

Case #2 – Locally Advanced Primary Breast Cancer: Multidisciplinary Management Part I

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**WHAT DOES THE PATIENT
WANT?**

...simply the best?

Who is a candidate for neoadjuvant systemic therapy?

Chemotherapy:

- Patients with locally advanced disease
- Patients in whom all information necessary to decide on the use of chemotherapy are available before surgery

Endocrine Therapy

- Patients, in whom all information necessary to decide on endocrine therapy are available before surgery

pCR and OS

<i>Study (year)</i>	<i>Pts</i>	<i>Regimen</i>	<i>pCR</i>	<i>5 y S of pCR</i>
Bonadonna (98)	536	CMF,A,M	3%	86% (8y)
NSABP B18 (98)	1523	AC	13%	90%
Kuerer (99)	451	FAC	12%	89%
Aberdeen (02)	162	CVAP+/-D	34%	90% (all)
NSABP B27 (03)	2411	AC+/-D	26%	92%
Dieras (04)	200	AT vs AC	16 vs 10%	91% (DFS)

Case #2

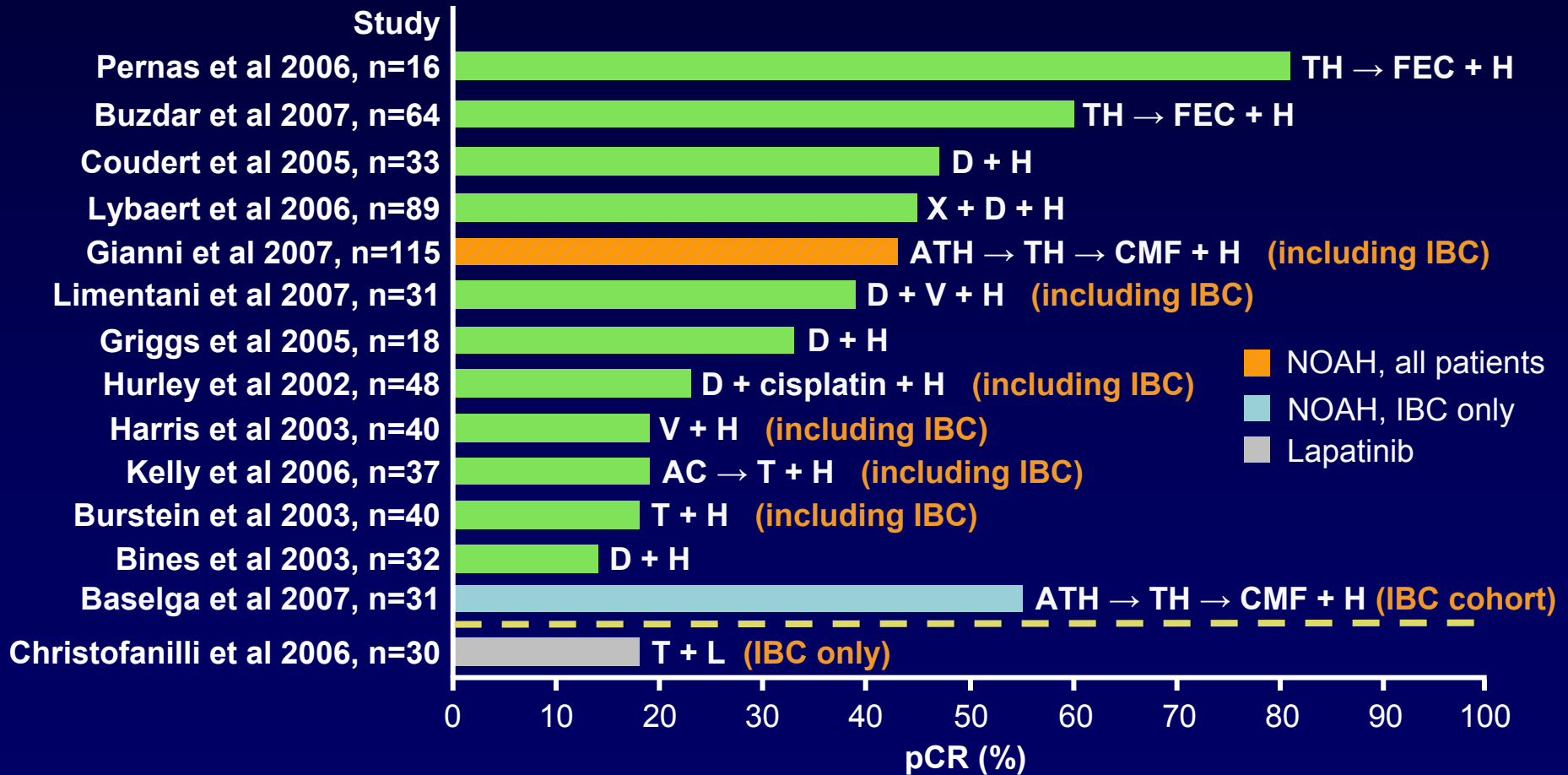
Locally Advanced Primary Breast Cancer: Multidisciplinary Management

Part I:

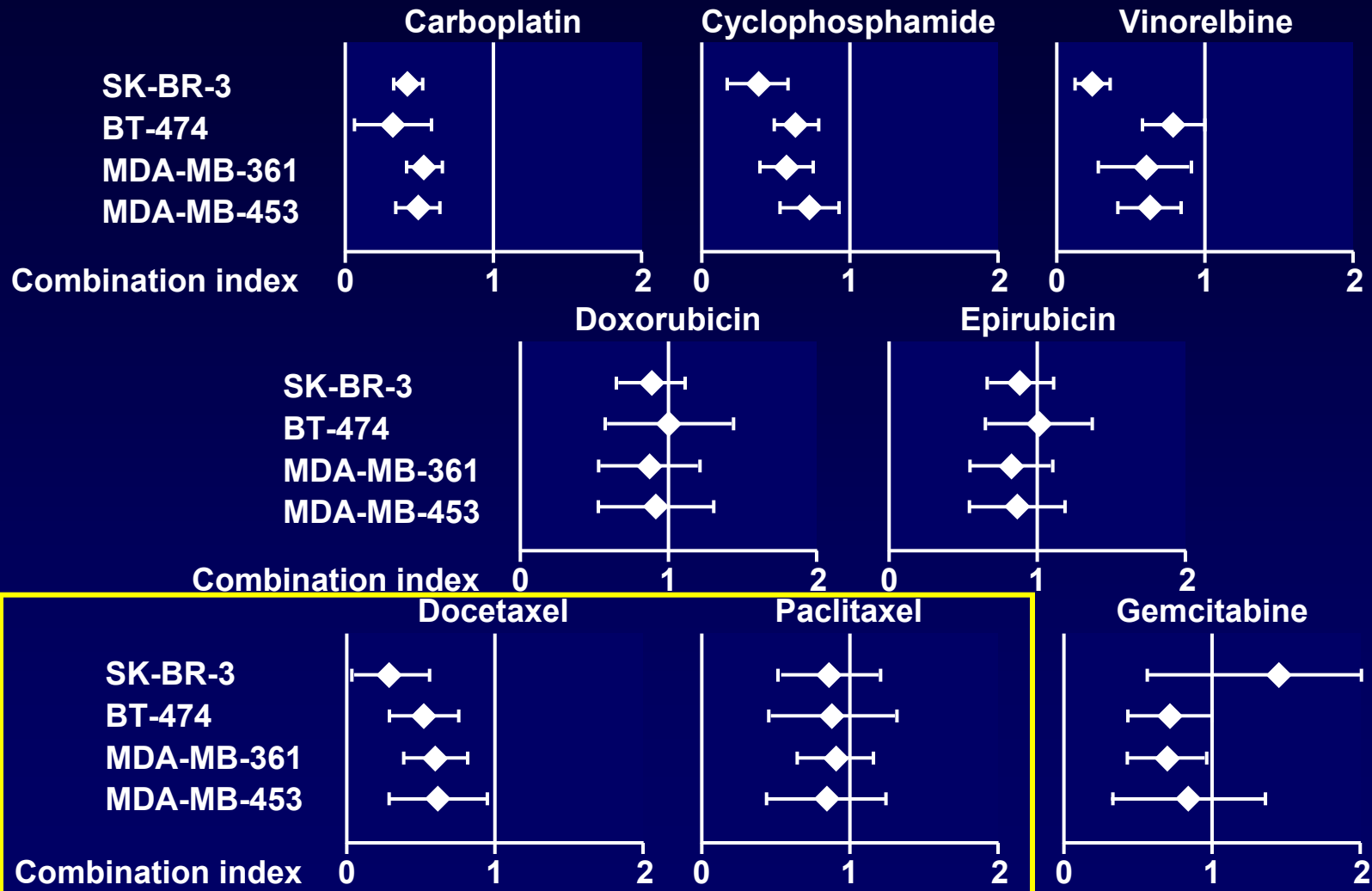
Which of the following neoadjuvant options would you recommend?

- Trastuzumab and a taxane
- Trastuzumab and vinorelbine (Navelbine®)
- Trastuzumab and pegylated liposomal doxorubicin (Caelyx®)
- Trastuzumab + docetaxel (Taxotere®) + carboplatin
- Trastuzumab and an aromatase inhibitor
- Chemotherapy or endocrine therapy alone, no trastuzumab
- Encourage participation in NEO ALTTO clinical trial

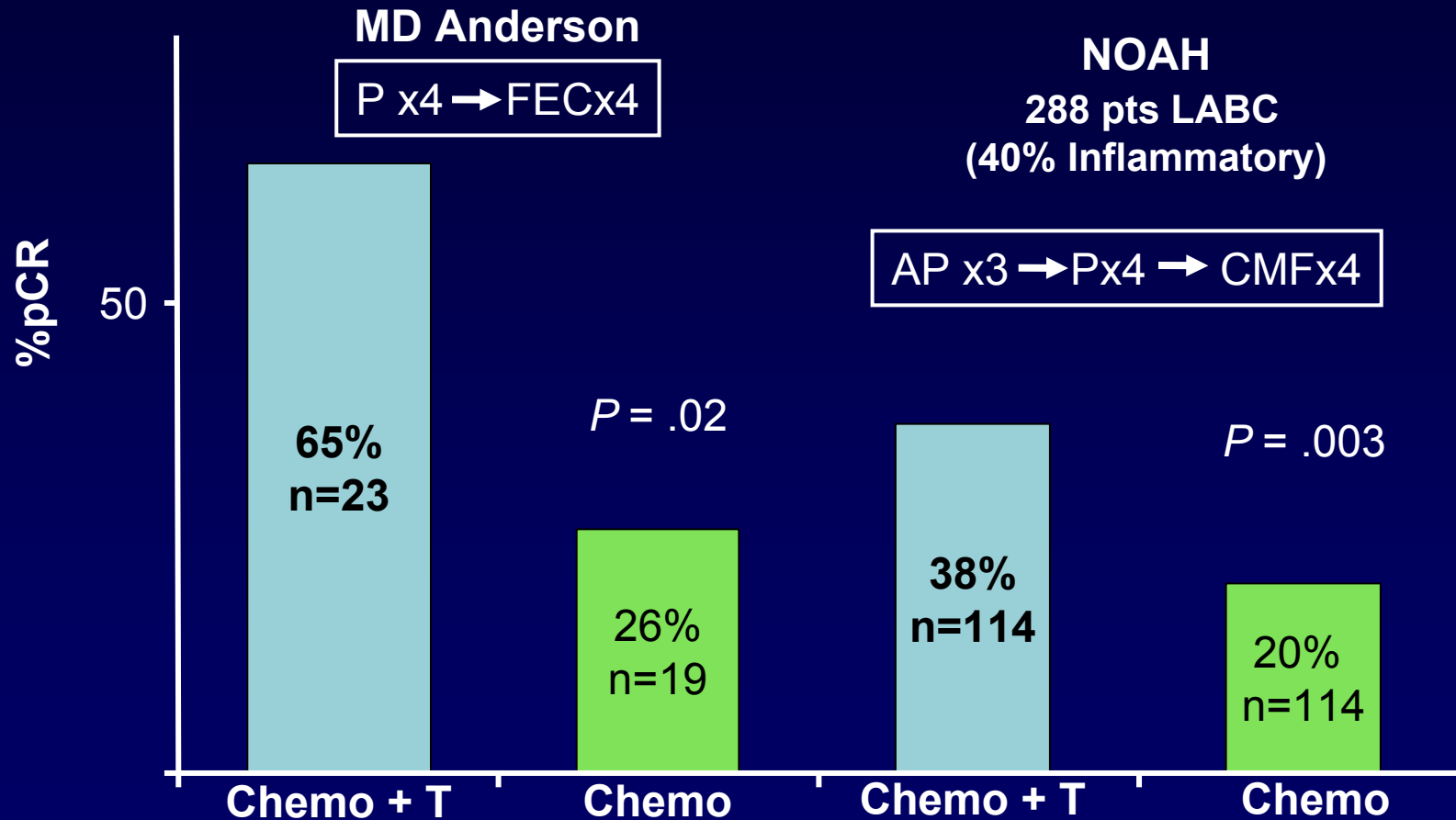
Preoperative Therapy: pCR Rates in HER2-Positive Disease



In Vitro Drug Interactions With Trastuzumab



Preoperative Chemo ± Trastuzumab Two Randomized Trials pCR Rates



MD Anderson Randomized Preoperative HER2+: Cardiac Safety

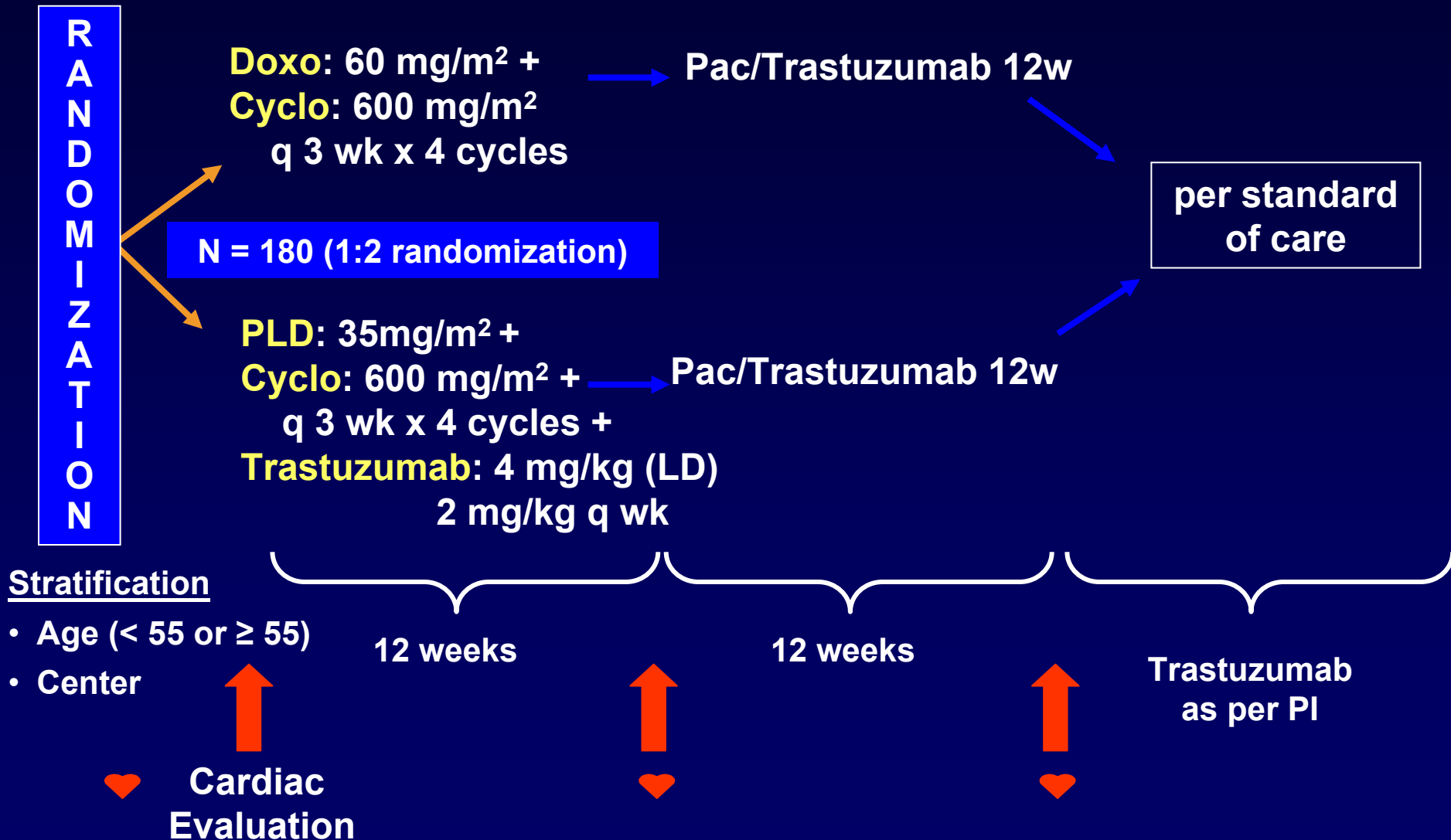
- Epirubicin dose was limited at 300 mg/m²
- No cases of CHF were observed during or immediately following treatment
- Two cases of clinical cardiac dysfunction with trastuzumab-containing regimen reported after longer follow-up
- Acknowledged only 45 pts; phase III trial planned to validate

NOAH Cardiac Safety Data at First Planned Interim Analysis, %

LVEF worst value	HER2-positive cohort		HER2-negative (n=97)
	With H (n=114)	Without H (n=113)	
No change	75	84	87
Absolute decrease $\geq 10\%$ <20%	21	15	12
Absolute decrease $\geq 20\%$	2	1	1
CHF responsive to treatment	2	0	0



Adjuvant Pegylated Liposomal Doxorubicin + Trastuzumab



Trastuzumab + vinorelbine

Objective response rate

%

100
80
60
40
20
0

■ First-line therapy

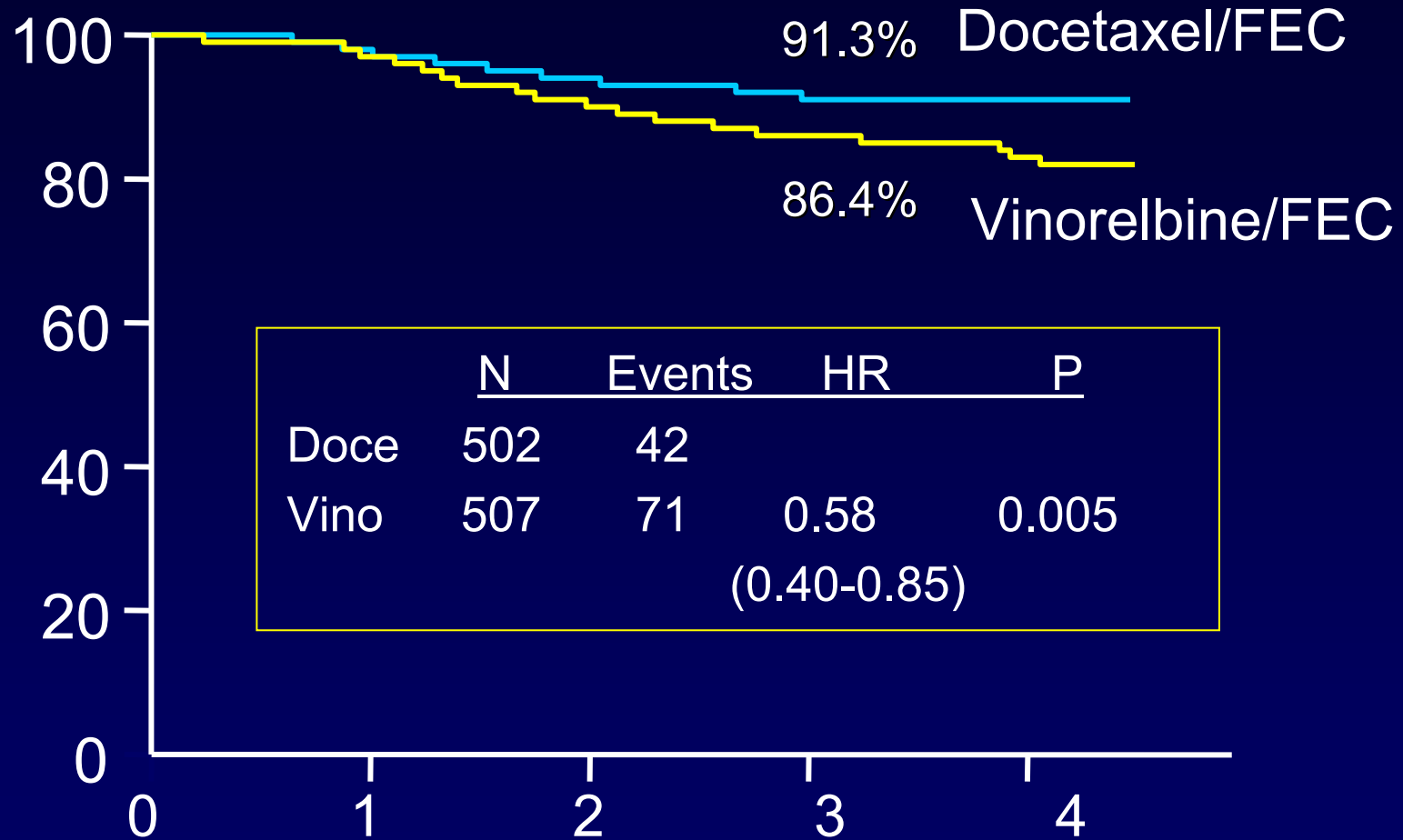
■ Second-or subsequent-line therapy

Jahanzeb et al., 30 mg/m²
Burstein et al., 25 mg/m²
Bernardo et al., 25 mg/m²
Chan et al., 30 mg/m²
de Wit et al., 25 mg/m²
Burstein et al., 25 mg/m²
Papaldo et al., 25 mg/m²
Bayo et al., 25 mg/m²
Glogowska et al., 35 mg/m²

Vinorelbine schedule

BUT FINHER IMPLIES VRL IS INFERIOR TO DOCE?

Recurrence-free Survival (%)



No. at Risk

Years

Docetaxel	502	491	431	250	83
Vinorelbine	507	492	411	233	82

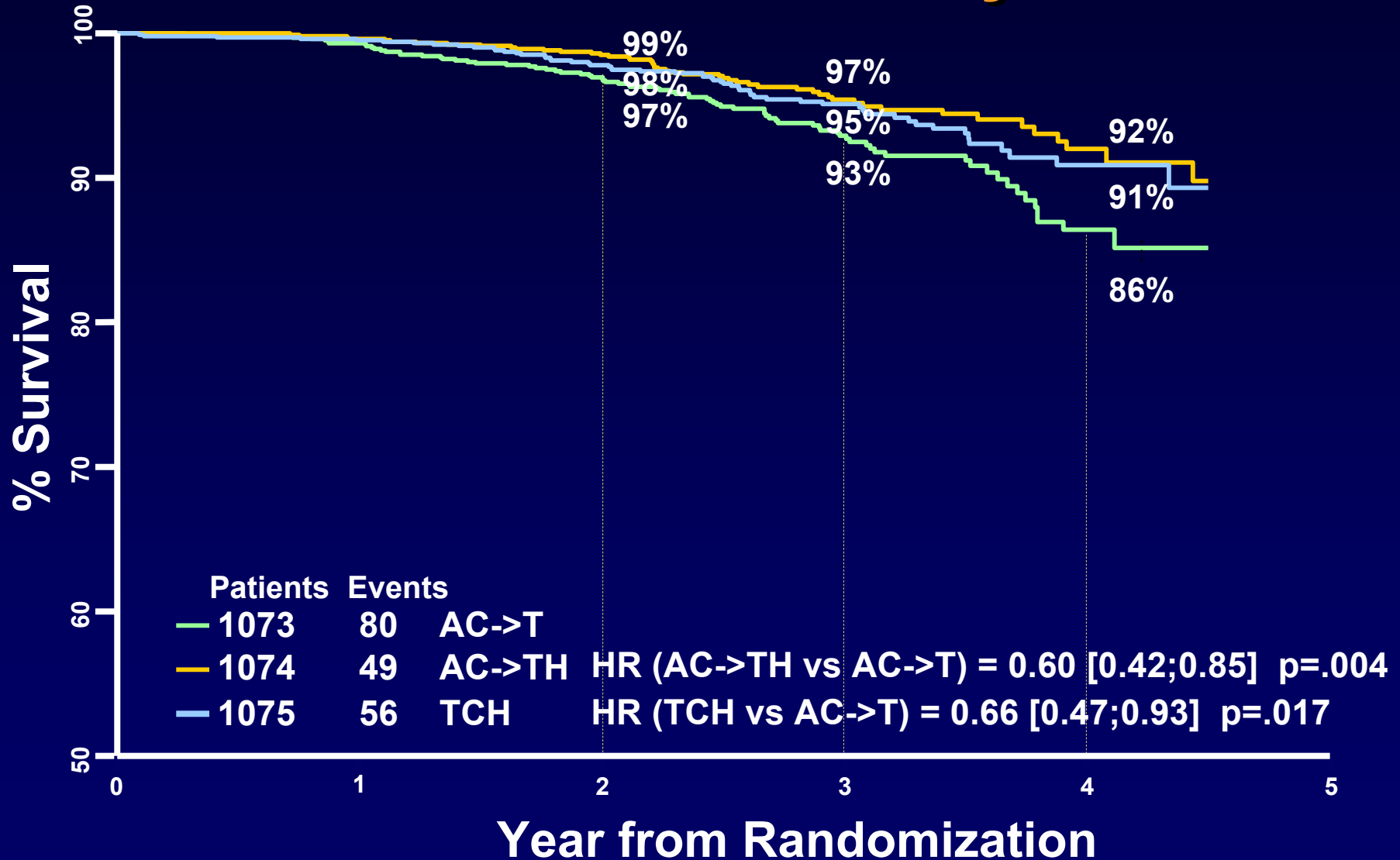
Trastuzumab + CAPECITABINE

- **48 pts without prior chemotherapy for MBC ; 43 evaluated**
- **Adjuvant chemotherapy (65%), including anthracycline (42%), docetaxel (9%), and paclitaxel (7%).**
- **ORR is 63% (n=27), including 8 CRs (19%) and 19 PRs (44%).**
- **Median progression-free and overall survival have not been reached.**

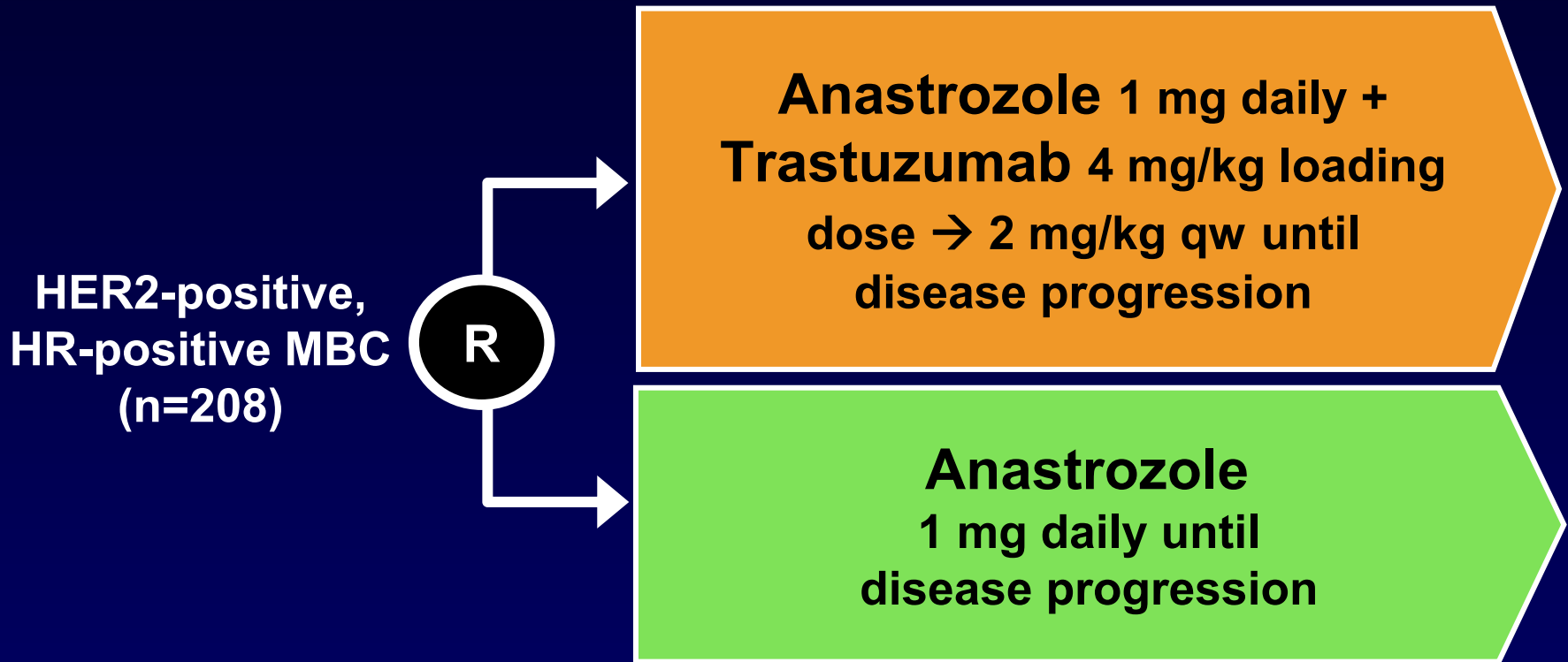
Phase II Preoperative HER2+ Docetaxel + Carboplatin + Trastuzumab

- n = 70, 6 cycles TCH
- T2/T3 (100%), N1/N2 (53%)
- Clinical response 95%
- Breast conservation 64%
- pCR in breast and nodes 39%
- Median f/up 25 months
 - 5 local recurrences
 - 8 distant recurrences

BCIRG 006: Overall Survival Second Interim Analysis



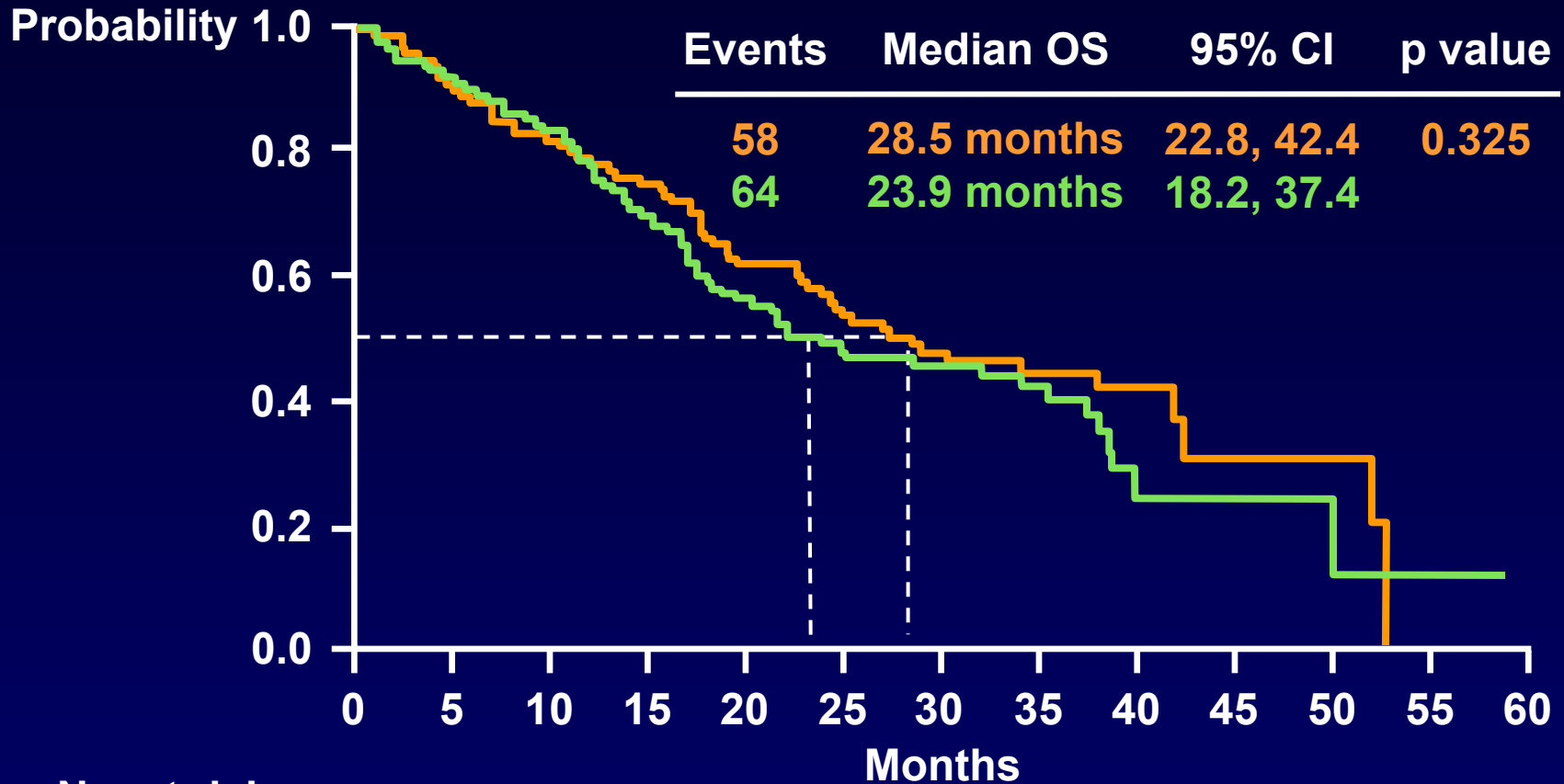
TAnDEM Study Design



- Crossover to receive trastuzumab was actively offered to all patients who progressed on anastrozole alone

HR, hormone receptor; MBC, metastatic breast cancer; R, randomisation

Overall Survival



No. at risk

— A + H	103	91	83	76	63	49	36	24	12	4	3	0	0
— A	104	96	87	73	58	42	34	22	5	2	1	1	0

73/104 patients (70%) received H later during the course of disease

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NEO-ALTTO: Study Design

