Primär systemische Therapie beim Mammakarzinom

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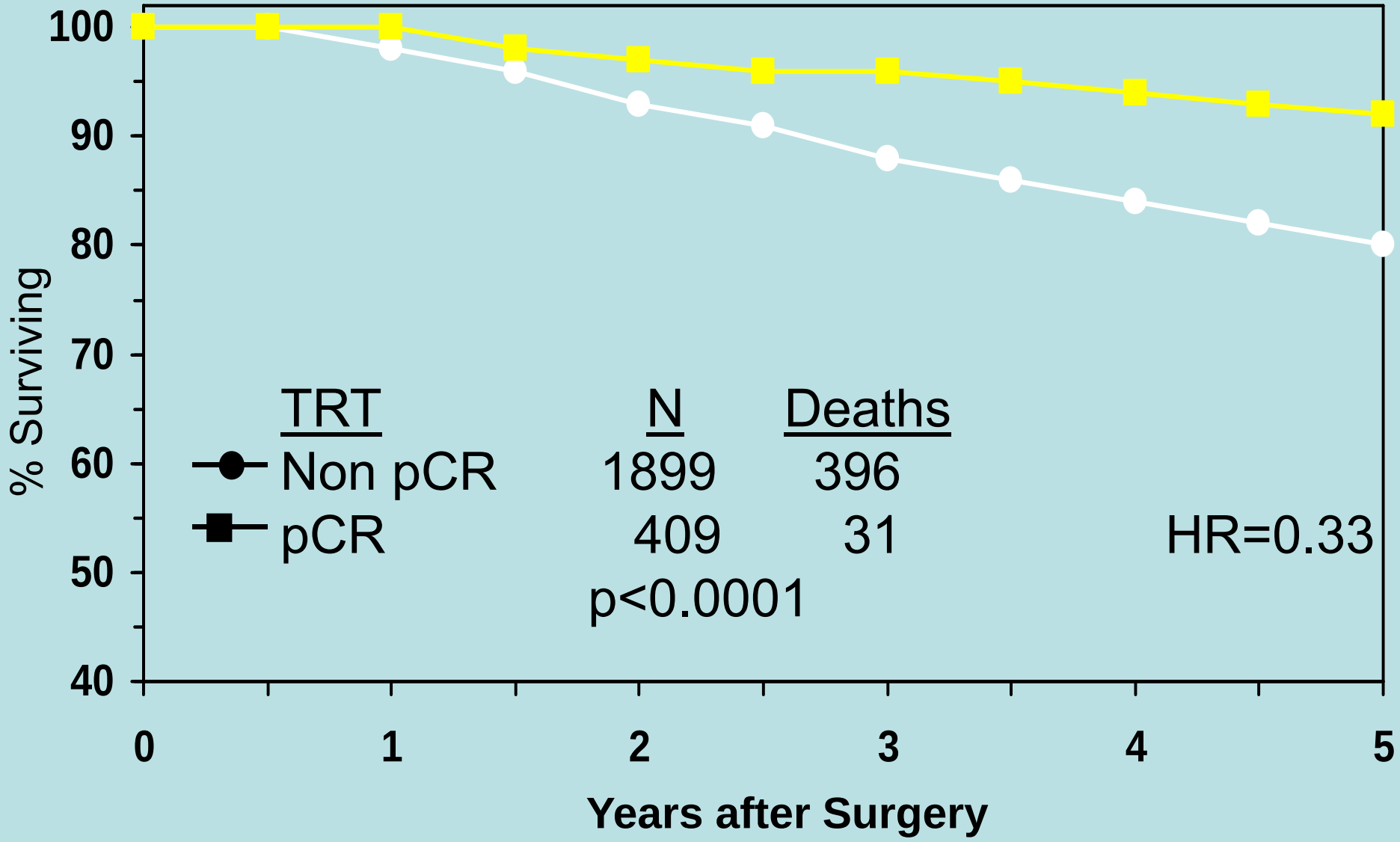
EUROPEAN SOCIETY OF MASTOLOGY
Eusoma Initial Accreditation 2006

Primär systemische Therapie

Chemotherapie +/- Herceptin oder endokrine Therapie

NSABP B-27: Survival
pCR vs. non-pCR Pat.



ECTO: Main Efficacy Outcome at 7 years

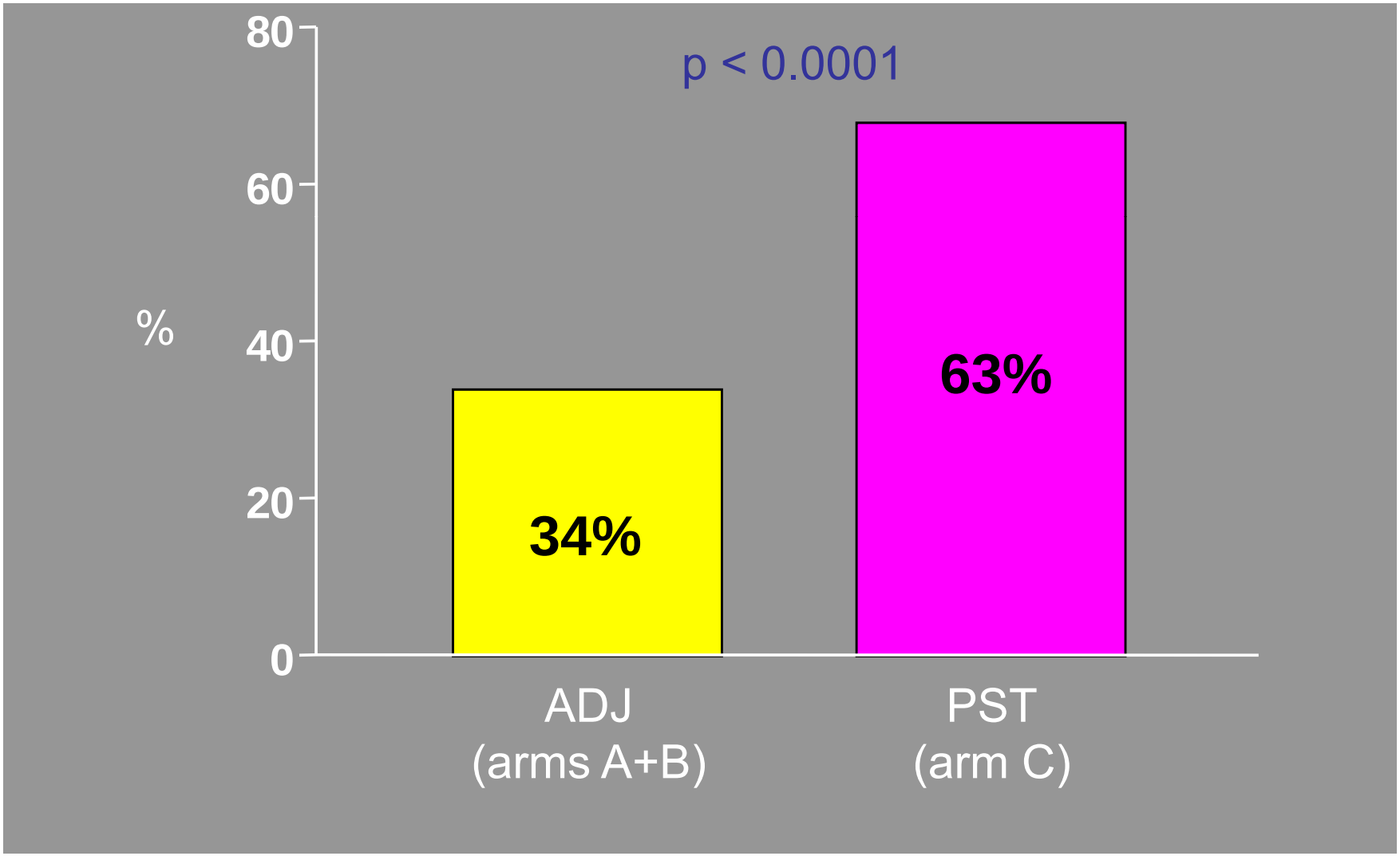
	Arm A S→A→CMF	Arm B S→AT→CMF	Arm C AT→CMF→S
RFS	69%	76%	72%
DRFS	77%	84%	80%
OS	82%	85%	84%
LBR			
Cons.	6.9%	5.2%	5.3%
Mast.	2.3%	3.5%	2.7%

Eiermann,ASCO breast 2008

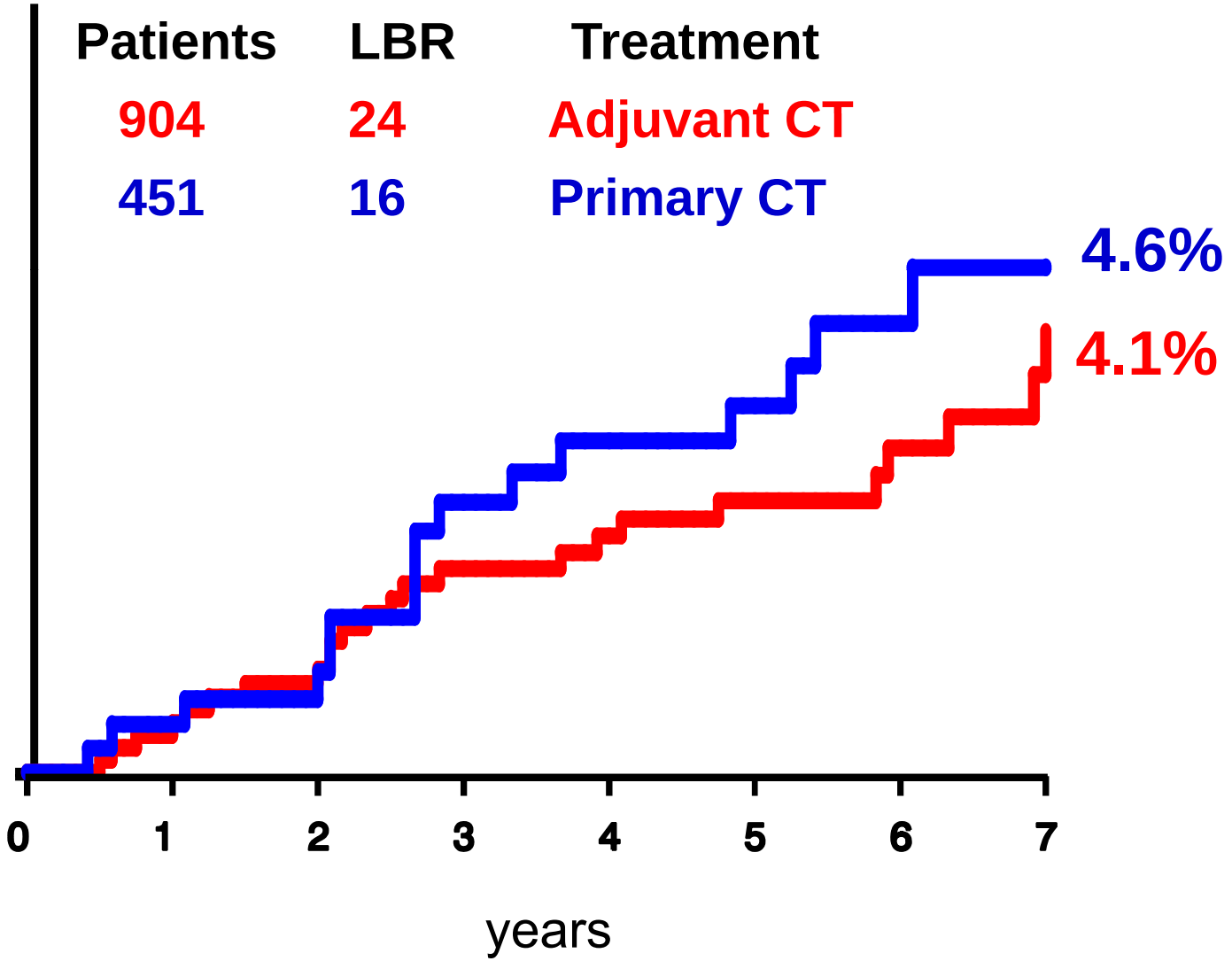
Primär systemische Therapie
Zusammenhang: Rezeptorstatus und pCR

Autor	Patienten-zahl	Regime	% HR negativ	% pCR in HR negativ	% pCR in HR positiv
Houston	1018	Pooled data	NA	**20,6**	**5,6**
Geparduo	913	dd AD/AC-doc	26,3	**22,8**	**6,2**
ECTO	**438**	**AP-CMF**	**38,2**	**42,2**	**11,6**
NSABP-B27	2411	AC vs AC-doc	32	**16,7**	**8,3**
Gepartrio	286	DAC/DAC-NX	31,9	**36,6**	**10,1**
Gepardo	250	dd AD +/Tam	43,9	**15,4**	**1,1**

ECTO: Rate of breast conserving surgery



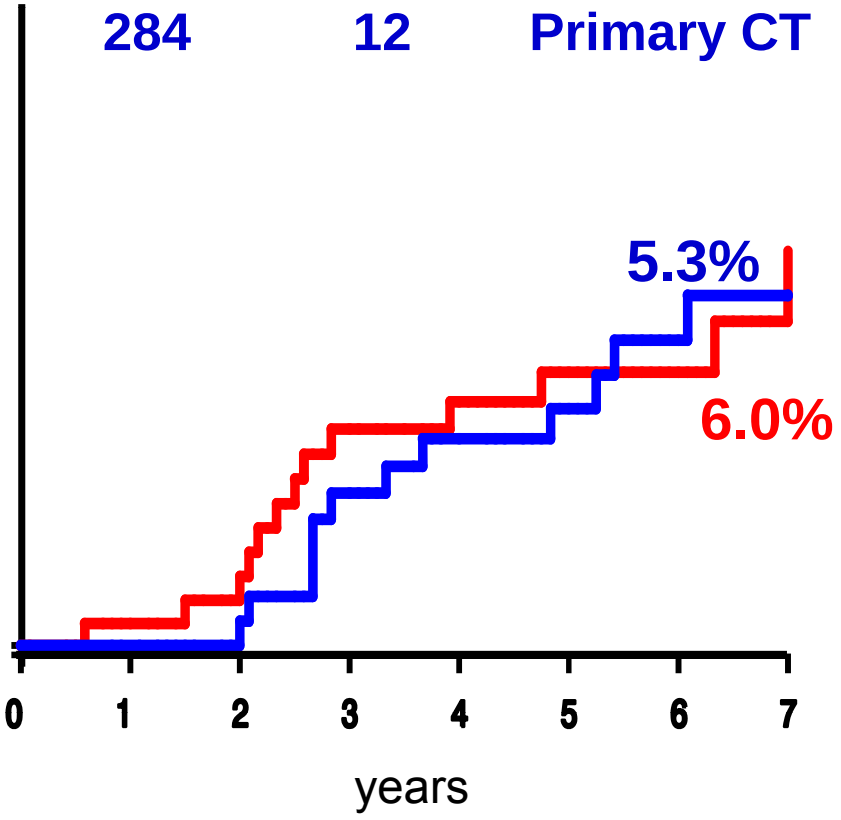
ECTO: Cumulative risk of LBR



ECTO: Cumulative risk of LBR

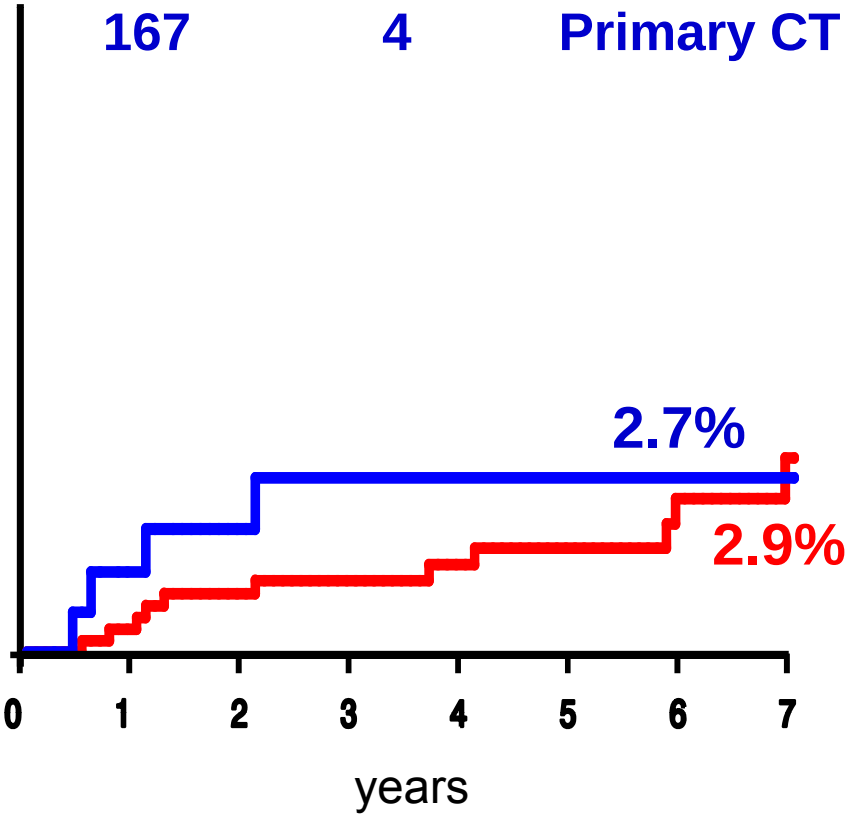
Conservative surgery

Patients	LBR	Treatment
307	13	Adjuvant CT
284	12	Primary CT



Mastectomy

Patients	LBR	Treatment
597	11	Adjuvant CT
167	4	Primary CT



Faktoren die eine hohe LRR nach PST mit BET vorhersagen

- **Klinisch N 2 – 3**
- **Verbliebener Tumor über 2 cm**
- **Multifokaler Resttumor nach PST**
- **Lymphangiosis**
- **Vaskuläre Invasion**

Eiermann etal ASCObreast 2008

Integrated meta-analysis on

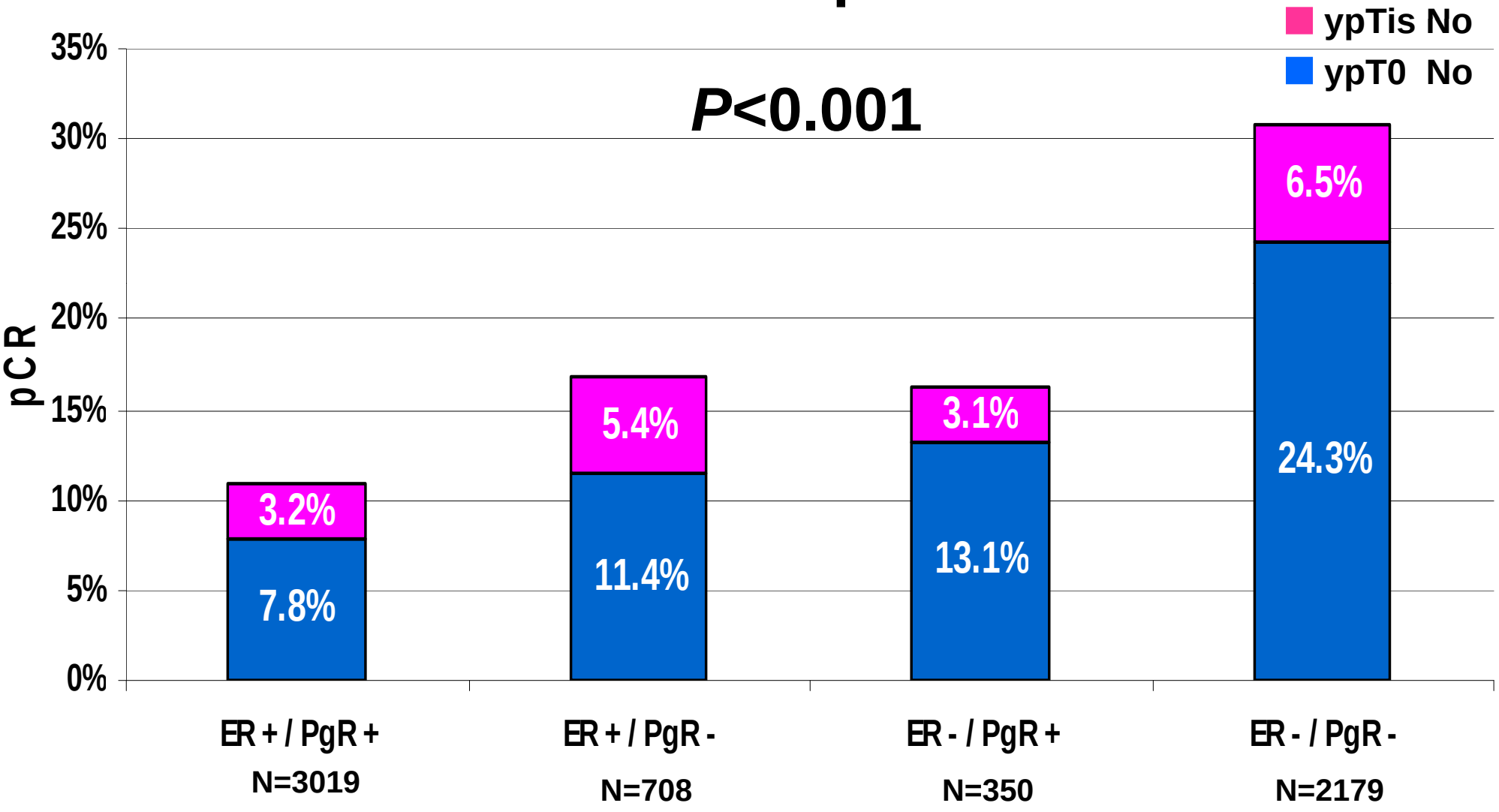
6634 patients with early breast cancer receiving neoadjuvant anthracycline-taxane +/- trastuzumab containing chemotherapy

von Minckwitz G, Kaufmann M, Kümmel S, Fasching P, Eiermann W, Blohmer JU, Costa SD, Loibl S, Mehta K, Untch

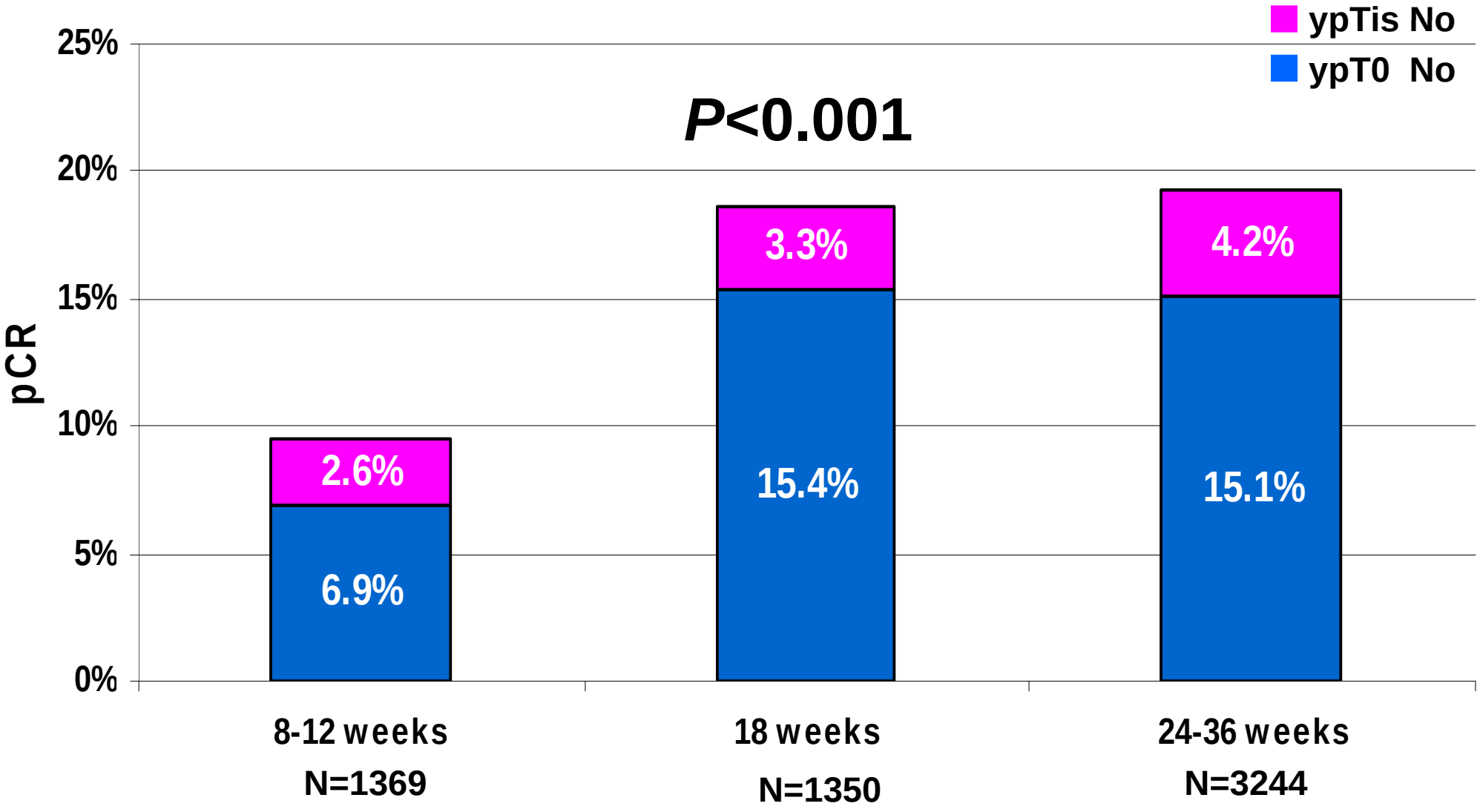
AGO

GBG GERMAN BREAST GROUP

Predictive Factors
Hormone Receptor Status

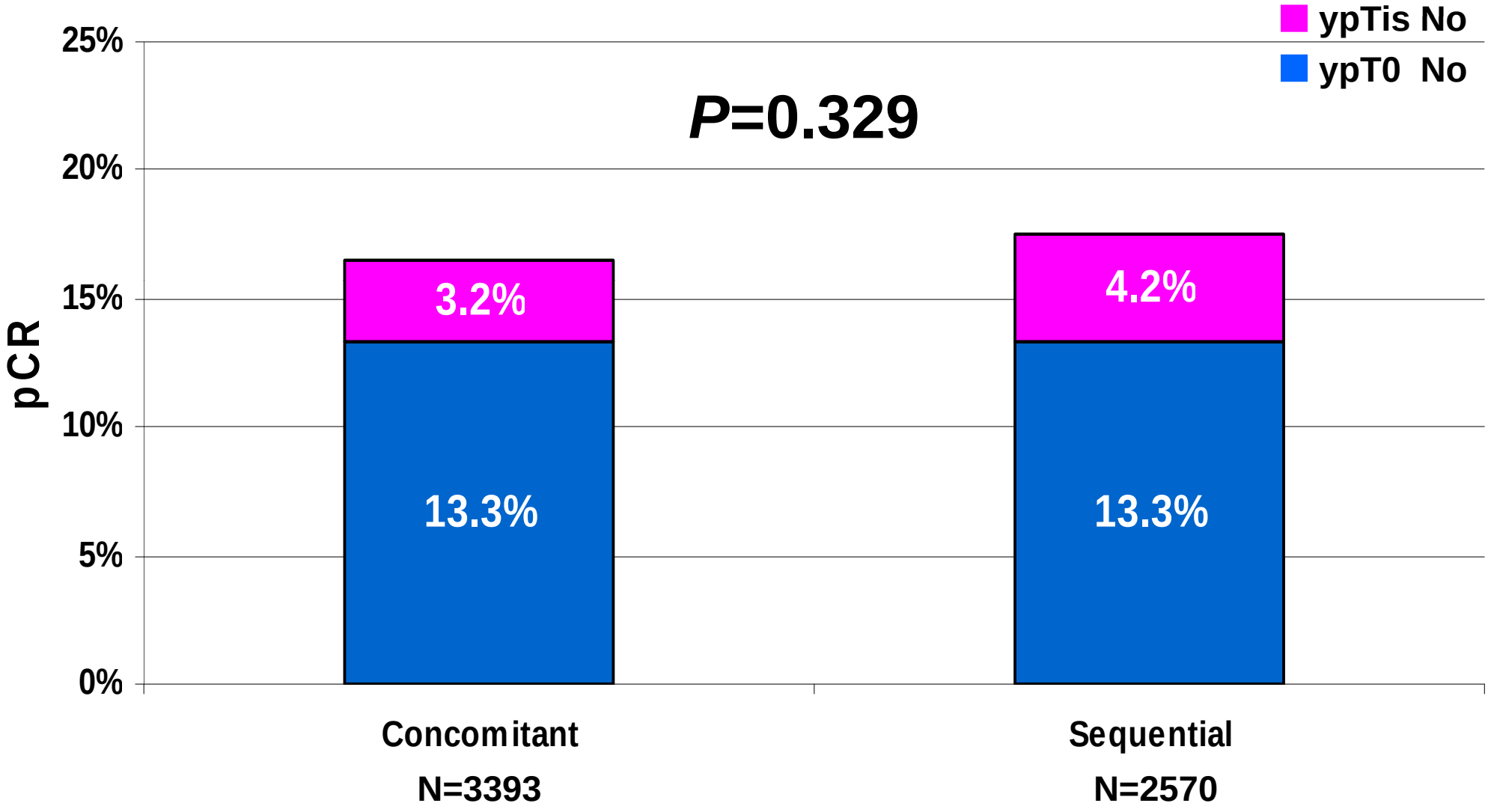


Treatment Group Effects*
Planned Duration of Regimen



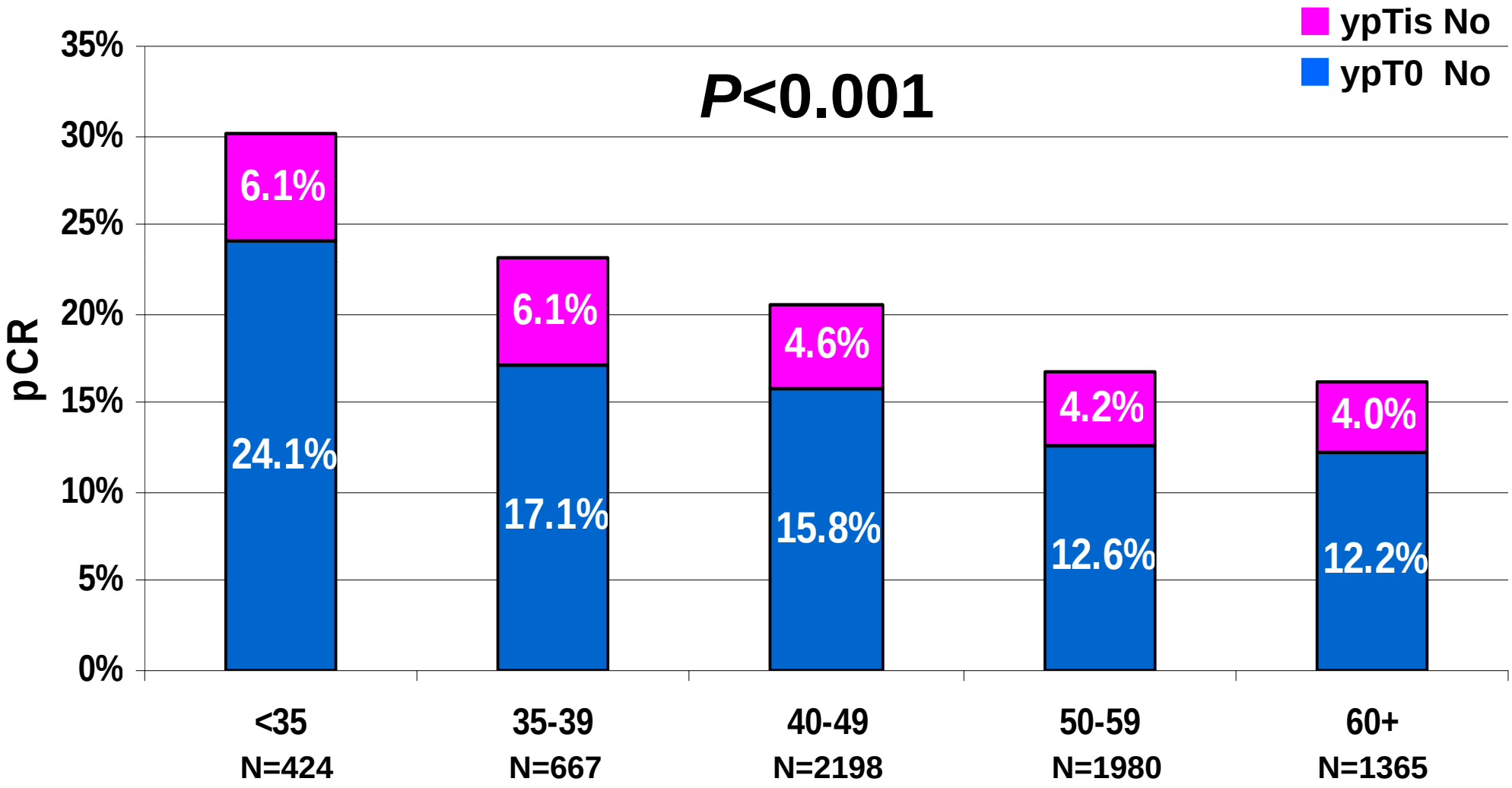
* excluding patients treated with trastuzumab

Treatment Group Effects*
Concomitant vs. Sequential

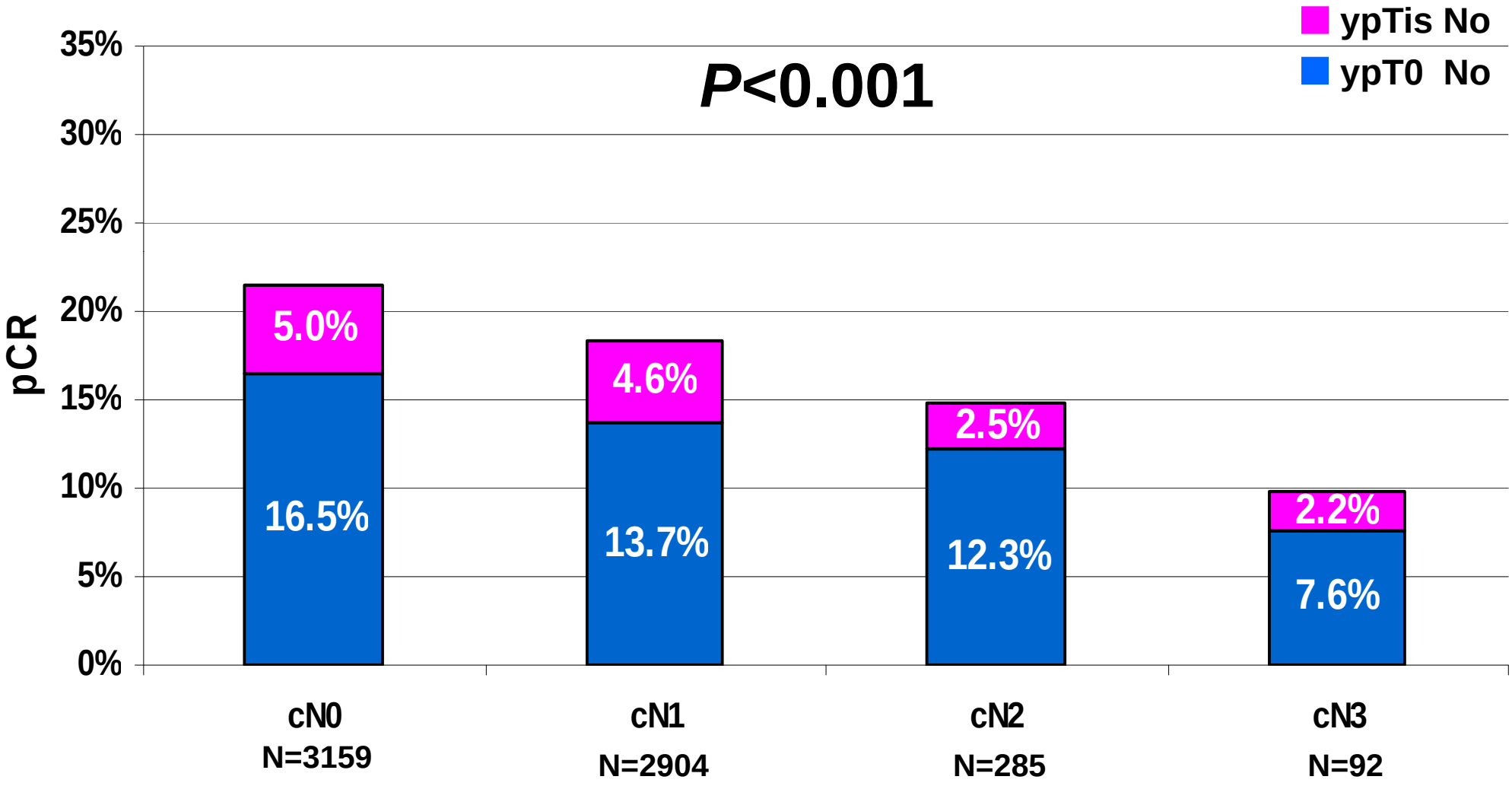


* excluding patients treated with trastuzumab

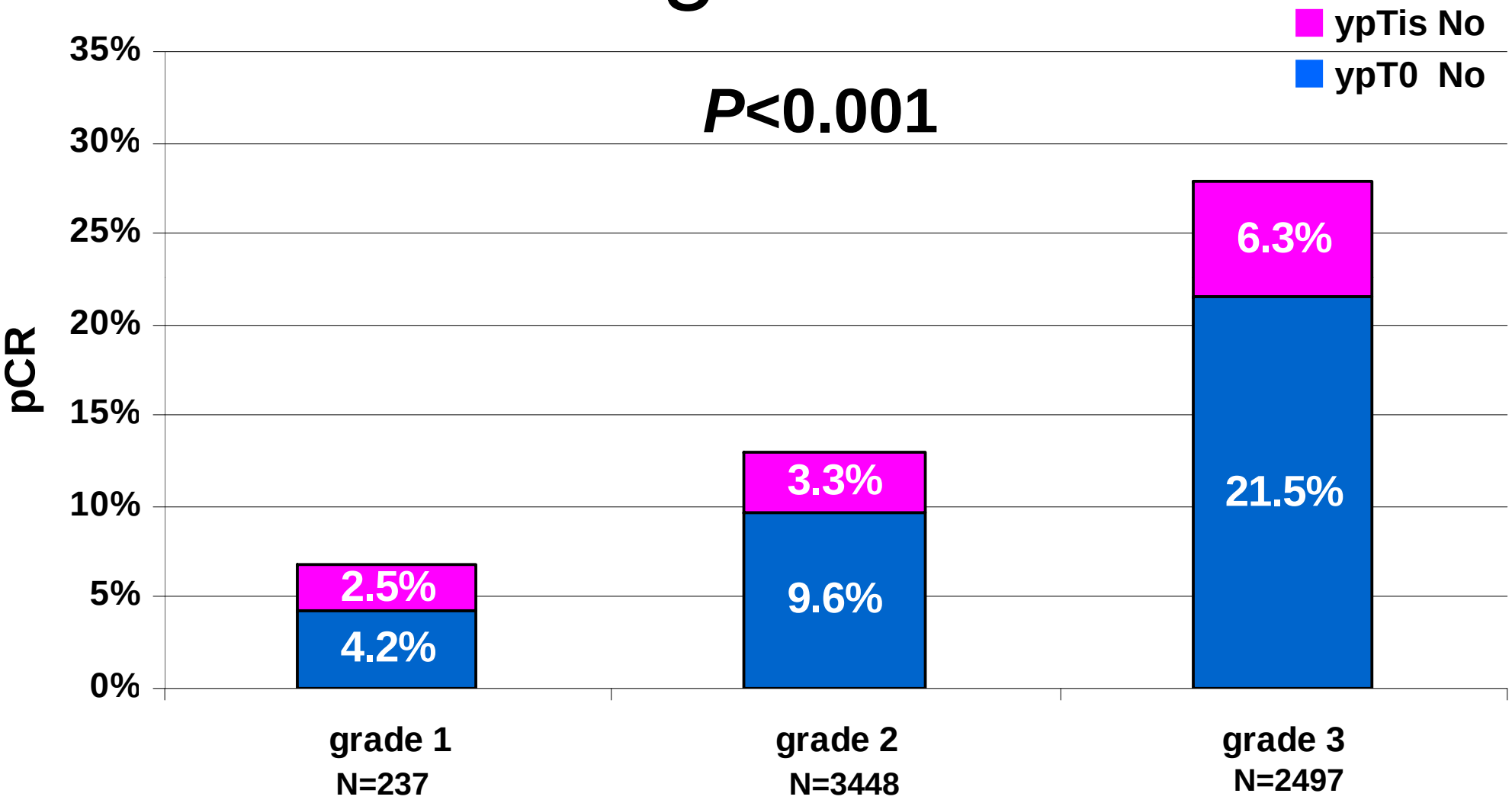
Predictive Factors
Age



Predictive Factors
Clinical Nodal Stage



Predictive Factors
Histological Grade



Hormonrezeptor pos. Mammakarzinom und PST

- **Niedrige pCR Rate ca. 10%**
- **Falls Brusterhaltende Therapie erwünscht sinnvoll**
- **Alternative Option präoperativ Aromatase-hemmer (Letrozol oder Anastrozol)**

GEPARTRIO

-frühes Ansprechen (2 Zyklen) prädiktiv für pCR

-aber die frühen Non responder zeigen trotzdem noch 5% pCR

Invasiv lobuläres Carcinom

pCR Rate bei 3% vs 20 % bei invasiv ductalem Ca.

Triple neg. Mamma Ca (TNBC)

- Höhere pCR Rate als non -TNBC 22 vs 11%

- Bei pCR vergleichbares OS (Liedtke 2008)

- Bei Resttumor nach Chemotherapie hat TNBC schlechteres OS im Vergleich zu non TNBC mit Resttumor

FONDAZIONE MICHELANGELO
avanzamento delle studie e cura dei tumori

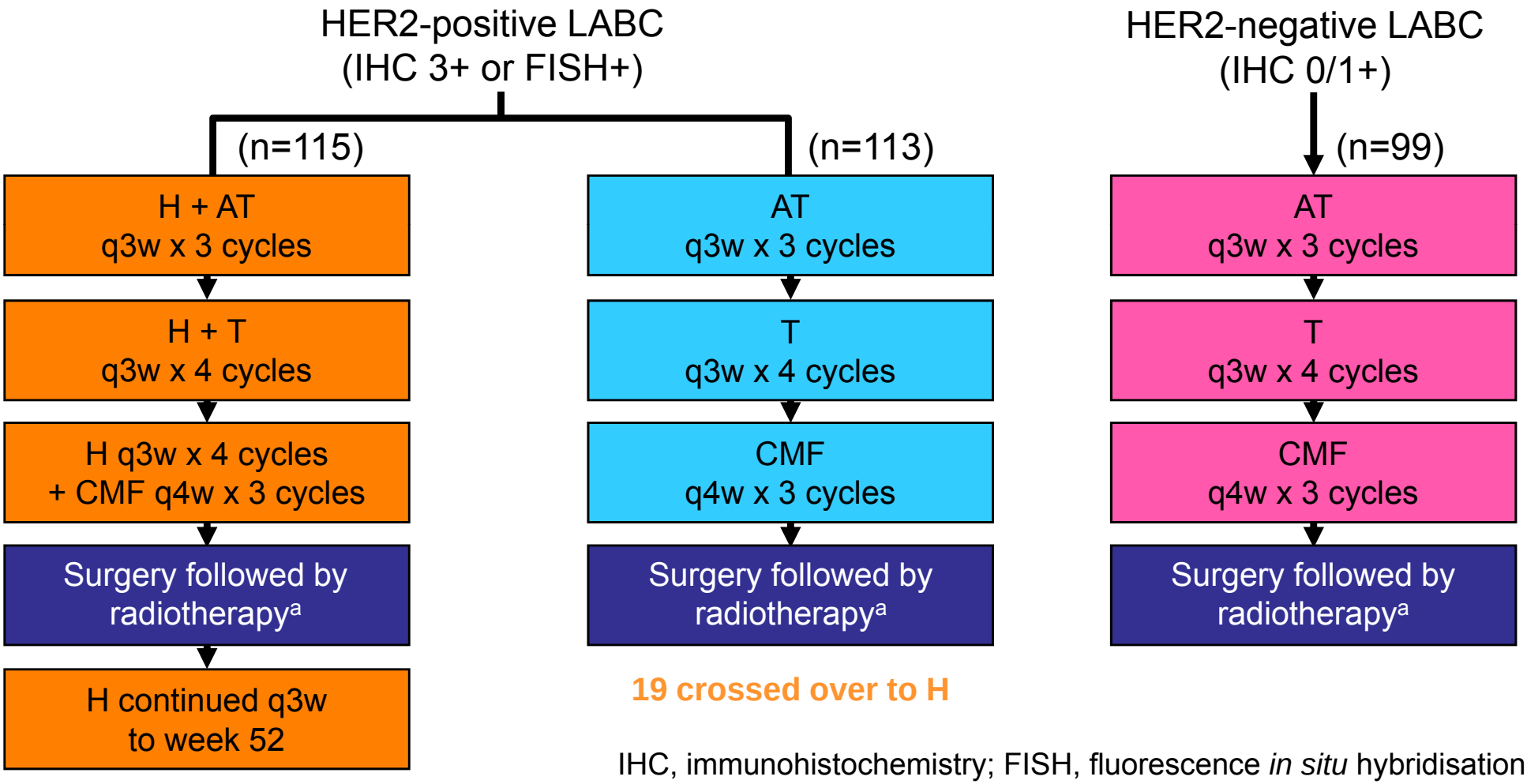
grupo SOLTI

Neoadjuvant trastuzumab in patients with HER2-positive locally advanced breast cancer: primary efficacy analysis of the NOAH trial

L Gianni, W Eiermann, V Semiglazov, GM Manikhas, A Lluch, S Tjulandin, A Feyereislova, P Valagussa, J Baselga

The study is co-sponsored by the Michelangelo Foundation and F Hoffmann-La Roche

NOAH study design



IHC, immunohistochemistry; FISH, fluorescence *in situ* hybridisation;
H, trastuzumab (8 mg/kg loading dose then 6 mg/kg); AT, doxorubicin (60 mg/m^2), paclitaxel (150 mg/m^2);
q3w, every 3 weeks; T, paclitaxel (175 mg/m^2); q4w, every 4 weeks
[a]Hormone receptor-positive patients will receive adjuvant tamoxifen

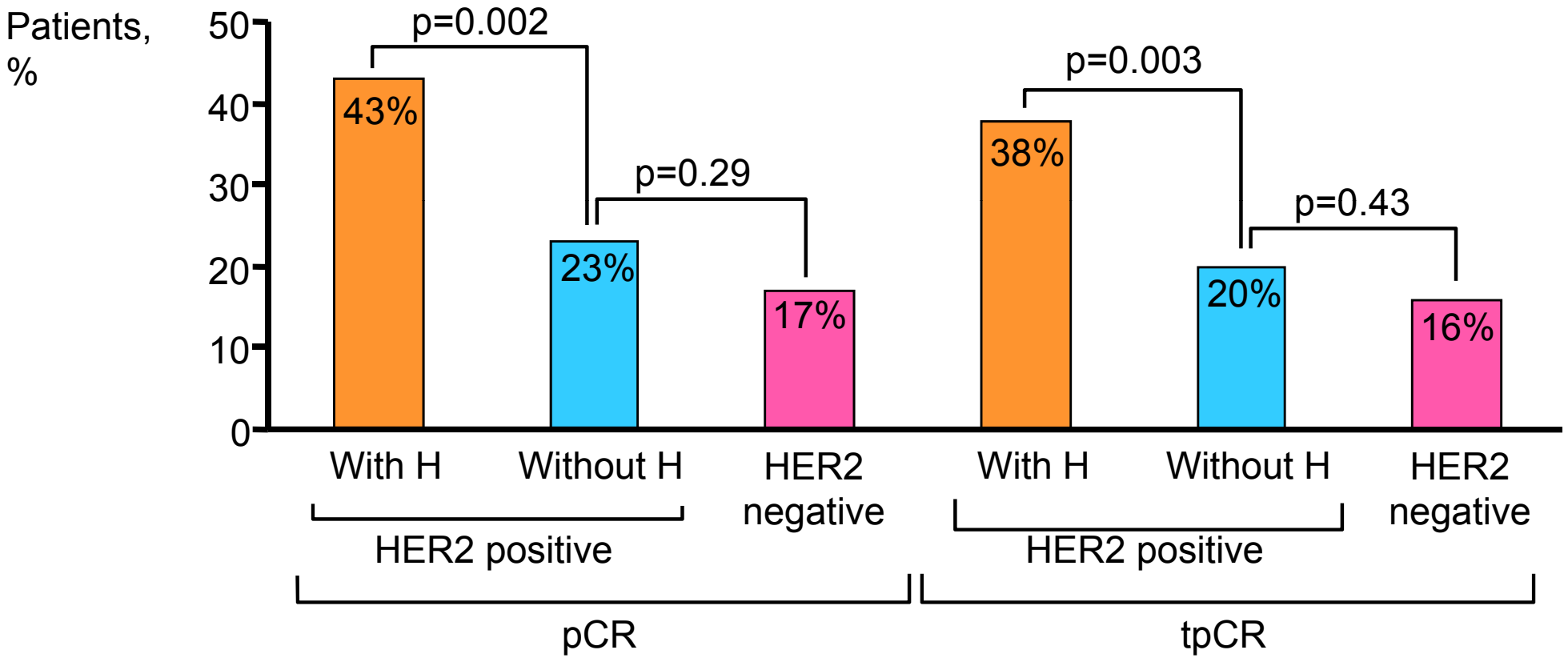
Baseline characteristics (1)

	HER2 positive		HER2 negative
	With H (n=115)	Without H (n=112[a])	(n=99)
Stage group, %			
T4, non-inflammatory	42	43	44
Inflammatory disease	27	27	14
N2 or ipsilateral nodes	31	30	41
Hormone receptor status, %			
ER and / or PgR positive	35	35	64
Both negative	65	65	36
Age group, %			
<50 years	46	41	51
≥50 years	54	59	49

[a]1/113 did not receive ethics approval for the last protocol amendment at the moment of the analysis

ER, oestrogen receptor; PgR, progesterone receptor

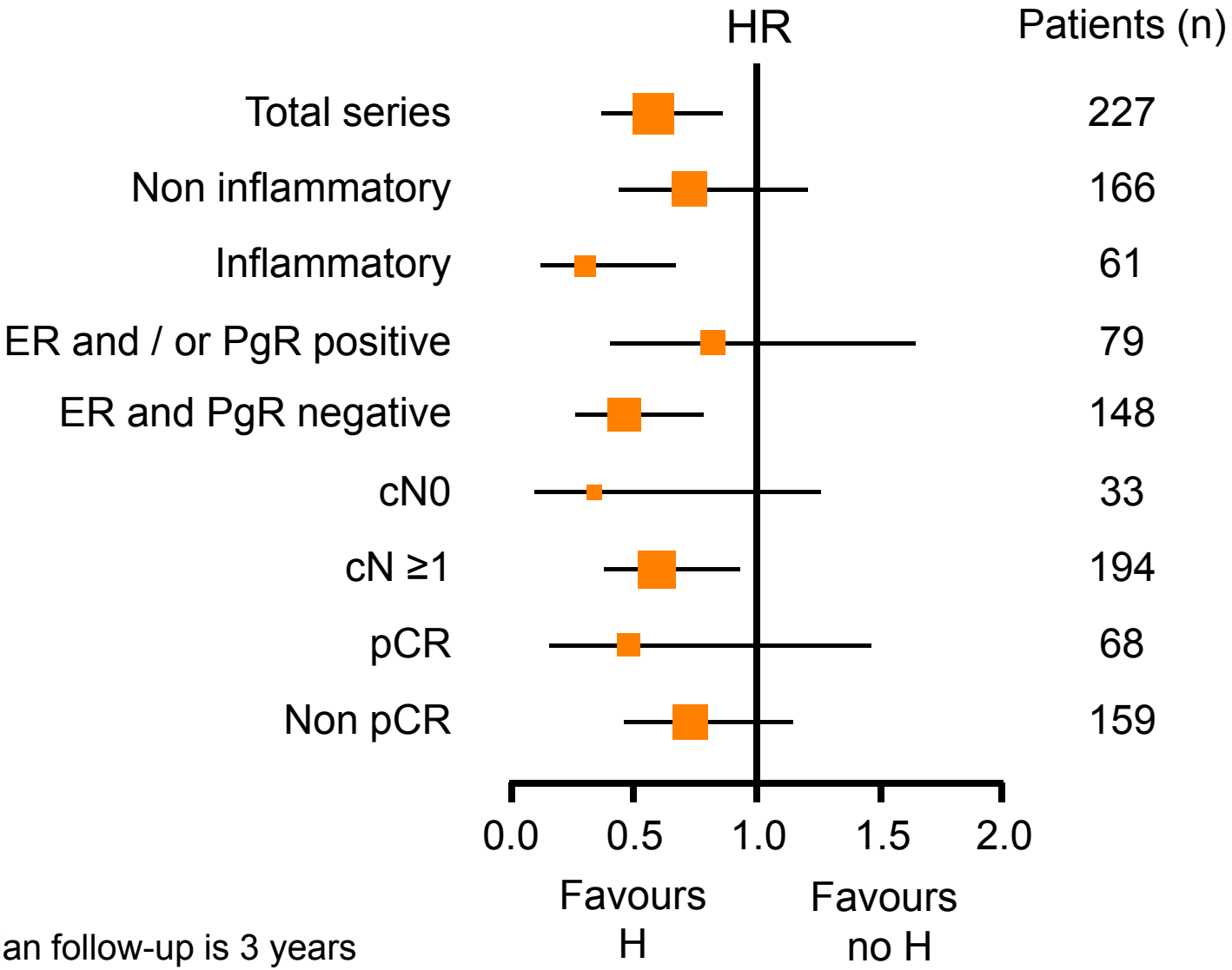
pCR of primary tumour: intent-to-treat population



tpCR: total pathologic complete response in breast and nodes

Eiermann et al 2008;
Semiglazov et al 2008

EFS by subgroup analysis of patients with HER2-positive disease: with vs without trastuzumab



Median follow-up is 3 years

Prim. systemische endokrine Therapie

Kein Standard

Ältere Pat. mit fortgeschrittenem Ca.

Bei Ablehnung einer Chemotherapie

Keine Daten i.d. Prämenopause

Beste Datenlage mit Letrozol

Primär systemische endokrine Therapie

Aromataseinhibitoren in der Postmenopause

Autor / Studie	Patienten-zahl	Therapie	cRR (%)	BCS (%)
Eiermann et al 2001	**337**	**Letrozol vs Tam**	**55 vs 36**	**45 vs 35**
Smith et al 2003 IMPACT	330	Anastrozol vs Tam vs Anastrozol+Tam	37 vs 36 vs 39	46 vs 22 vs 26
Gil et al 2004	55	Exemestan	45	42
Paepke et al 2003	33	Letrozol (4 Mo) Vs Letrozol (8 Mo)	57 vs 90	67
Semiglazov et al 2004	121	Chemo Vs Anastrozol Vs Exemestan	76 vs 76 vs 82	24 vs 32 vs 34

Welchen Pat. ist Prim.syst. Therapie als Alternative zur Adj.Therapie zu empfehlen?

1. Primär inoperables bzw. nicht brusterhaltend operables Ca.
2. Inflammatorisches Ca.
3. Stadium IIIA-B oder T3 oder Beteiligung ipsilateraler supra –oder infraclav. Lnn (N3)
4. Rezeptorneg. und / oder HER2 neu pos. Befund nach Stanzbiopsie
5. Kontraindikation für Chirurgie

Behandlungsvorschläge ausserhalb klin. Studien die empfohlen werden können.

Regime	Dosierung (mg/m²)	Zeitablauf
AC/EC–D (P)	A75, E90, C600, D100	Jeweils 4 Zyklen 3 wöchentlich
DAC/DEC	D75, A50, E75, C500	6 Zyklen 3 wöch.
AP-CMF	A60, P200, CMF i.v.	4 Zyklen 3 wöch. 4 Zyklen Tag 1+8, q 28

A=Doxorubicin, C=Cyclophophamide, E=Epirubicin, D=Docetaxel, P=Paclitaxel,
M=Methotrexate, F=5-Fluorouracil

Primär systemische Chemotherapie
MammaCa - Vorteile

- **In vivo Chemosensitivitäts-Test**
- **Schnelle Beurteilung der Effektivität neuer Therapieregime**
- **Beurteilung von Tumoransprechen durch Patientin**
- **Vergleich von Biomarkern mit Tumoransprechen (prädiktive Faktoren, Resistenz-Faktoren)**
- **Erhöhte BET-Rate**
- **Plattform für Phase III – Studien adjuvant**