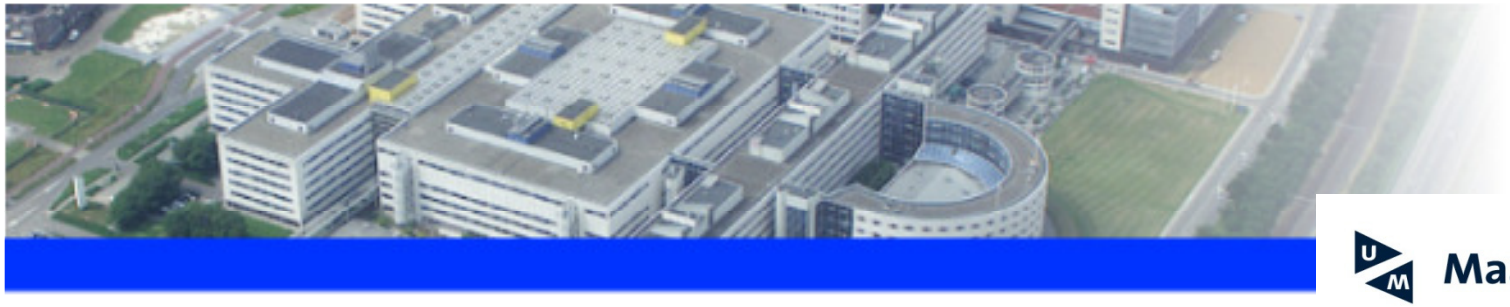


azM

Maastricht University

Berichten uit San Antonio

CTRC-AACR
SAN ANTONIO BREAST CANCER SYMPOSIUM **2010**

Birgit Vriens
Medisch oncoloog
MUMC, Maastricht

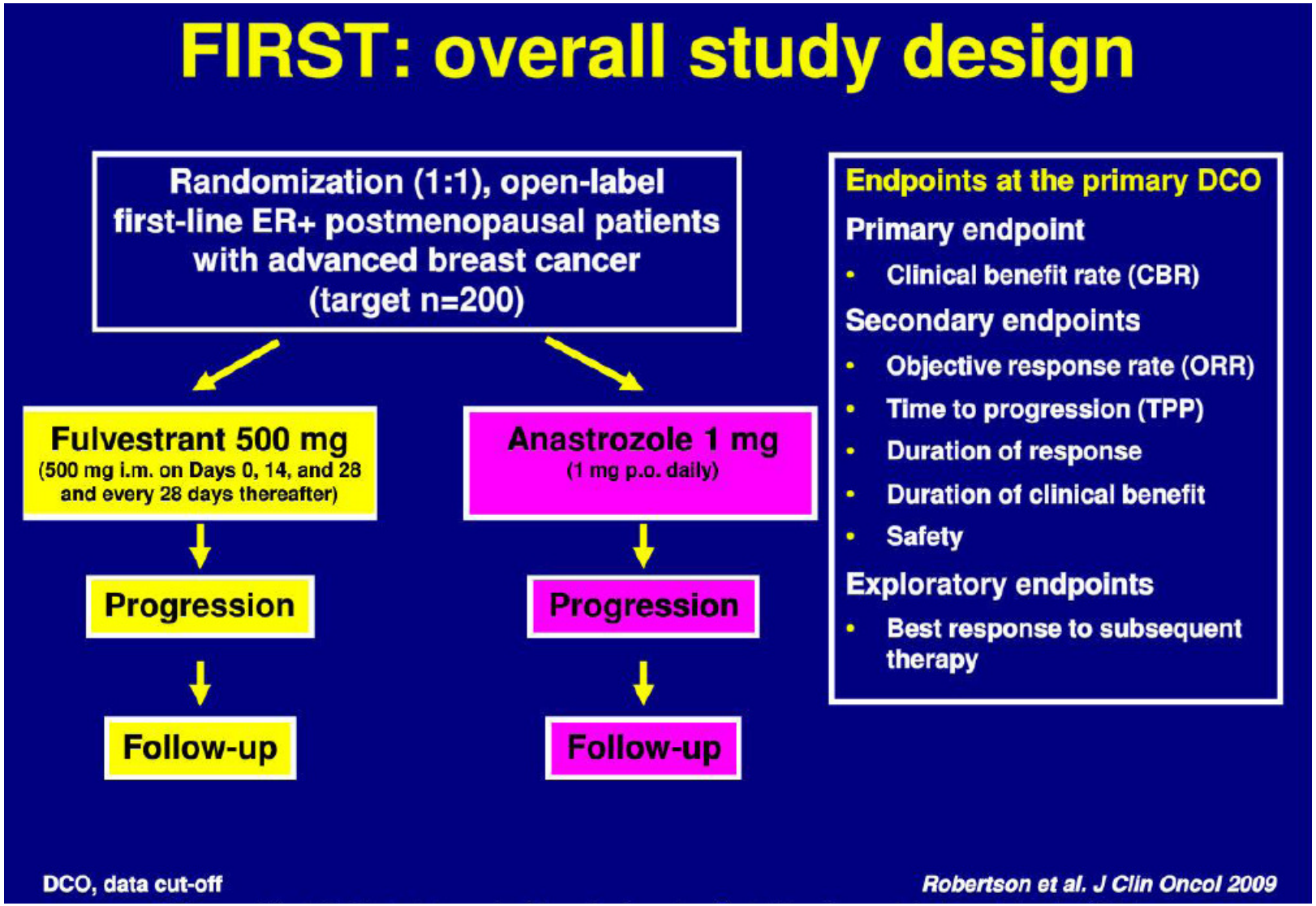
2e Mammacongres Harderwijk
28 januari 2011

- **Endocriene therapie**
  - Fulvestrant (fase II)
- **Chemotherapie**
  - BCIRG 001
- **Targeted therapie**
  - Geparquinto
  - Neosphere (fase II)
- **Verandering hormoonreceptorstatus**
  - primaire tumor vs recidief
- **Preventieve lymfedrainage**
- **AZURE trial**

A comparison of fulvestrant 500 mg with anastrozole as first-line treatment for advanced breast cancer: follow up analysis from the FIRST study

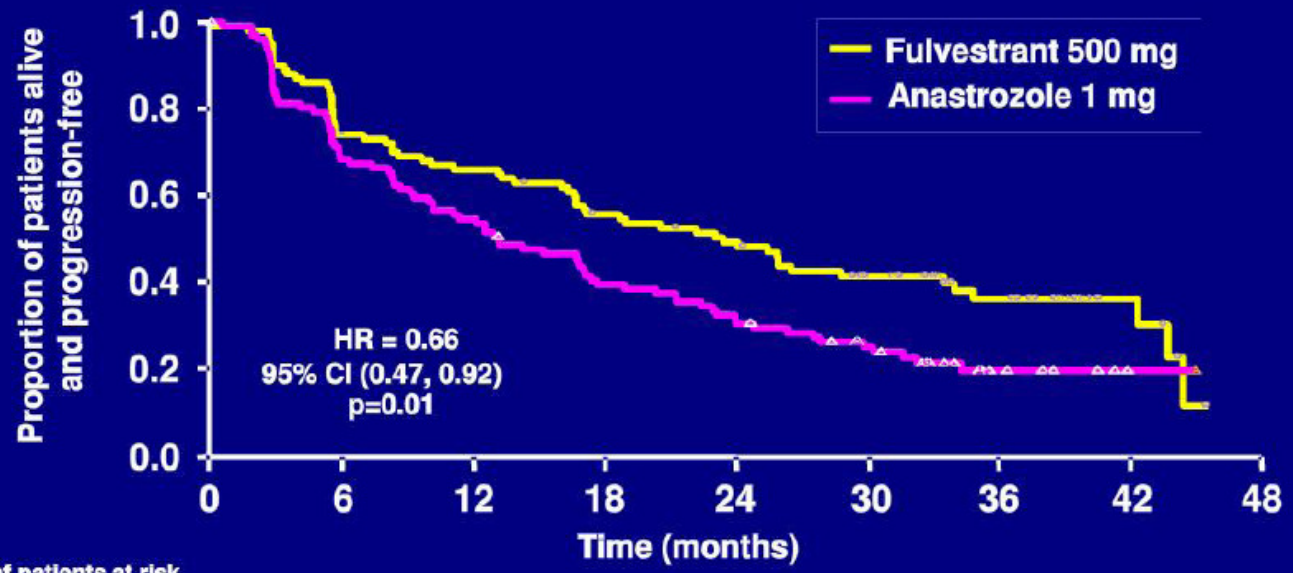
John F. R. Robertson, Justin P.O. Lindemann
et all.

Design


FIRST: overall study design
Randomization (1:1), open-label first-line ER+ postmenopausal patients with advanced breast cancer (target n=200)
Fulvestrant 500 mg
(500 mg i.m. on Days 0, 14, and 28 and every 28 days thereafter)
Anastrozole 1 mg
(1 mg p.o. daily)
Progression
Progression
Follow-up
Follow-up
Endpoints at the primary DCO
Primary endpoint
• Clinical benefit rate (CBR)
Secondary endpoints
• Objective response rate (ORR)
• Time to progression (TPP)
• Duration of response
• Duration of clinical benefit
• Safety
Exploratory endpoints
• Best response to subsequent therapy
DCO, data cut-off
Robertson et al. J Clin Oncol 2009

Results

TTP: updated analysis



Number of patients at risk

Fulvestrant 500 mg	102	74	65	52	45	34	20	6	0
Anastrozole 1 mg	103	69	55	39	30	21	8	2	0

	Fulvestrant 500 mg n=102 (%)	Anastrozole 1 mg n=103 (%)
Number of progressions (%)	63 (61.8)	79 (76.7)
Median (months)	23.4	13.1

After primary DCO, progression was determined by investigator opinion

Conclusion

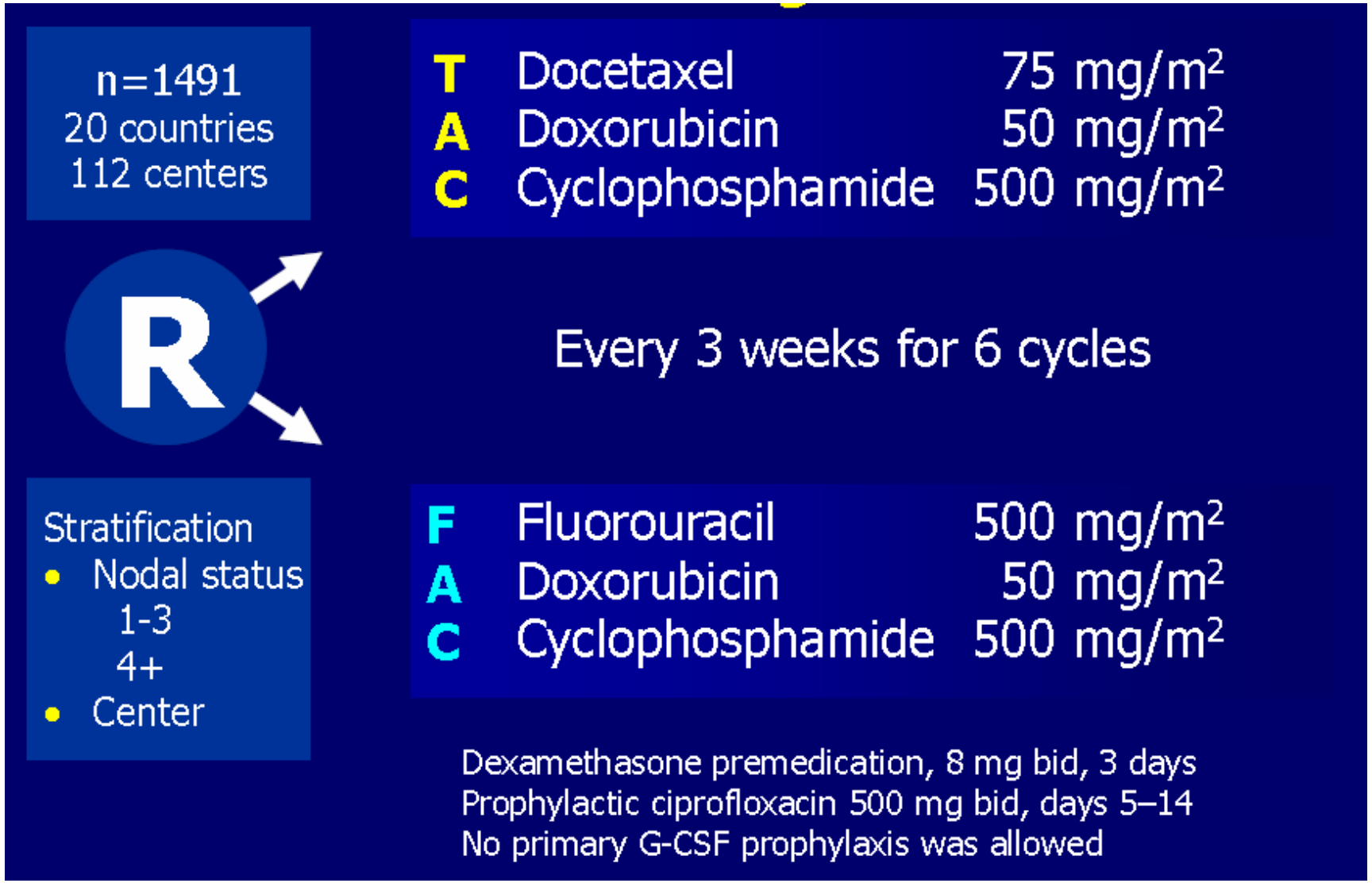
- Significante verbetering TTP, fulvestrant vs anastrozol als endocriene 1e lijns therapie in ER+ mammacarcinoom, MBC
- Voordeel TTP is consistent in alle subgroepen
- Fase II trial, kleine aantallen
- Mogelijk voordeel tgv verschillend werkingsmechanisme

Ten-year follow-up analysis of the BICRG 001 trial confirms superior DFS and OS benefit of adjuvant TAC (docetaxel, doxorubicin, cyclophosphamide) over FAC (fluorouracil, doxorubicin, cyclophosphamide) in women with operable node-positive breast cancer

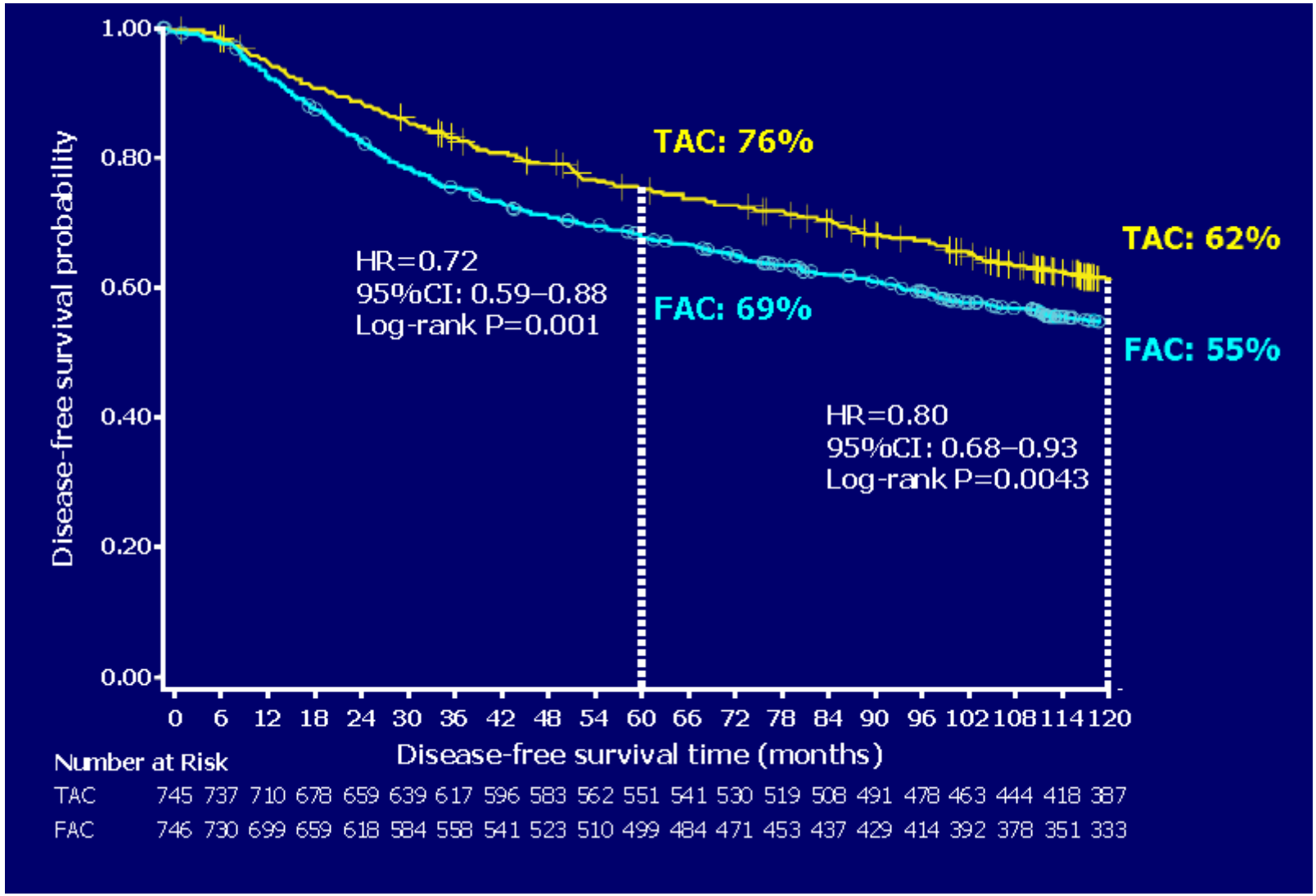
Martin M, Mackey J, Pienkowski T, Rolski J, Guastalla JP, Sami A, Glaspy J, Juhos E, Wardley A, Fornander T, Hainsworth J, Coleman R, Modiano M, Vinholes J, Pinter T, Childs B, Roessner M, Wilson V, Rupin M, Vogel C
on behalf of the BCIRG 001 Investigators

NCT00688740
Sponsored by sanofi-aventis

Trial design

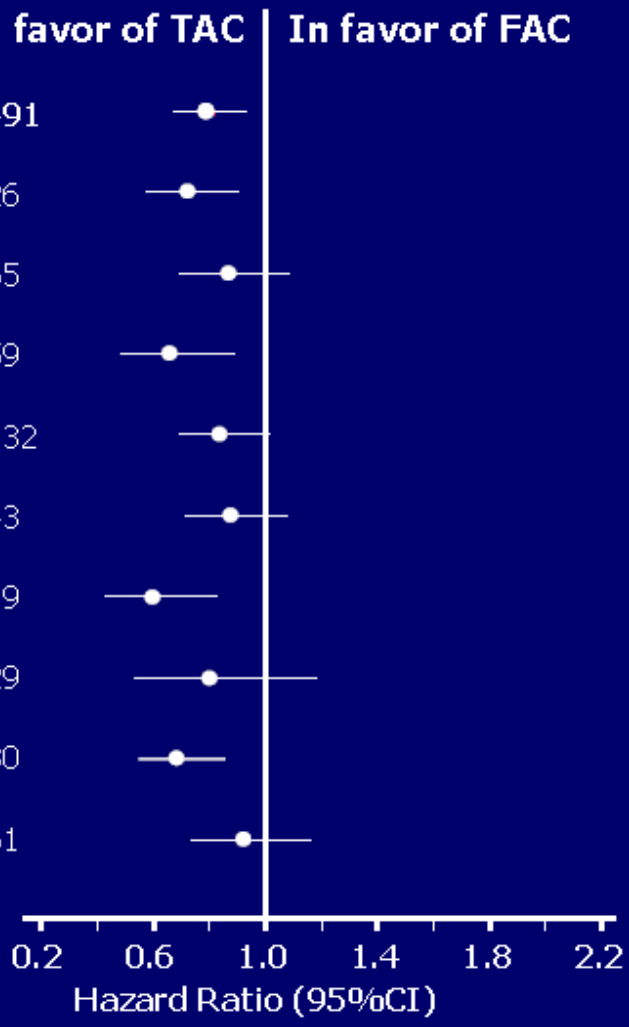


DFS at median 10y FU



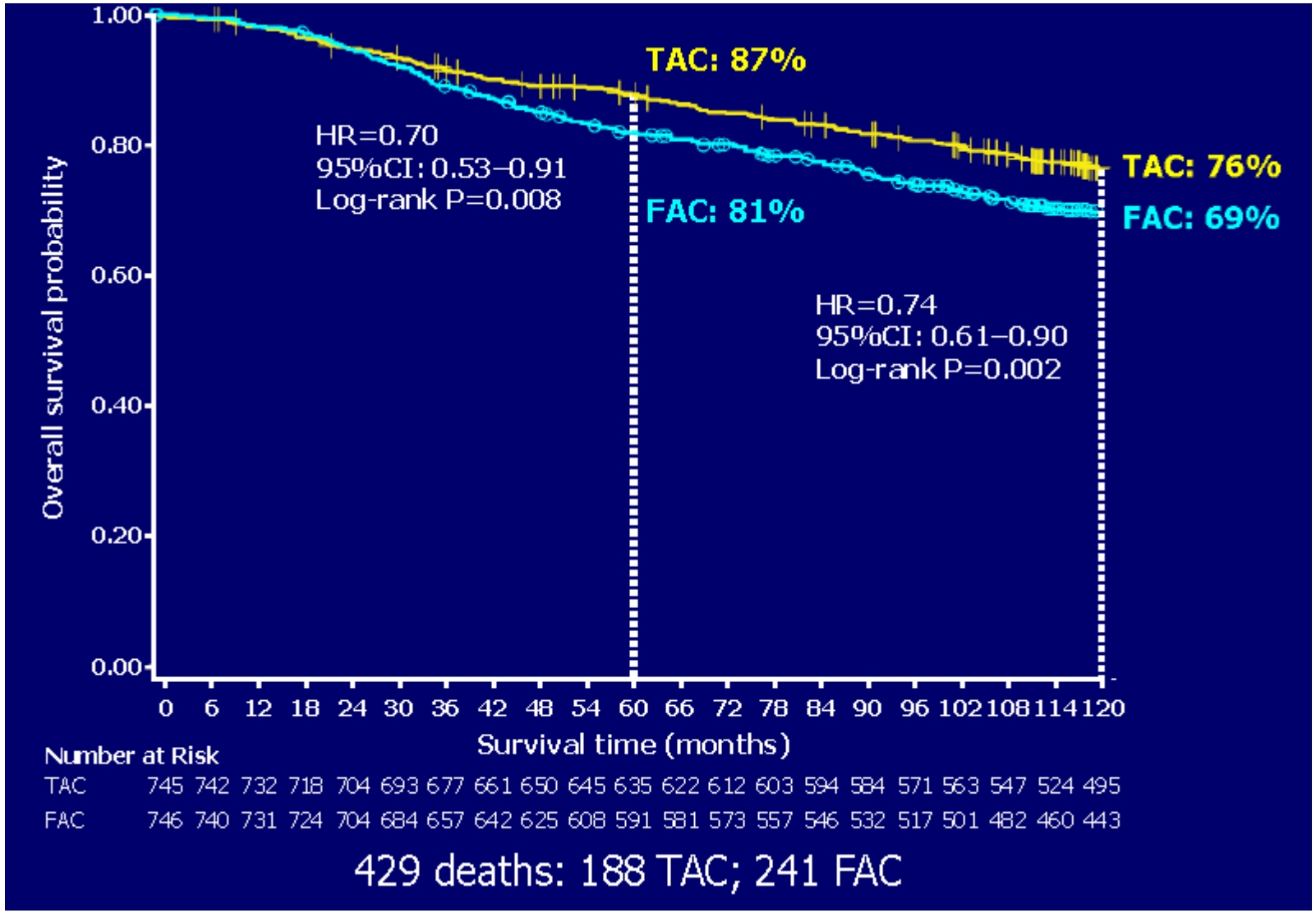
DFS at pre-defined subgroups

				In favor of TAC / In favor of FAC
Overall	ITT Adjusted*	0.80 (0.68 to 0.93)	1491	
Number of positive nodes	[1-3]	0.72 (0.58 to 0.91)	926	
Number of positive nodes	[4+]	0.87 (0.70 to 1.09)	565	
Hormonal Receptor status	Negative	0.66 (0.49 to 0.89)	359	
Hormonal Receptor status	Positive	0.84 (0.70 to 1.01)	1132	
HER2/NEU status	Negative	0.88 (0.72 to 1.08)	943	
HER2/NEU status	Positive	0.60 (0.43 to 0.83)	319	
HER2/NEU status	Unknown	0.80 (0.54 to 1.18)	229	
Menopausal status	Pre-menopausal	0.69 (0.55 to 0.86)	830	
Menopausal status	Post-menopausal	0.93 (0.74 to 1.16)	661	



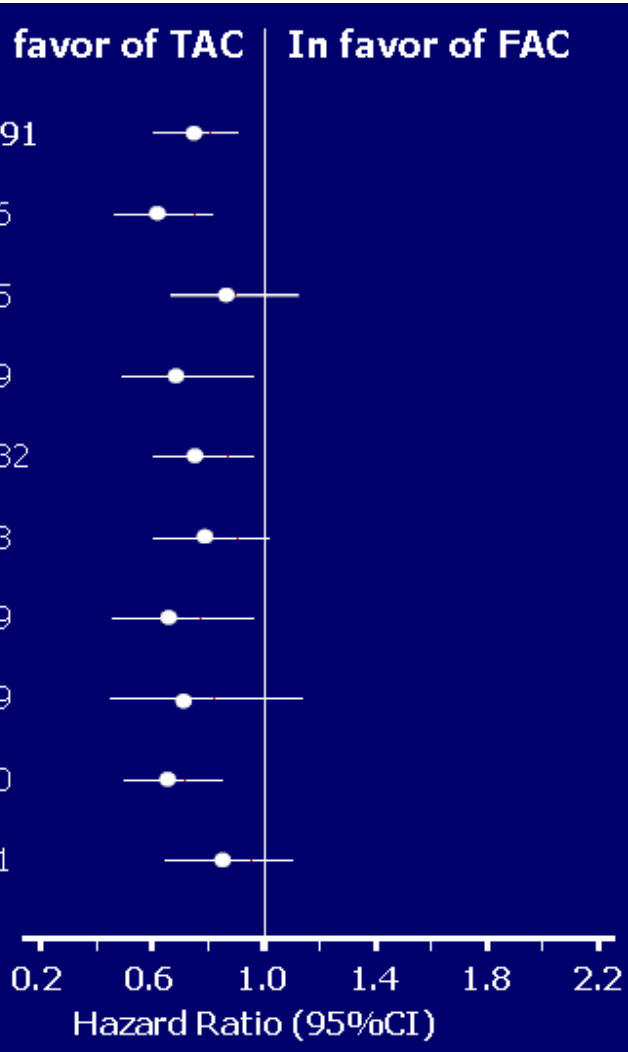
*Adjusted for nodal status

OS at a median 10y FU



DFS at pre-defined subgroups

Overall	**ITT Adjusted***	**0.74 (0.61 to 0.90)**	**1491**
Number of positive nodes	[1–3]	0.62 (0.46 to 0.82)	926
Number of positive nodes	[4+]	0.87 (0.67 to 1.12)	565
Hormonal Receptor status	Negative	0.69 (0.49 to 0.96)	359
Hormonal Receptor status	Positive	0.76 (0.60 to 0.96)	1132
HER2/NEU status	Negative	0.79 (0.61 to 1.01)	943
HER2/NEU status	Positive	0.66 (0.45 to 0.96)	319
HER2/NEU status	Unknown	0.71 (0.44 to 1.14)	229
Menopausal status	Pre-menopausal	0.65 (0.49 to 0.85)	830
Menopausal status	Post-menopausal	0.85 (0.65 to 1.11)	661



*Adjusted for nodal status

Conclusie

- Ook na 10 jaar betere DFS en OS na TAC therapie tov FAC bij N+ mammacarcinoom
- Geen onverwachte toxiciteit op langere termijn
- Toekomst: Ook taxaan bij N0 mammacarcinoom

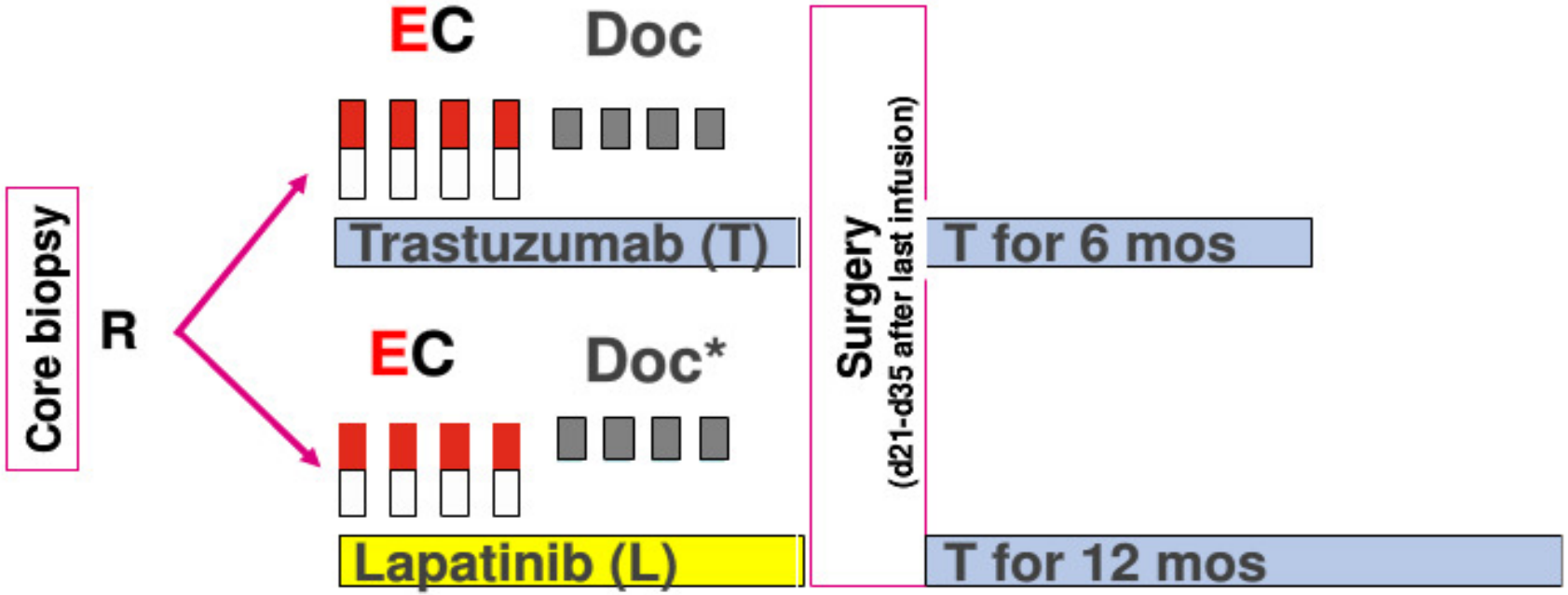
Geparquinto

LAPATINIB VS TRASTUZUMAB IN COMBINATION WITH NEOADJUVANT ANTHRACYCLINE-TAXANE-BASED CHEMOTHERAPY: PRIMARY EFFICACY ENDPOINT ANALYSIS OF THE GEPARQUINTO STUDY (GBG 44)

Untch M, Loibl S, Bischoff J, Eidtmann H, Kaufmann M, Blohmer JU, Hilfrich J, Strumberg D, Fasching P, Kreienberg R, Tesch H, Hanusch C, Gerber B, Rezai M, Jackisch C, Huober J, Kühn T, Nekljudova V, von Minckwitz G for the

Design

HER2-positive Study Design



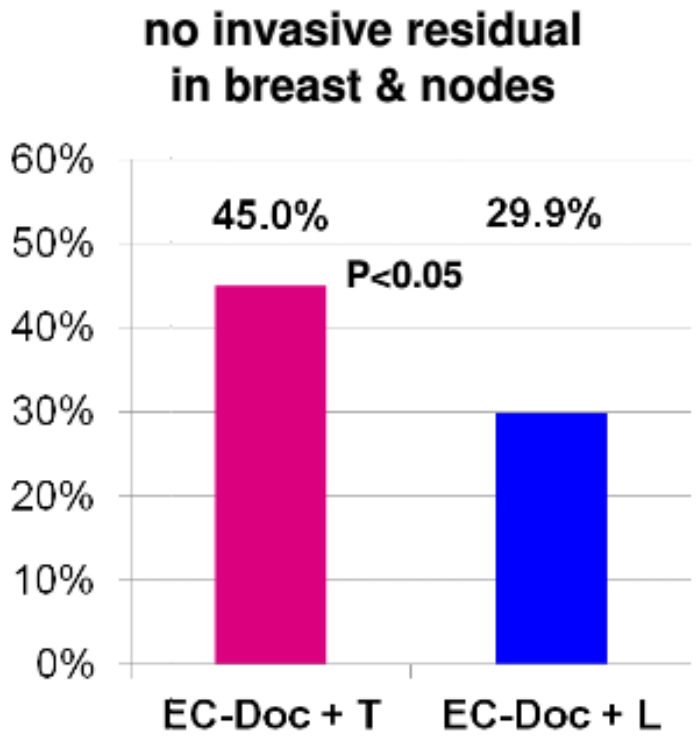
E: Epirubicin 90 mg/m²
C: Cyclophosphamide 600 mg/m²
Doc: Docetaxel 100mg/ m² *+ G-CSF

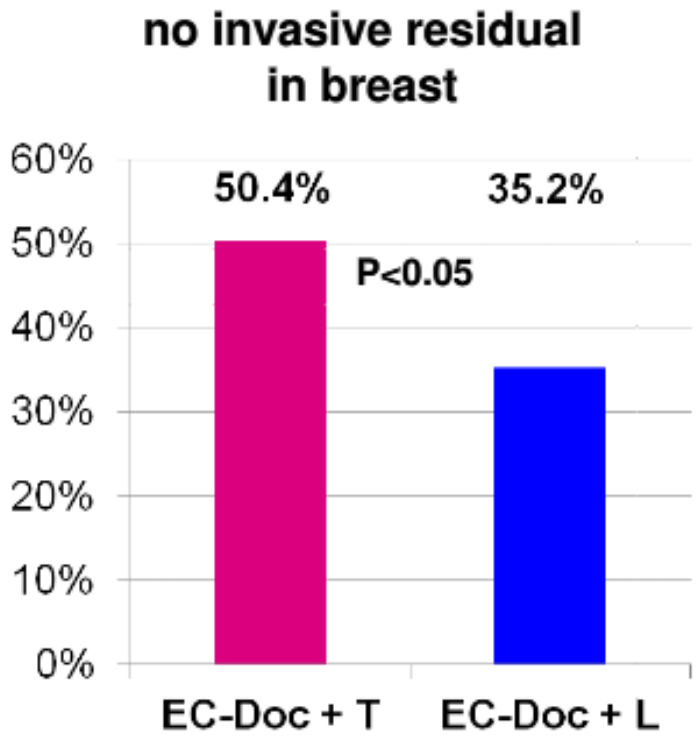
T: Trastuzumab 6 (8) mg/kg
L: 1250-1000 mg/ d p.o.
(all 3 week cycles)

pCR

San Antonio Breast Cancer Symposium - Cancer Therapy and Research Center at UT Health Science Center – December 8-12, 2010

pCR Rates According to Other Definitions



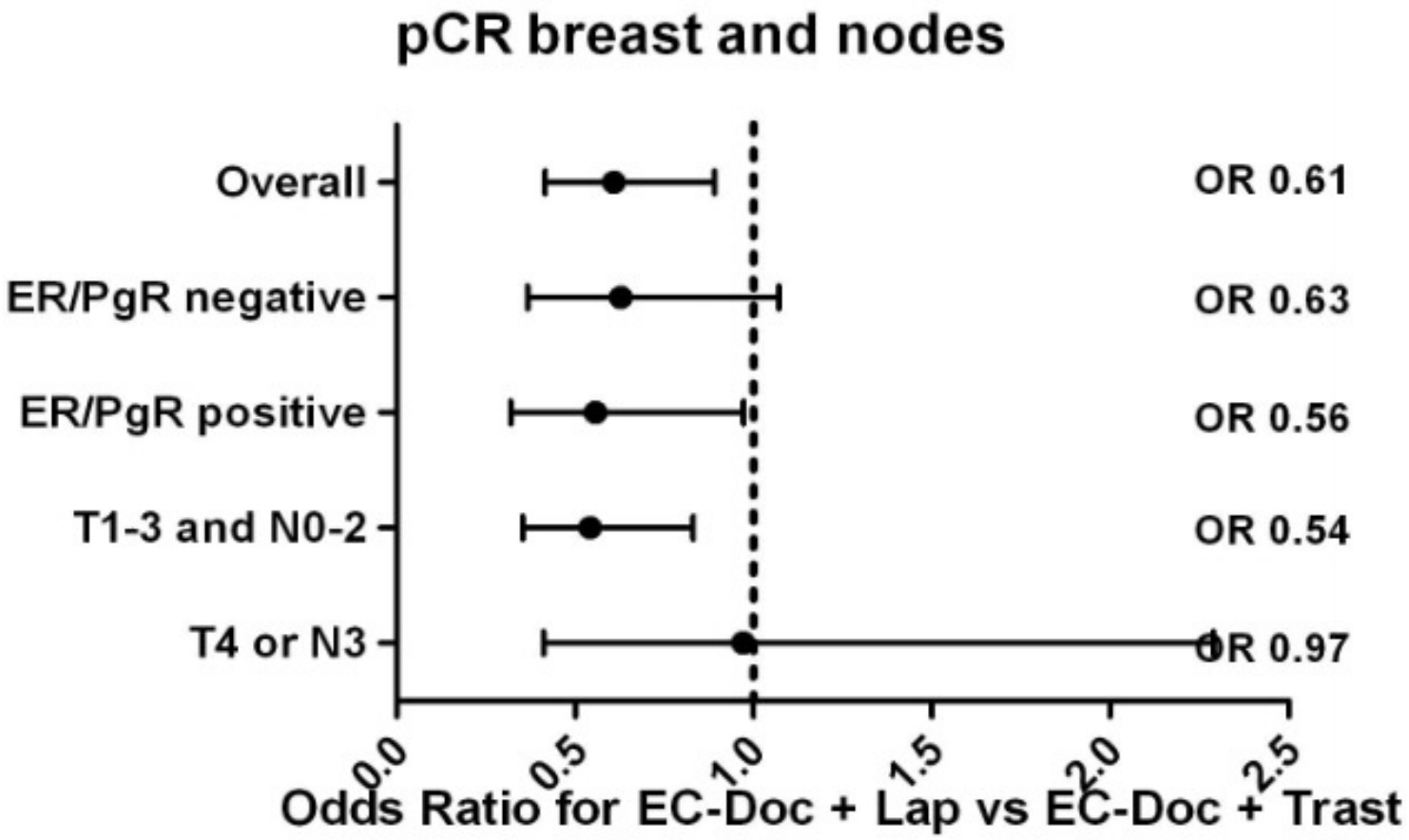


pCR according to subtype

San Antonio Breast Cancer Symposium - Cancer Therapy and Research Center at UT Health Science Center – December 8-12, 2010

pCR According to Subtypes

(predefined and stratified)



Conclusie

- Significant hogere pCR rate van 50% in de arm met trastuzumab
- Chemotherapie en lapatinib resulteerde in een pCR rate van 35%, waarschijnlijk deels door toxiciteit
- Lapatinib lijkt minder aantrekkelijk
- Geen veranderingen in beleid

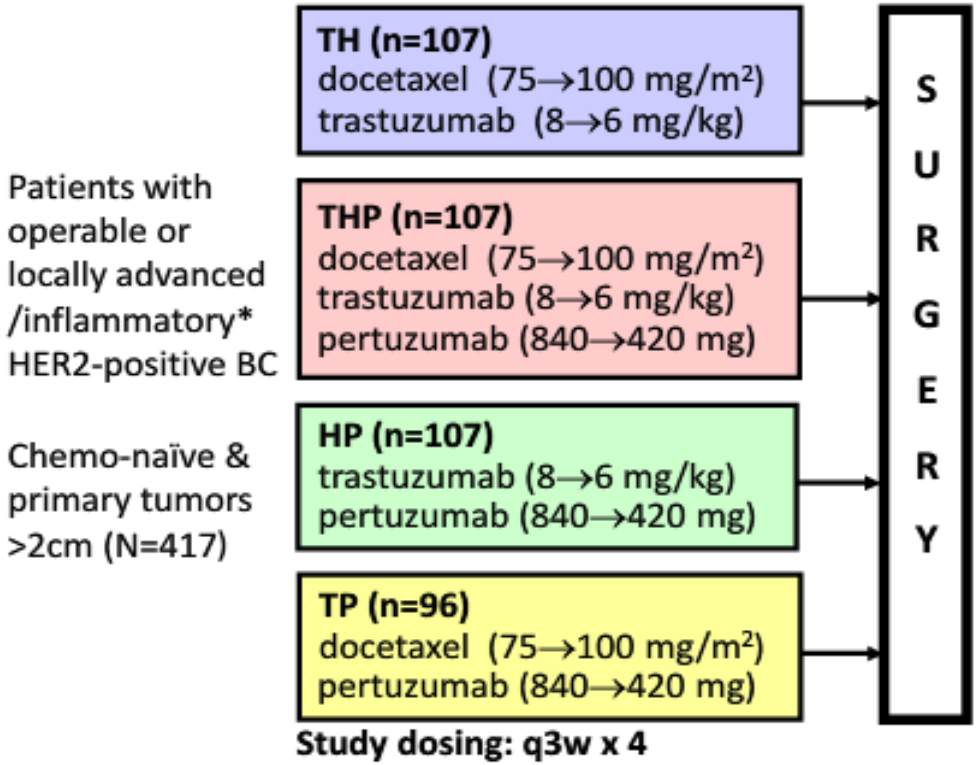
Neoadjuvant pertuzumab (P) and trastuzumab (H): Antitumor and safety analysis of a randomized phase II study ('NeoSphere')

L Gianni, T Pienkowski, Y-H Im, L Roman, L-M Tseng, M-C Liu,
A Lluch-Hernandez, V Semiglazov, T Szado, G Ross

on behalf of the 'NeoSphere' study investigators

Fase II study

NeoSphere: study design and objectives

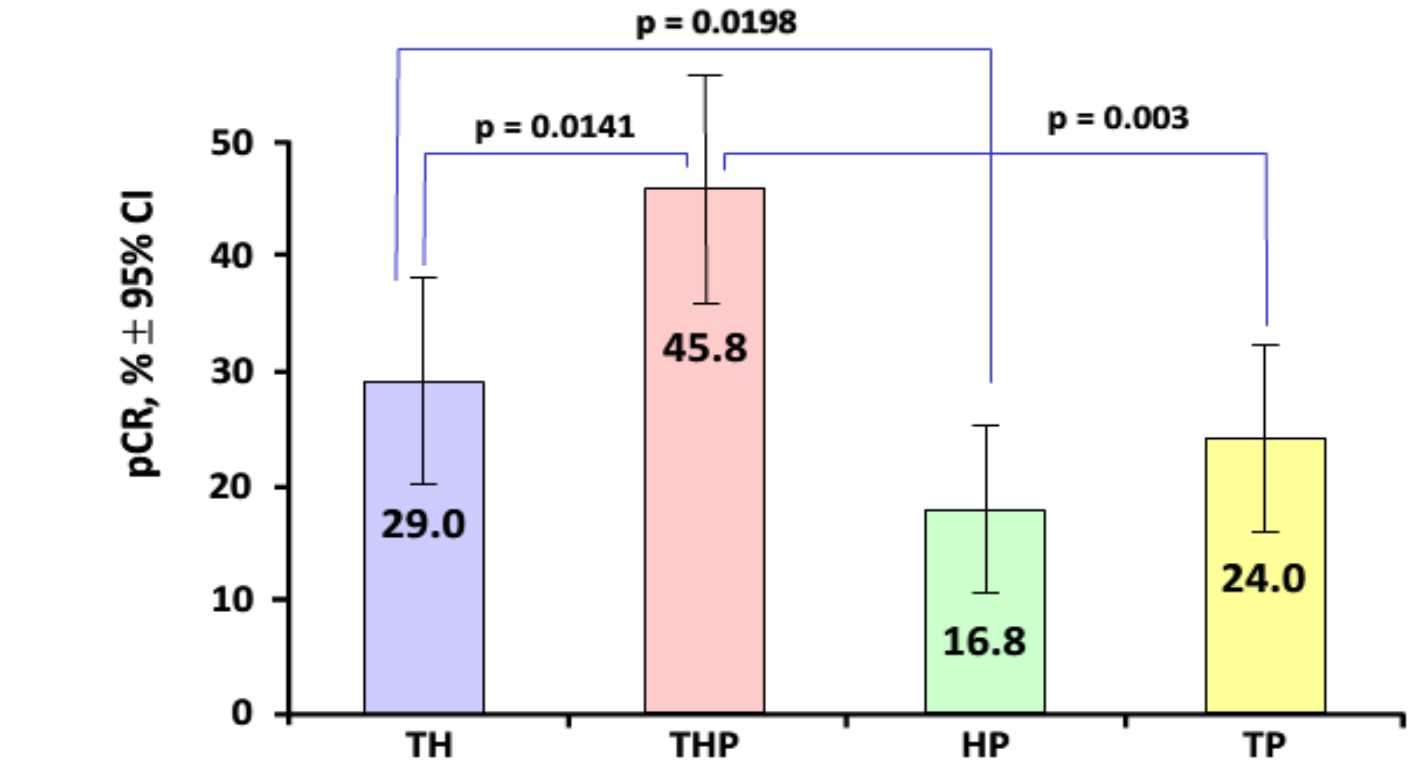


- **Phase II design**
- **Primary endpoint:**
  - comparison of pCR rates
    - TH vs THP
    - TH vs HP
    - THP vs TP
- **Secondary endpoints:**
  - Clinical response
  - DFS
  - Breast conservation rate
  - Biomarker evaluation

BC, breast cancer; FEC, 5-fluorouracil, epirubicin and cyclophosphamide
*Locally advanced=T2–3, N2–3, M0 or T4a–c, any N, M0; operable=T2–3, N0–1, M0; inflammatory = T4d, any N, M0
H, trastuzumab; P, pertuzumab; T, docetaxel

pCR

NeoSphere pCR rates: ITT population summary



H, trastuzumab; P, pertuzumab; T, docetaxel

Conclusie

- Significant hogere pCR rate (45.8%) met docetaxel, trastuzumab in combinatie met pertuzumab
- Substantieel antitumor effect met trastuzumab en pertuzumab zonder chemotherapie (pCR rate van 16.8%!)
- Therapie wordt goed verdragen

Discordance in hormone and HER2 receptor status in breast cancer during tumor progression

Linda Lindstrom, Eva Karlsson, Ulla Wilking, Lambert Skoog, Jonas Bergh

Dept of oncology and pathology, Karolinska Institut and University Hospital, Stockholm, Sweden

Results

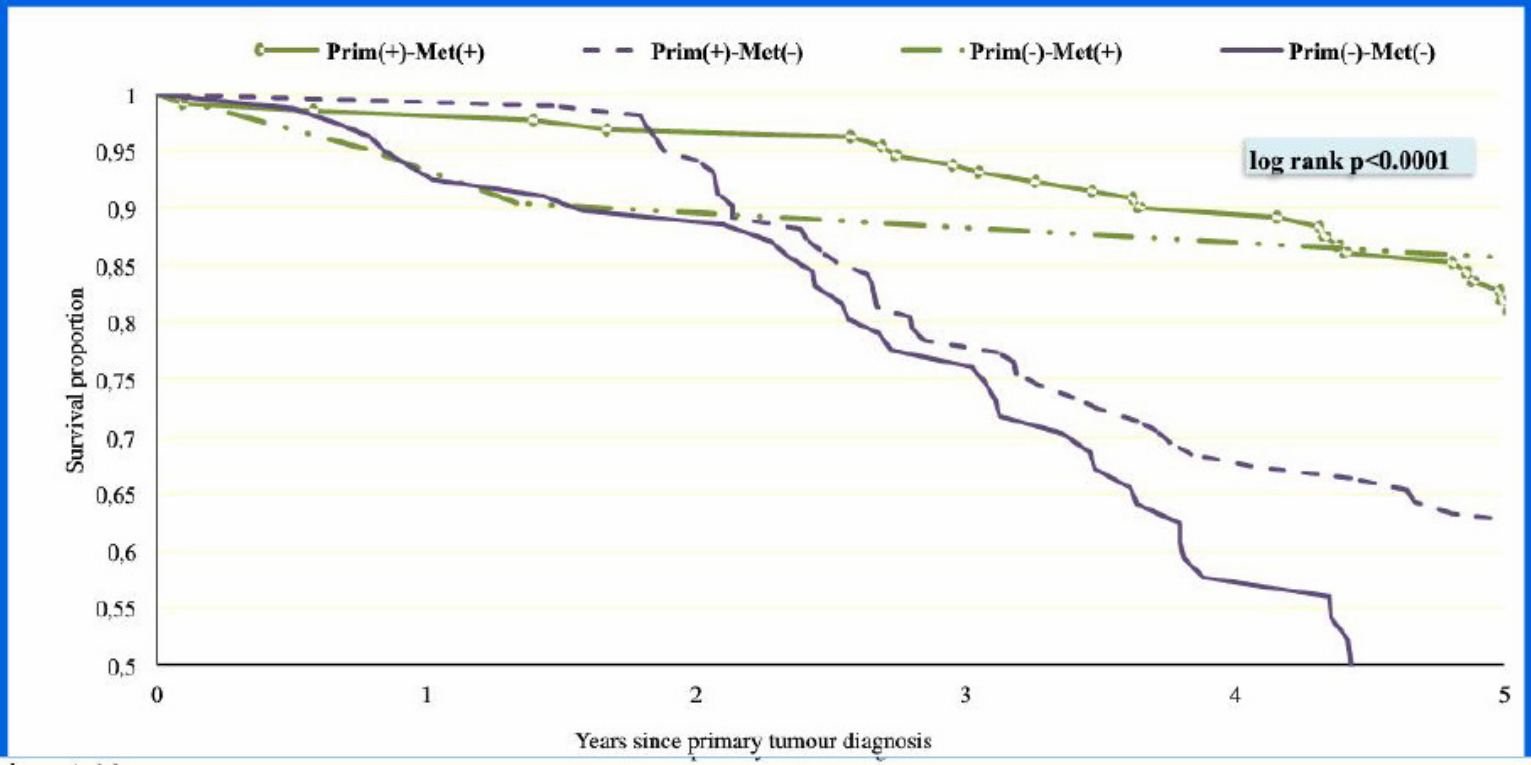
Intra-individual ER, PR and HER2 status in primary tumour and relapse

Intra-individual ER, PR and HER2 status in primary tumor and relapse				
Hormonal receptor and HER2	Local and systemic relapse		Systemic relapse	
Status	Number	Percent	Number	Percent
ER status				
Prim(+)/Rel(+)	202	44.0	131	39.1
Prim(+)/Rel(-)	121	26.4	103	30.7
Prim(-)/Rel(+)	31	6.7	21	6.3
Prim(-)/Rel(-)	105	22.9	80	23.9
Total number	**459**		**335**	
PR status				
Prim(+)/Rel(+)	92	21.1	53	16.2
Prim(+)/Rel(-)	157	35.9	129	39.4
Prim(-)/Rel(+)	21	4.8	14	4.3
Prim(-)/Rel(-)	167	38.2	131	40.1
Total number	**437**		**327**	
HER2 status				
Prim(+)/Rel(+)	25	21.2	18	18.4
Prim(+)/Rel(-)	8	6.8	6	6.1
Prim(-)/Rel(+)	4	3.4	4	4.1
Prim(-)/Rel(-)	81	68.6	70	71.4
Total number	**118**		**98**	

*Cut-off value of 0.05 fmol/µg DNA and 10%, for monoclonal antibody based biochemical and IHC/ICC methods, respectively

Receptorstatus and OS

Overall breast cancer survival from primary tumor diagnosis to death or censoring

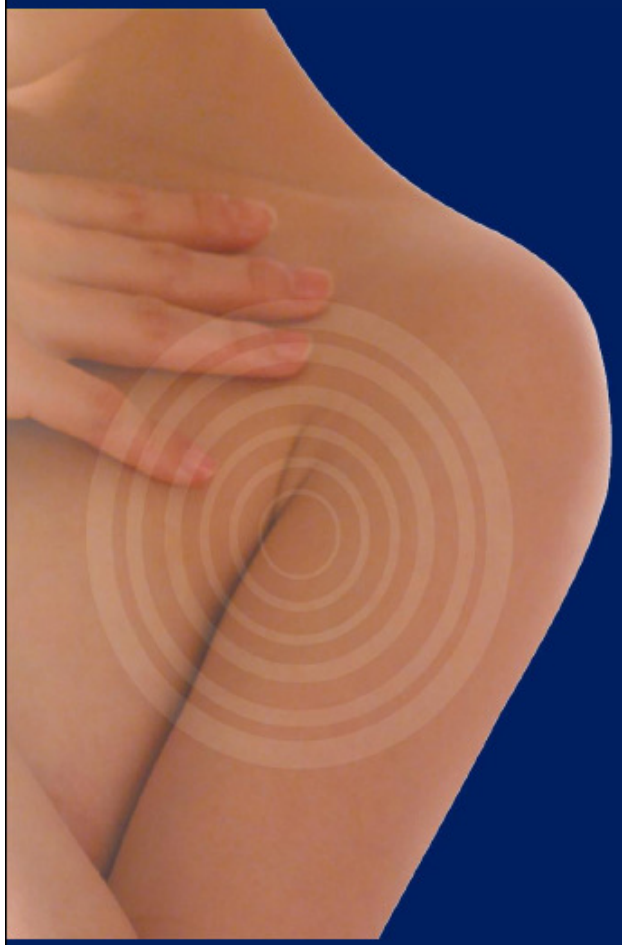


Numbers at risk						
Prim(+)-Met(+)	131	130	128	124	121	112
Prim(+)-Met(-)	103	102	100	96	79	65
Prim(-)-Met(+)	21	20	19	17	17	17
Prim(-)-Metl(-)	80	79	73	64	51	30

Linda Lindström & Jonas Bergh SABCS 2010

Conclusie

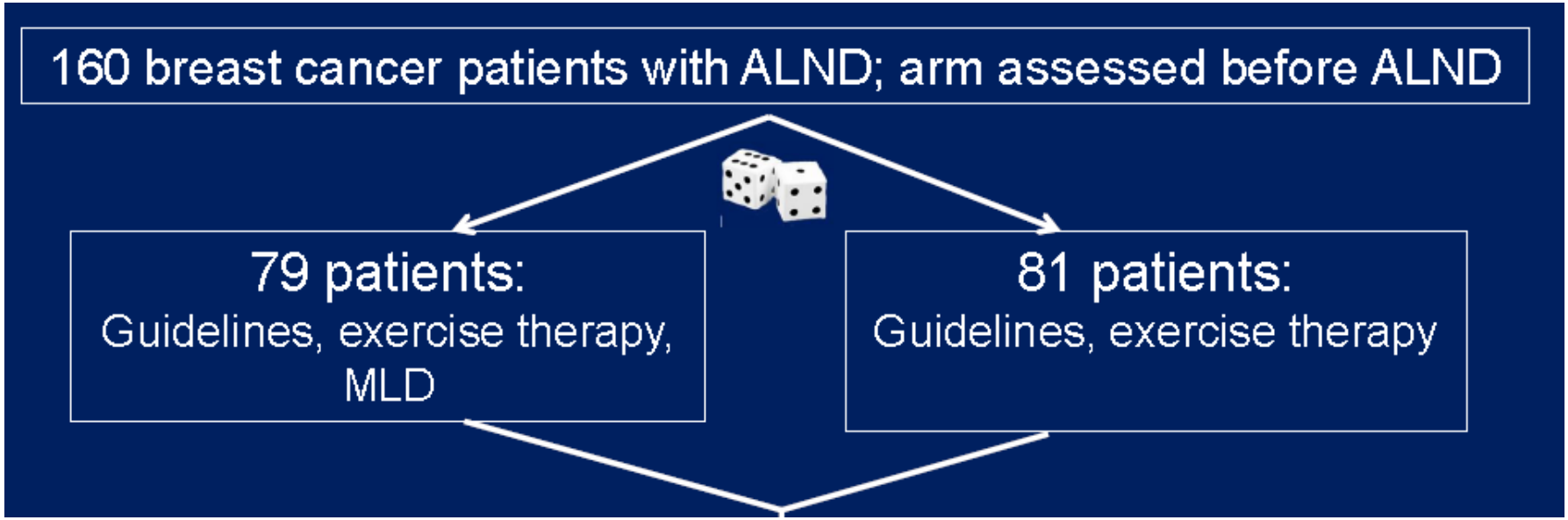
- 1/3 recidieven heeft een veranderde hormoonstatus tov primaire tumor
- 1/10 recidieven heeft een veranderde HER2 status tov de primaire tumor
- Mogelijke oorzaken
  - Cytologie geen histologie verkregen!!
  - Receptor status primair niet goed bepaald
  - Sampling error



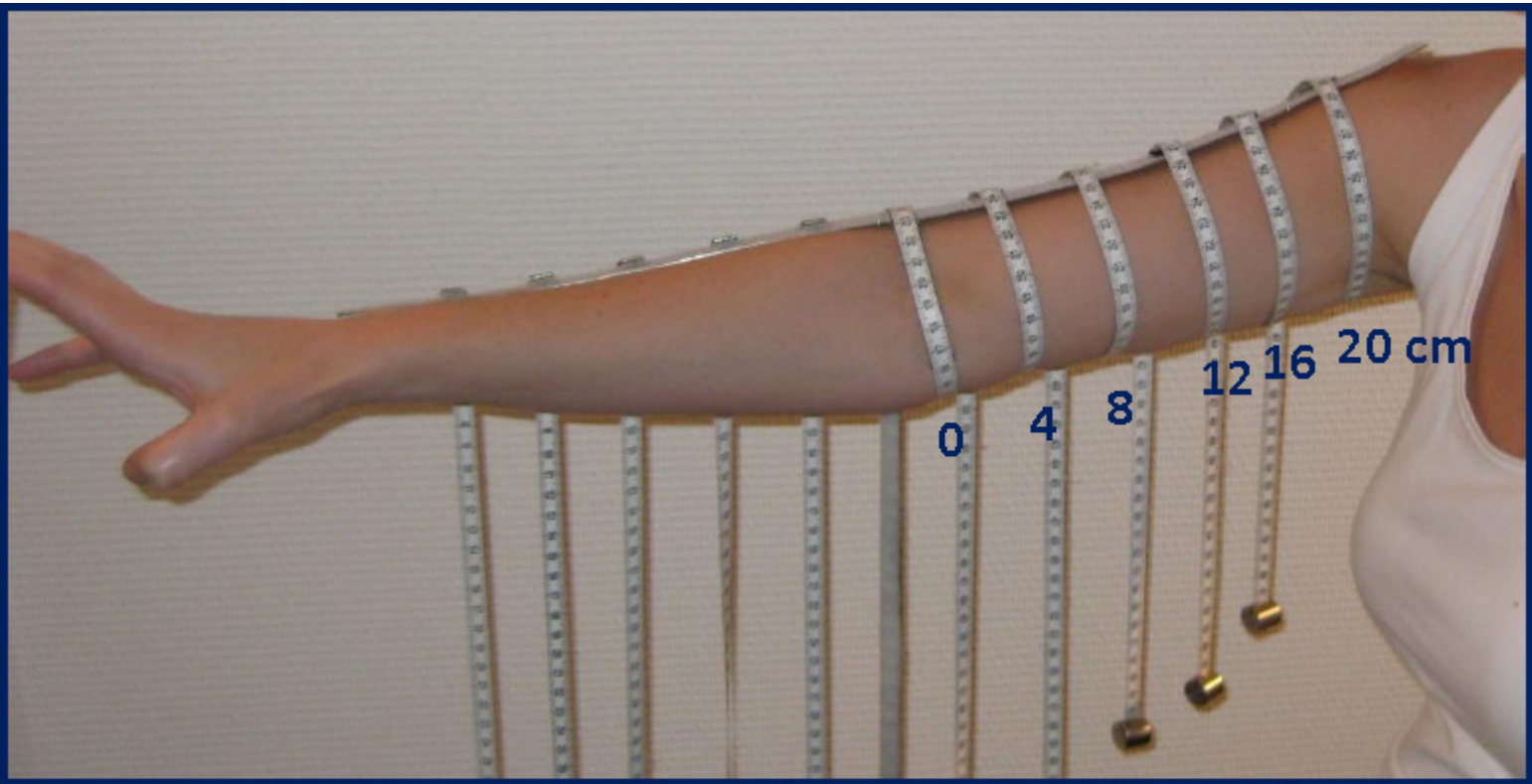
Is manual lymph drainage effective to prevent breast cancer-related lymph edema?

N Devoogdt, MR Christiaens, I Geraerts, S Truijen, A Smeets, K Leunen, P Neven, M Van Kampen
Department of Physiotherapy and Multidisciplinary Breast Clinic, University Hospitals Leuven, Belgium

Design

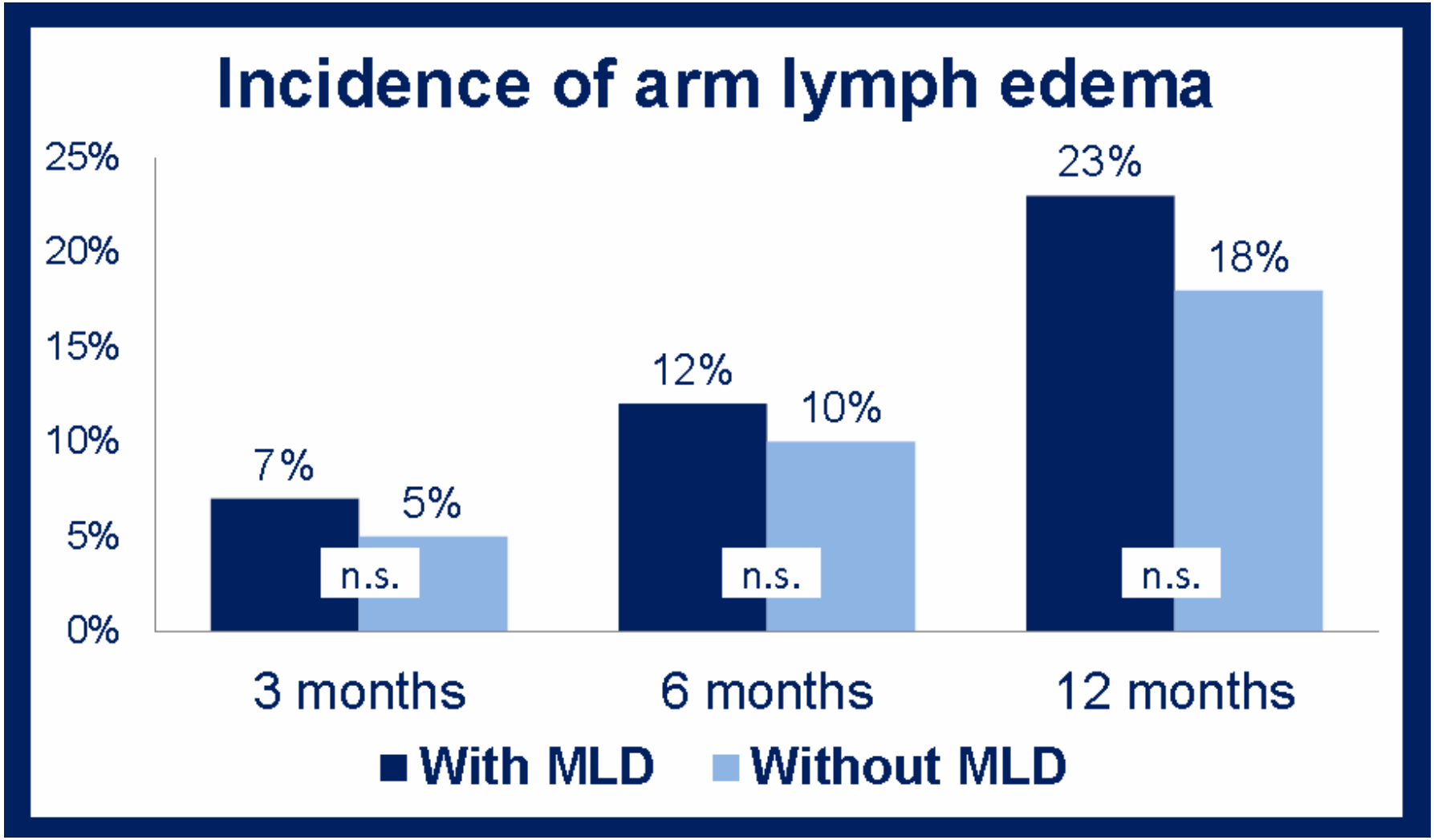

160 breast cancer patients with ALND; arm assessed before ALND
79 patients:
Guidelines, exercise therapy, MLD
81 patients:
Guidelines, exercise therapy

Primary endpoint



Incidence of arm lymph edema, defined as:
2.0 cm or more increase at two adjacent points of pre-surgical value

Results


Incidence of arm lymph edema
25%
20%
15%
10%
5%
0%
7%
5%
n.s.
12%
10%
n.s.
23%
18%
n.s.
3 months
6 months
12 months
With MLD
Without MLD

Results

With and without MLD: comparable results

- Time to develop lymph edema (Log Rank p=n.s.)
- Increase arm volume (p=n.s.)
- Mental and physical health-related quality of life (p=n.s.)
- Functioning problems related to arm lymph edema (p=n.s.)

Conclusie

- Manuele lymfedrainage na okselklierdissectie bij mammacarcinoom is niet effectief ter preventie van lymfe-oedeem van de arm op korte termijn

- Patienten met okselklierdissectie wordt wel geadviseerd zelf oefeningen te doen ter preventie van lymfe-oedeem

Adjuvant Treatment With Zoledronic Acid in Stage II/III Breast Cancer. The AZURE Trial (BIG 01/04)

Coleman RE, Thorpe H, Cameron D, Dodwell D, Burkinshaw R, Keane M, Gil M, Houston SJ, Grieve RJ, Barrett-Lee PJ, Ritchie D, Davies C & Bell R.
on behalf of the AZURE Investigators.

The University Of Sheffield.

UNIVERSITY OF LEEDS

NHS
National Institute for Health Research

Design

AZURE: Study Design

Accrual September 2003 - February 2006

3,360 Breast Cancer Patients Stage II/III

R

Standard therapy

Standard therapy + Zoledronic acid 4 mg

6 doses Q3-4 weeks	8 doses Q 3 months	5 doses Q 6 months

Months 6 30 60

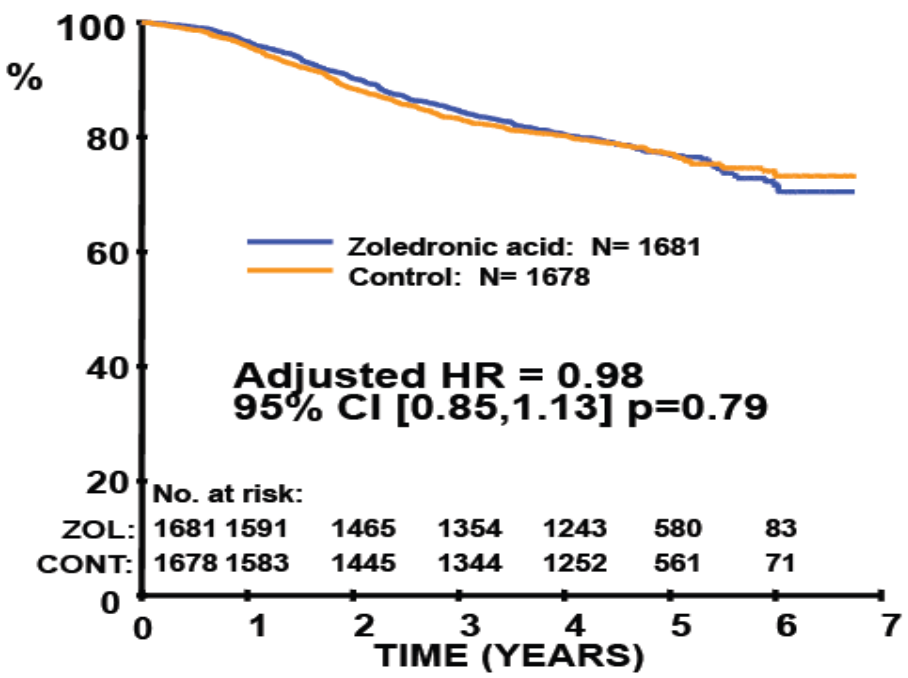
Zoledronic acid treatment duration 5 years

Countries	Centres	Patients
UK	123	2710
Eire	10	247
Australia	28	226
Spain	8	107
Portugal	1	32
Thailand	2	25
Taiwan	2	13

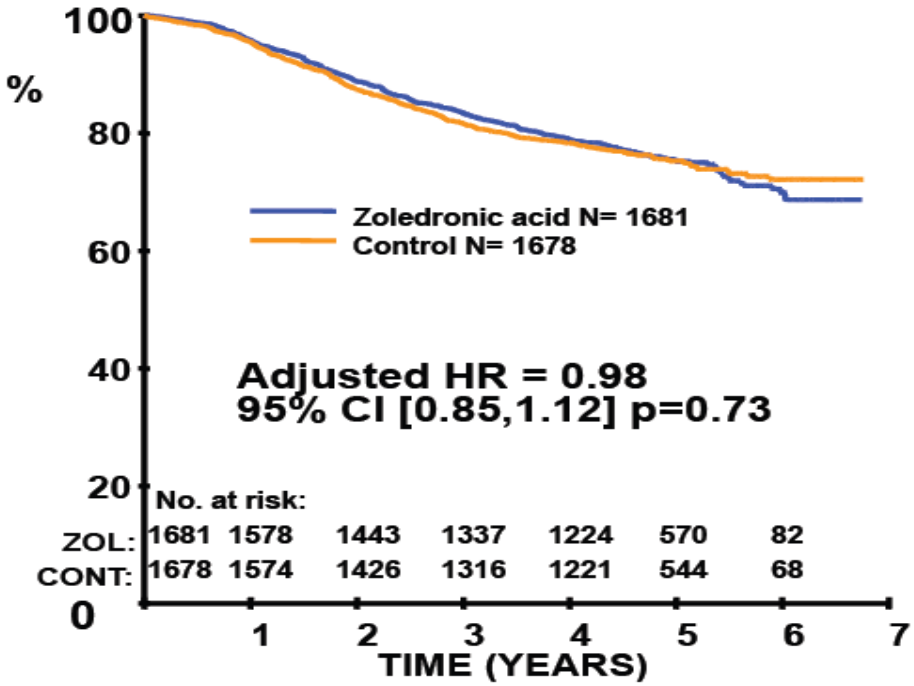
Results

AZURE: Disease (DFS) and Invasive Disease Free Survival (IDFS)

DFS

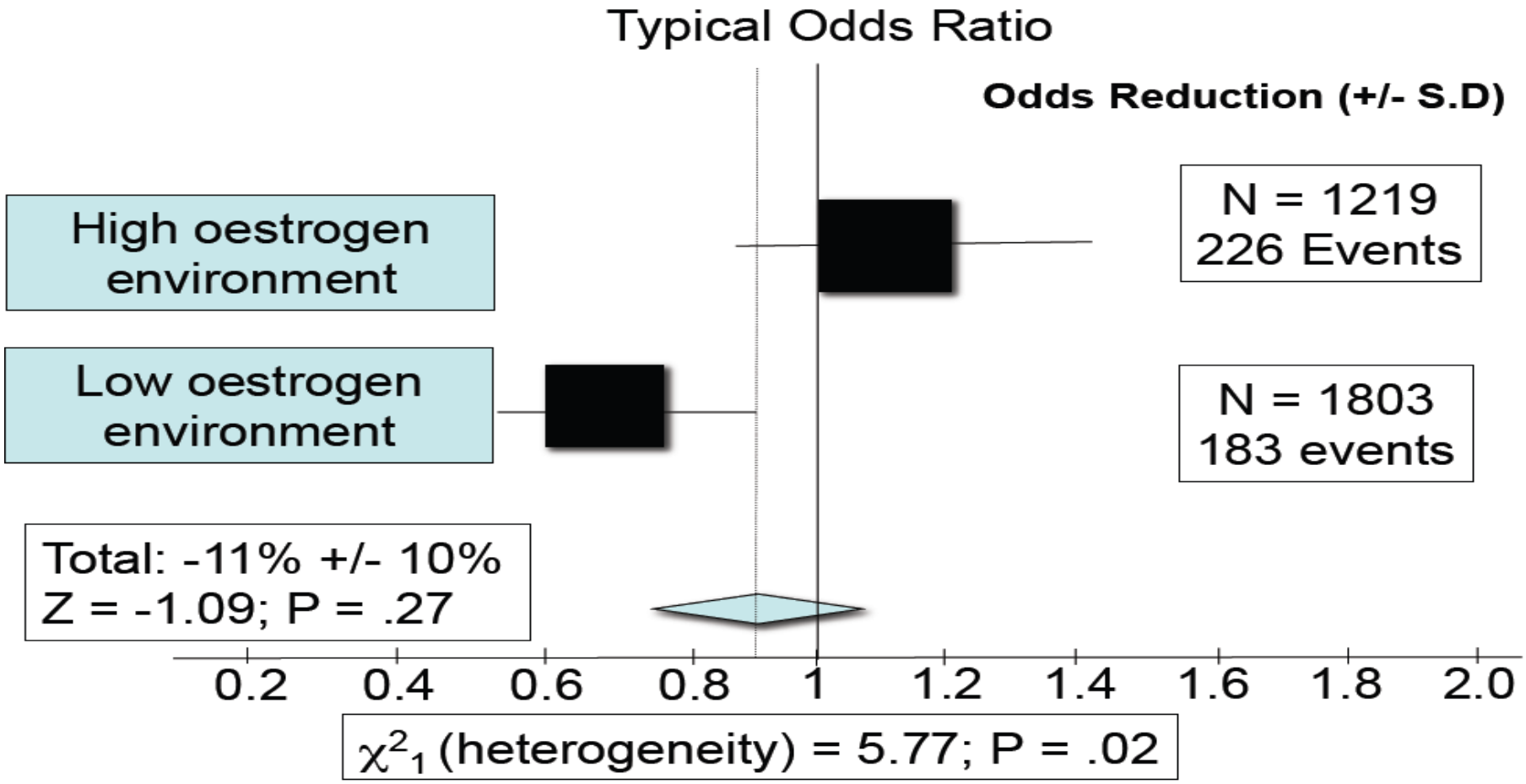


IDFS



Comparison DFS AZURE-ABCSG XII

DFS Comparison Between AZURE and ABCSG XII



Conclusie

- Toevoeging van zolendronaat aan adjuvante chemotherapie verbetert de DFS niet
- Mogelijke verklaring: hoge oestrogeen niveau's bij pre-menopausale patienten in deze studie itt ABCSG XII (meer gosereline)
- Theorie: lage oestrogeen spiegels-> oesteopenie/osteoporose->homing van tumorcellen in ontkalkt bot-> later activiteit en vorming van metastasen