IBZ
Interdisziplinäres
Brustzentrum München

Pojektgruppe Mammakarzinom
20.01.2011

Metastasiertes Mammakarzinom: Neues aus San Antonio

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Endokrine Therapie MBCA

- S1-6: Tamoxifen und RAD001
- S1-3: Fulvestrant in der first-line

S1-6: Tamoxifen und RAD001

TAMRAD: a GINECO randomized phase II trial of everolimus in combination with tamoxifen versus tamoxifen alone in patients with hormone receptor–positive, HER2-negative metastatic breast cancer with prior exposure to aromatase inhibitors

Thomas BACHELOT, Céline BOURGIER, Claire CROPET, Jean-Paul GUASTALLA, Jean-Marc FERRERO, Claire LEGER-FALANDRY, Patrick SOULIE, Jean-Christophe EYMARD, Marc DEBLED, Dominique SPAETH, Eric LEGOUFFE, Thierry DELOZIER, Claude EL KOURI and Jean CHIDIAC

GINECO

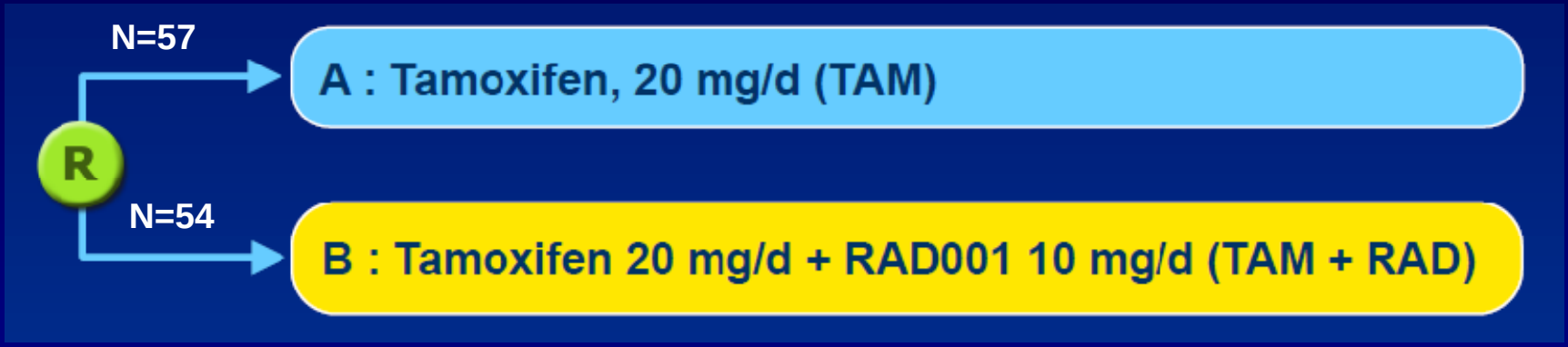
Everolimus (RAD001)

- Oraler mTOR-Inhibitor
- Phase I/II, neoadjuvant
- Zulassung für Nierenzellkarzinom

TAMRAD-Studie

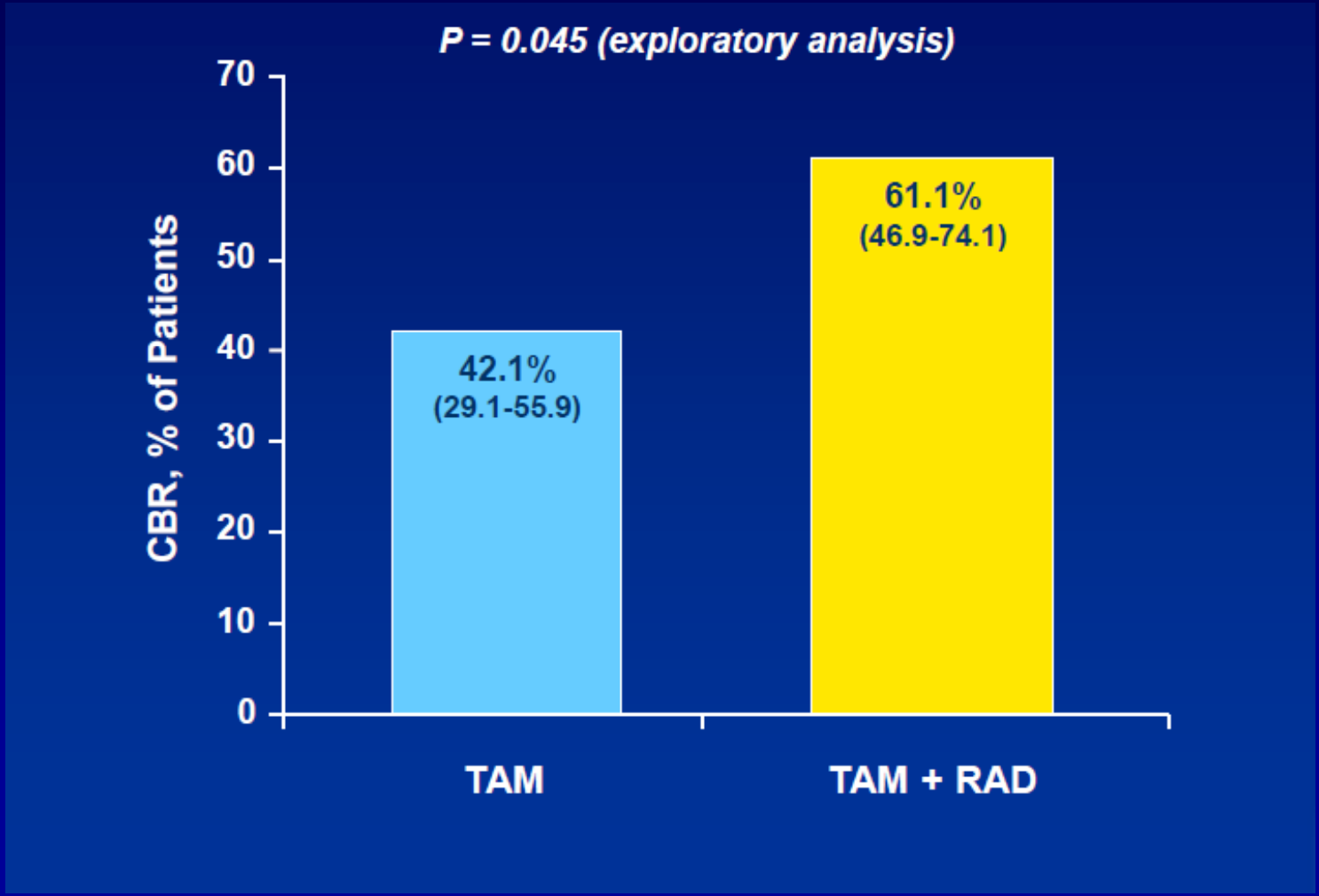
- Randomisierte Phase II (111 Pat.)
- Postmenopausale Patientinnen mit MBCA und vorheriger Aromatasehemmereinnahme
- HR positiv,HER2 negativ
- früheres TAM in der Adjuvans erlaubt
- frühere CTX erlaubt

TAMRAD-Protokoll



- **Stratifizierung: primäre oder sekundäre Hormonresistenz**
  - **primär: Progress unter AI (adj. oder < 6 Mon. metast.)**
  - **sekundär: späterer Progreß (> 6 Mon)**
- **Endpunkte:**
  - **primär: CBR (CR+PR+SD)**
  - **sekundär: TTP, OAS, Toxizität**

Clinical Benefit Rate

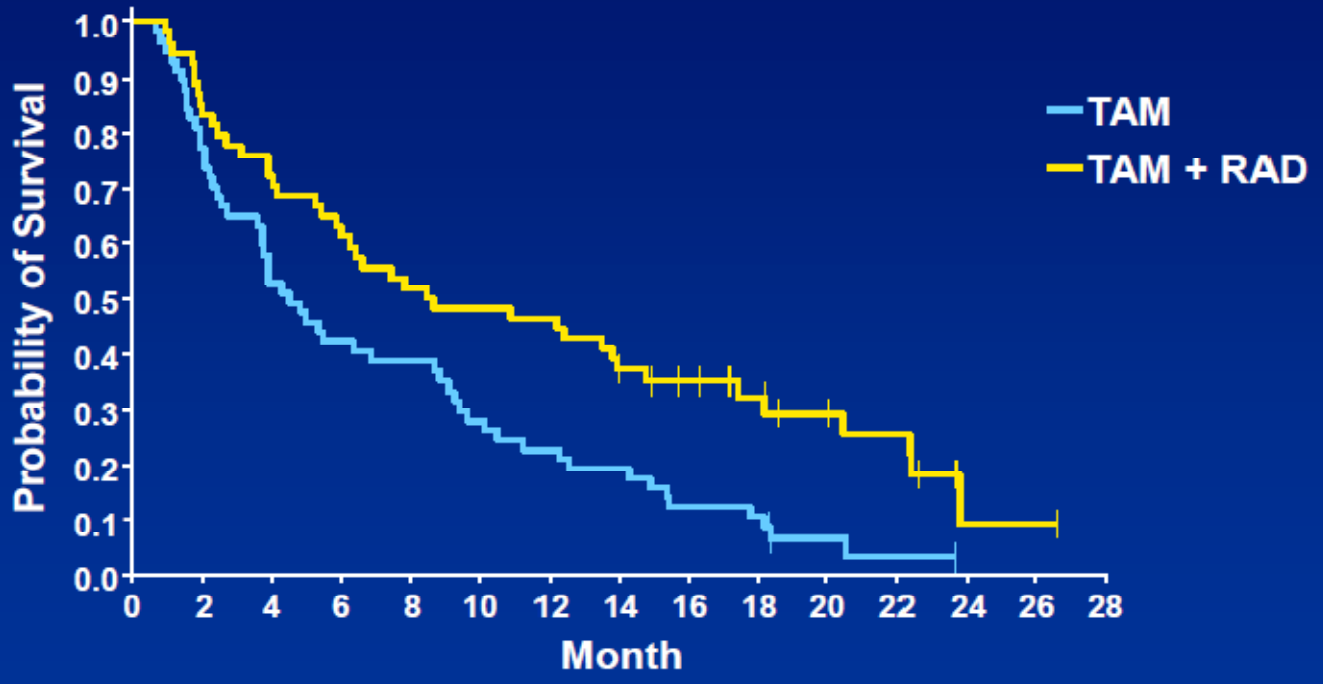


Time to Progression

Time to Progression

TAM: 4.5 mo.
TAM + RAD: 8.6 mo.

Hazard Ratio (HR) = 0.53; 95% CI (0.35-0.81)
Exploratory log-rank: *P* = 0.0026



Patients at risk															
TAM + RAD: n =	54	45	39	34	28	26	25	19	16	12	9	7	1	1	0
TAM : n =	57	44	30	24	22	16	13	11	7	6	2	1	0	0	0

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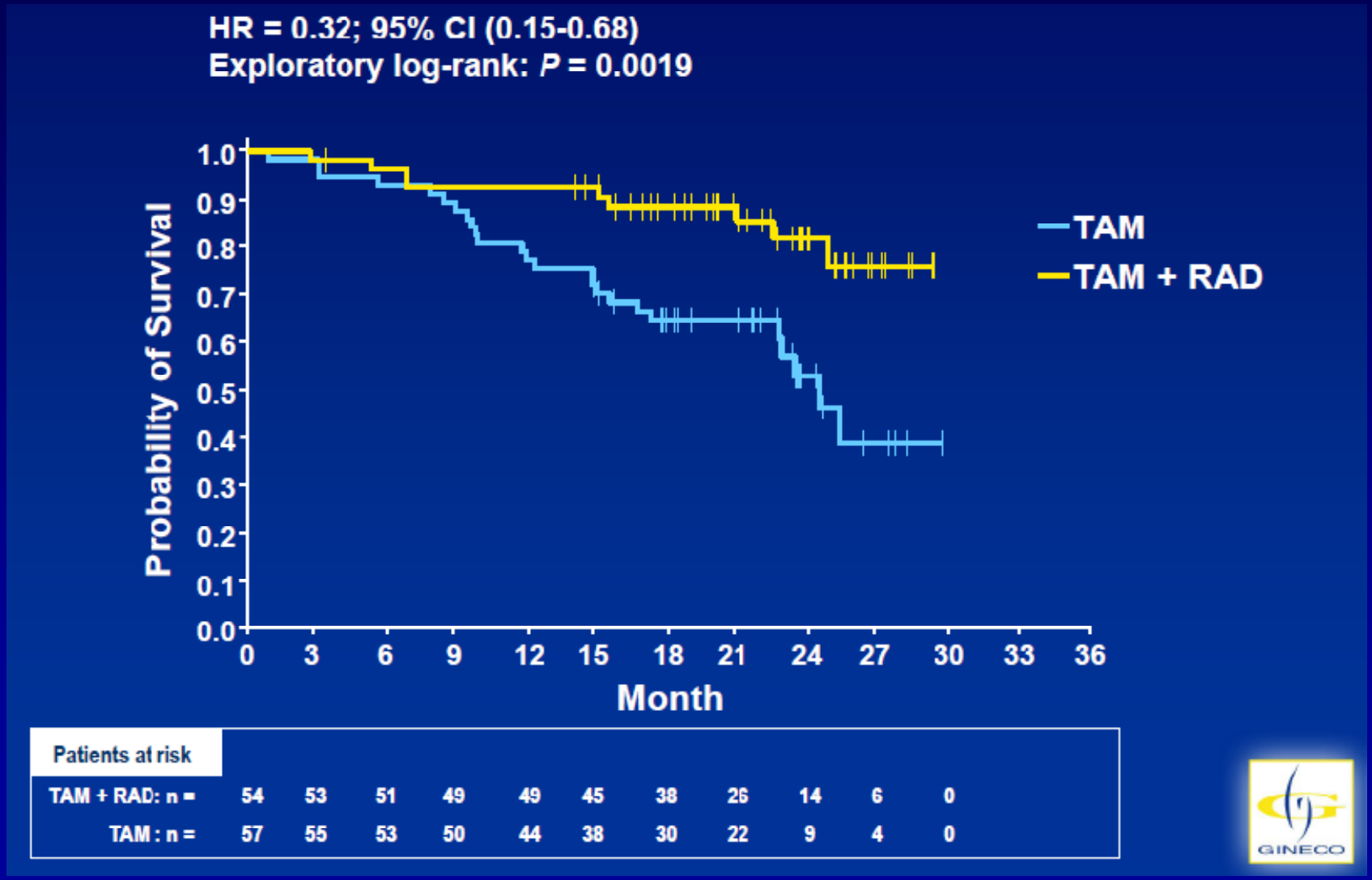
Overall Survival

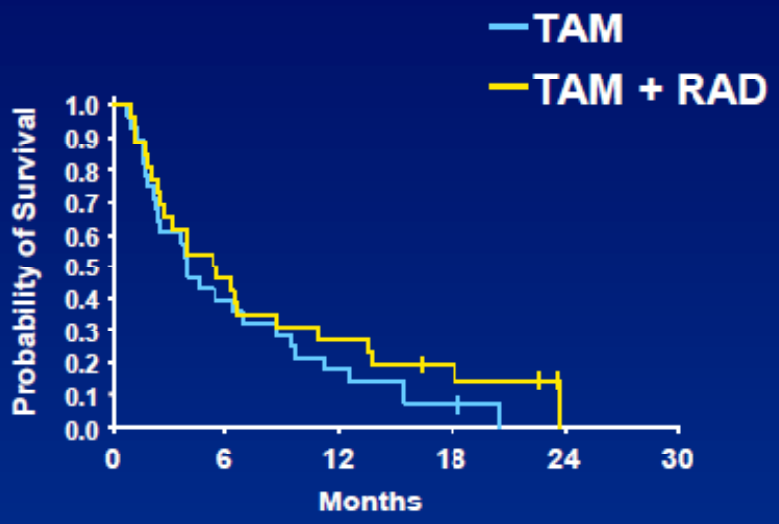


Toxizität

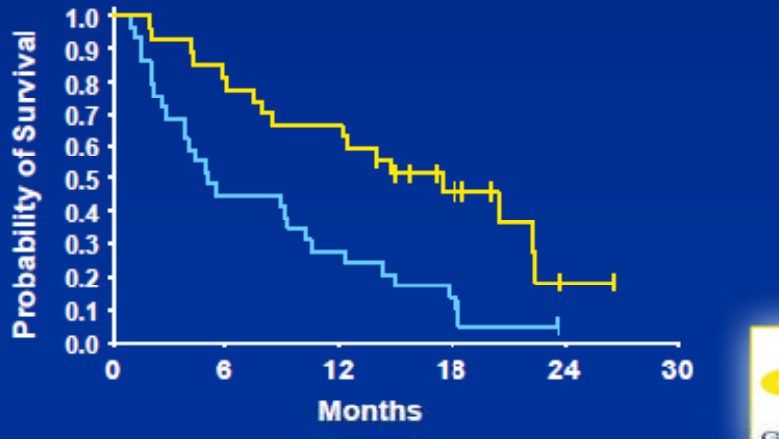
Incidence, n (%)	TAM n = 57		TAM + RAD n = 54	
Grade	Any	3/4	Any	3/4
Most Common Adverse Events (AE)				
Fatigue	30 (52.6)	6 (10.5)	40 (74.1)	3 (5.6)
Stomatitis	4 (7.0)	0	28 (51.9)	6 (11.1)
Rash	3 (5.3)	1 (1.8)	21 (38.9)	3 (5.6)
Anorexia	10 (17.5)	2 (3.5)	24 (44.4)	5 (9.3)
Diarrhea	5 (8.8)	0	21 (38.9)	1 (1.9)
Nausea	19 (33.3)	0	18 (33.3)	2 (3.7)
Vomiting	7 (12.3)	2 (3.5)	9 (16.7)	0
Pneumonitis	2 (3.5)	2 (3.5)	9 (16.7)	1 (1.9)
Thromboembolic	4 (7.0)	4 (7.0)	7 (13.0)	3 (5.6)
Pain	48 (84.2)	11 (19.3)	42 (77.8)	5 (9.3)
Dose reduction due to AE	0 (0)		15 (28)	
Treatment discontinuation due to AE	4 (7.0)		3 (5.6)	

TTP und Art der Hormonresistenz

- **Primary hormone resistance (n = 54)**
  - TAM: 3.9 mo.
  - TAM + RAD: 5.4 mo.
  - *HR = 0.74 (0.42-1.3)*



- **Secondary hormone resistance (n = 56)**
  - TAM: 5.0 mo.
  - TAM + RAD: 17.4 mo.
  - *HR = 0.38 (0.21-0.71)*



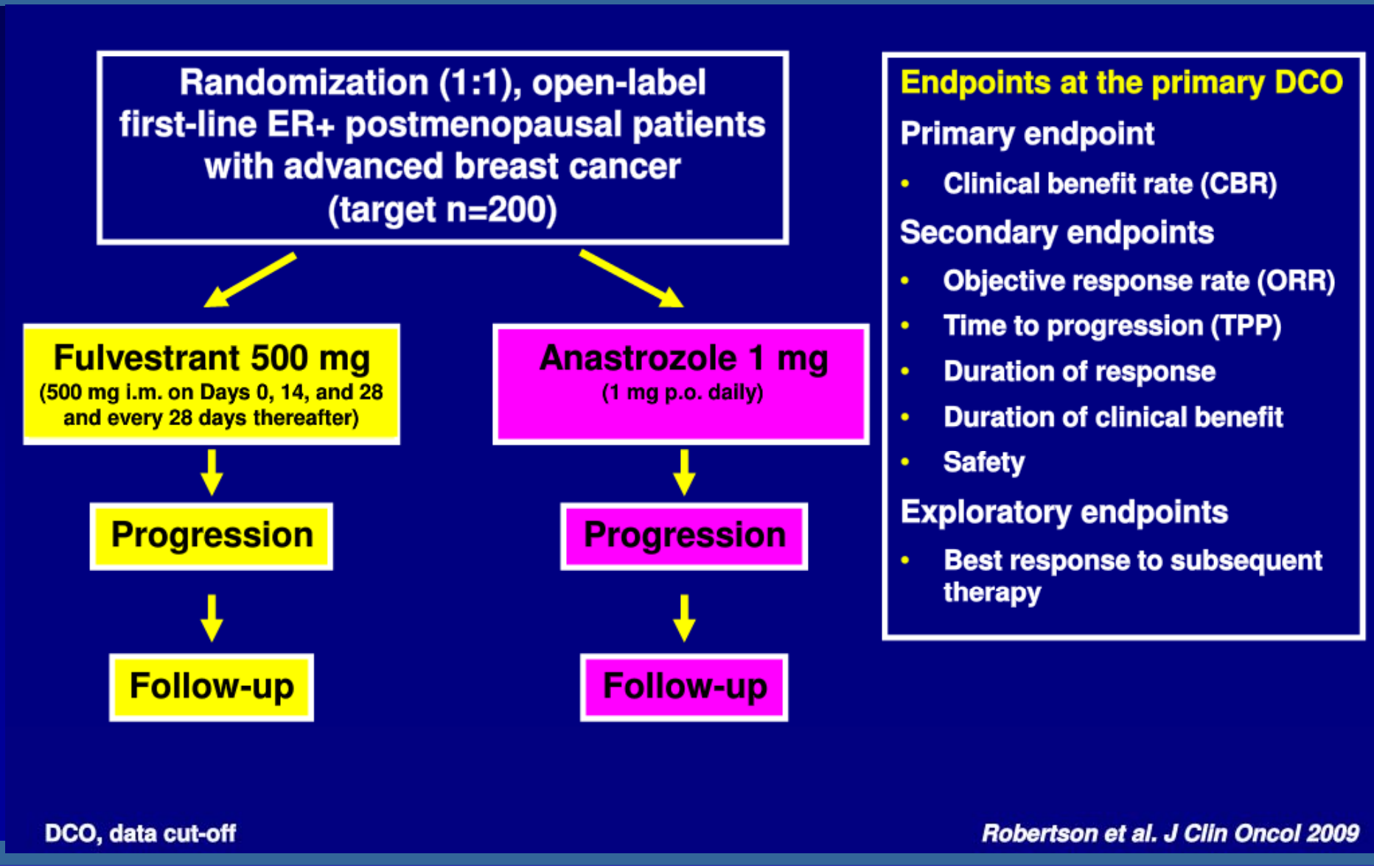
GINECO

S1-3: Fulvestrant in der first-line

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, Antonio Llombart-Cussac, Janusz Rolski, David Feltl, John Dewar, Laura Emerson, Andrew Dean, Matthew J. Ellis

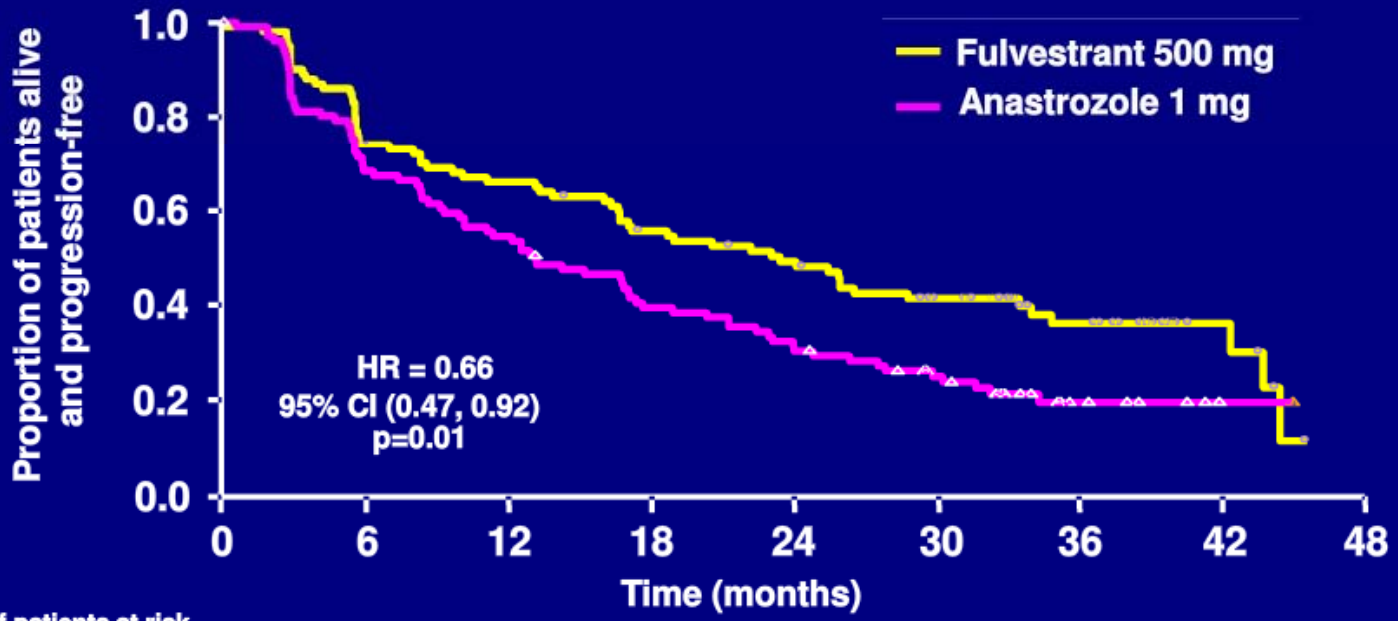
FIRST-Studie



DCO, data cut-off

Robertson et al. J Clin Oncol 2009

Update TTP



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

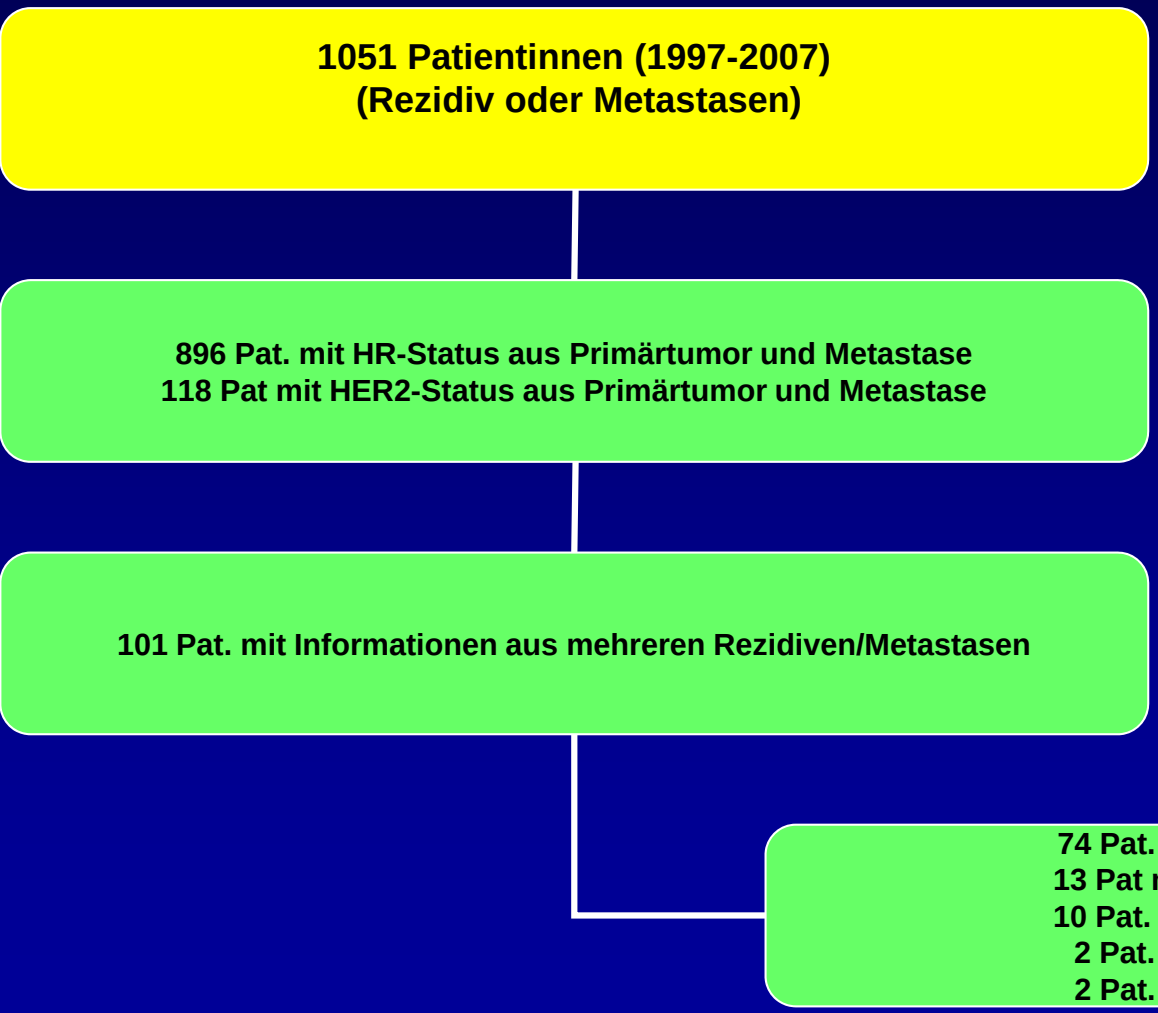
After primary DCO, progression was determined by investigator opinion

Response unter nachfolgender endokrinen Therapie

	Number (%) of patients	
	Fulvestrant 500 mg n=102	Anastrozole 1 mg n=103
Number of patients who progressed	63	79
Patients who have received a subsequent endocrine breast cancer therapy	34	50
Complete response	0	0
Partial response	3 (8.8)	7 (14.0)
Total responders	3 (8.8)	7 (14.0)
SD ≥24 weeks	11 (32.4)	14 (28.0)
Total with clinical benefit	14 (41.2)	21 (42.0)
SD <24 weeks	10 (29.4)	16 (32.0)
Progressive disease	3 (8.8)	8 (16.0)
Not evaluable	7 (20.6)	5 (10.0)

Histologie und Tumorprogression

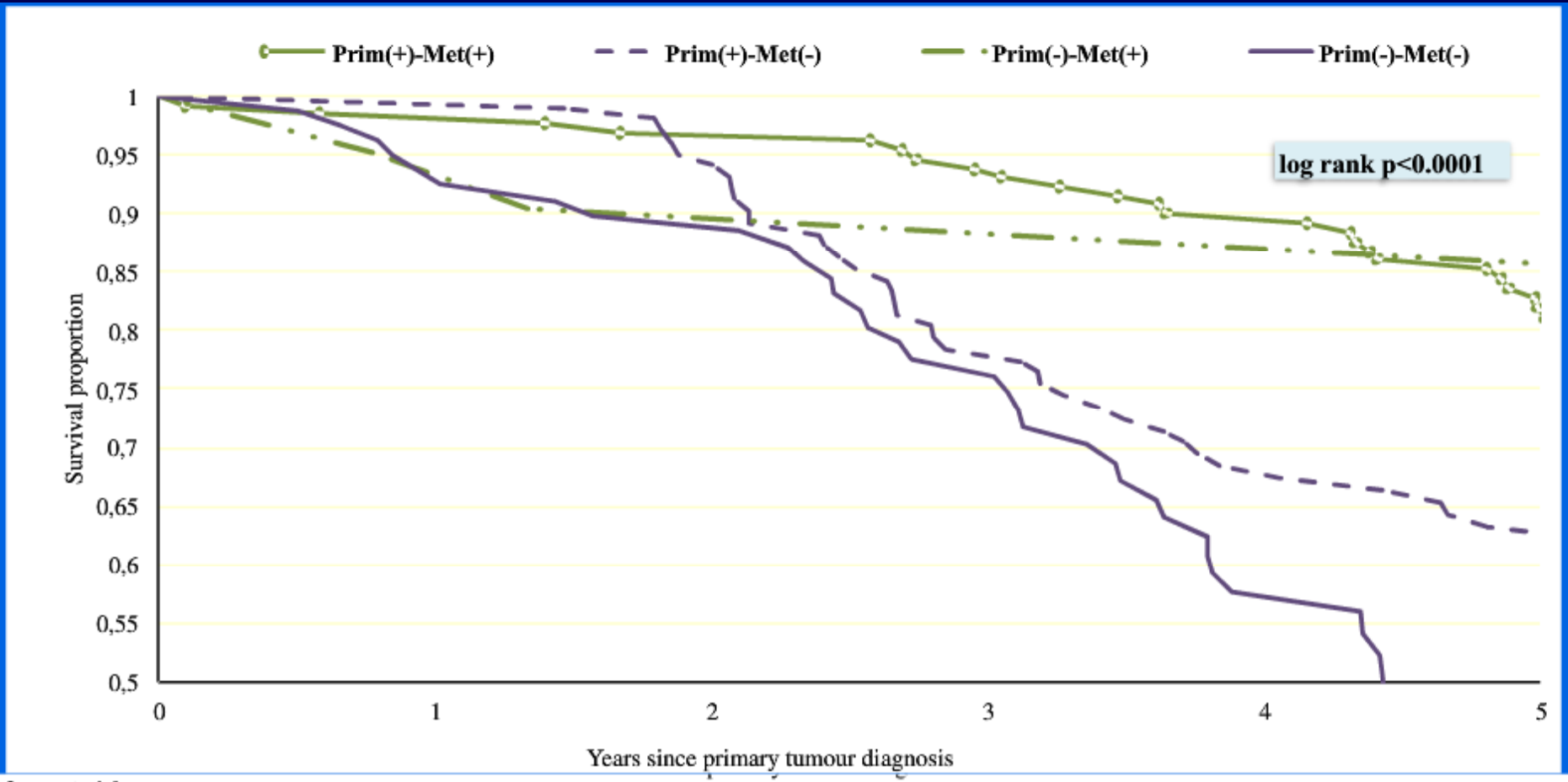
Karolinska-Kohorte



Ändert sich der Hormonstatus und der Her2-Status im Laufe der Tumrprogression ?

Hormonal receptor and HER2 Status	Local and systemic relapse Number	Percent
ER status		
Prim(+)/Rel(+)	202	44.0
Prim(+)/Rel(-)	121	26.4
Prim(-)/Rel(+)	31	6.7
Prim(-)/Rel(-)	105	22.9
Total number	**459**	
PR status		
Prim(+)/Rel(+)	92	21.1
Prim(+)/Rel(-)	157	35.9
Prim(-)/Rel(+)	21	4.8
Prim(-)/Rel(-)	167	38.2
Total number	**437**	
HER2 status		
Prim(+)/Rel(+)	25	21.2
Prim(+)/Rel(-)	8	6.8
Prim(-)/Rel(+)	4	3.4
Prim(-)/Rel(-)	81	68.6
Total number	**118**	

OAS und ER-Diskordanz



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

ER-Status im Vgl. zu erstem Rezidiv

Intra-individual ER status at relapse (only individuals with information on two or more relapse sites included)		
ER status change	Number of patients	Percent
Stable positive	34	33.7
Stable negative	38	37.6
Positive to negative	11	10.9
Negative to positive	12	11.9
Heterogeneity	6	5.9
	101	100

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Vielen Dank für Ihre Aufmerksamkeit!