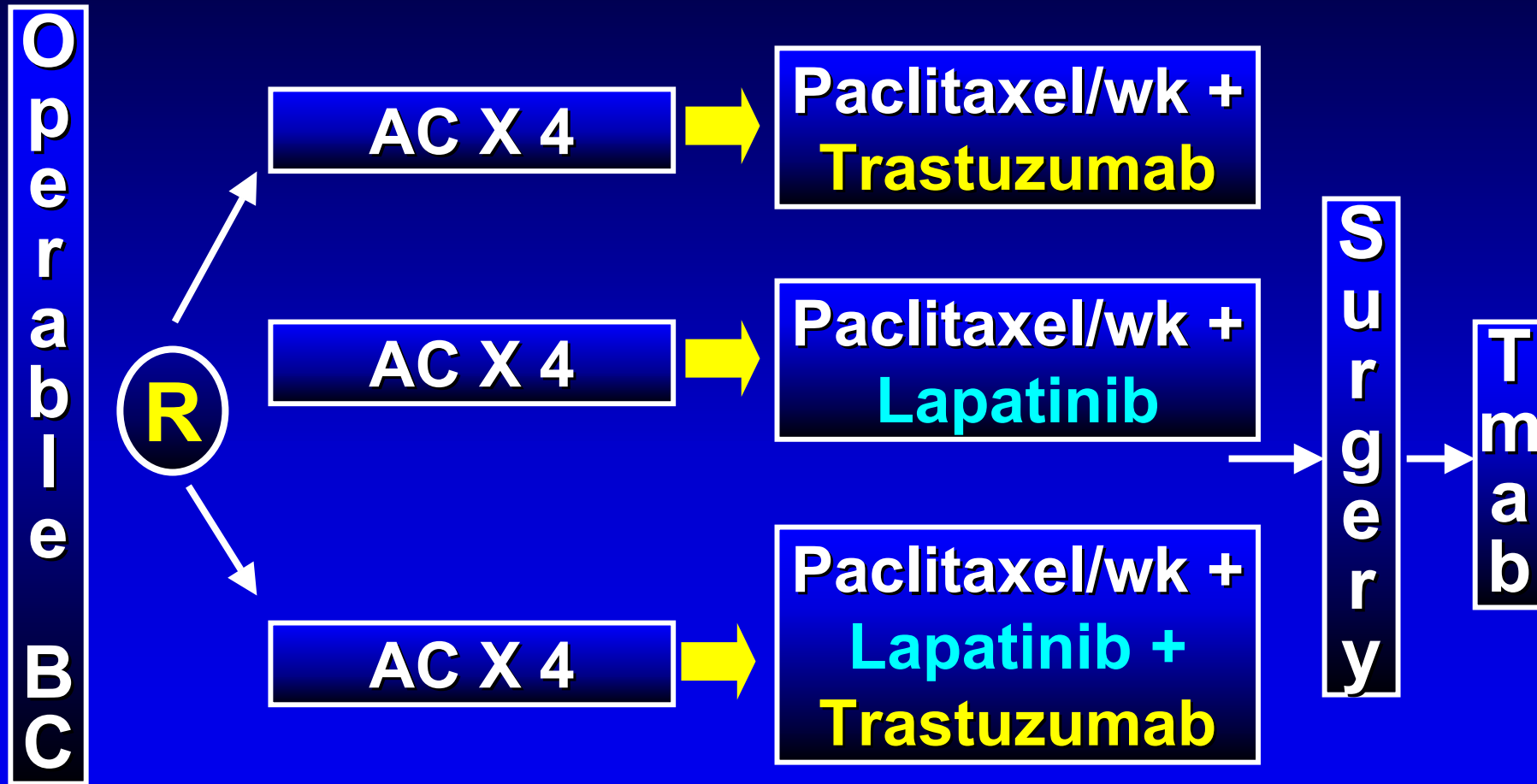


S
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r
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B
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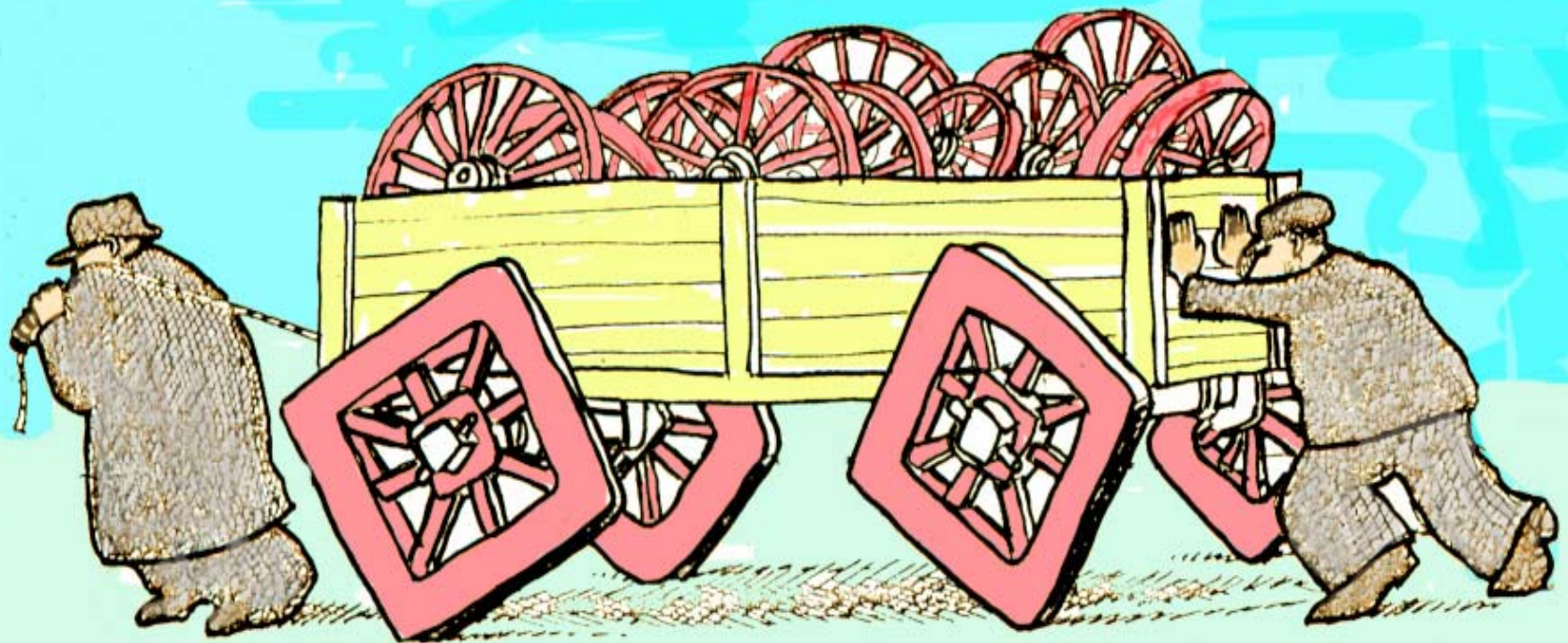
Endpoints: pCR; 2^o endpoint: pCR Δ (29 \rightarrow 38%)
DFS N=1200 Started: 11-07

NSABP B-41 Her2 Pos



N=522; pCR Δ 22% (42 \rightarrow 64%)

Deeper Meanings



Kliban



Mediocrity for a new millennium