Med. Klinik für Onkologie und Hämatologie
Charité Campus Mitte
Universitätsmedizin Berlin

Mamma-Ca: Therapeutische Chancen

K. Possinger

special article

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Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007

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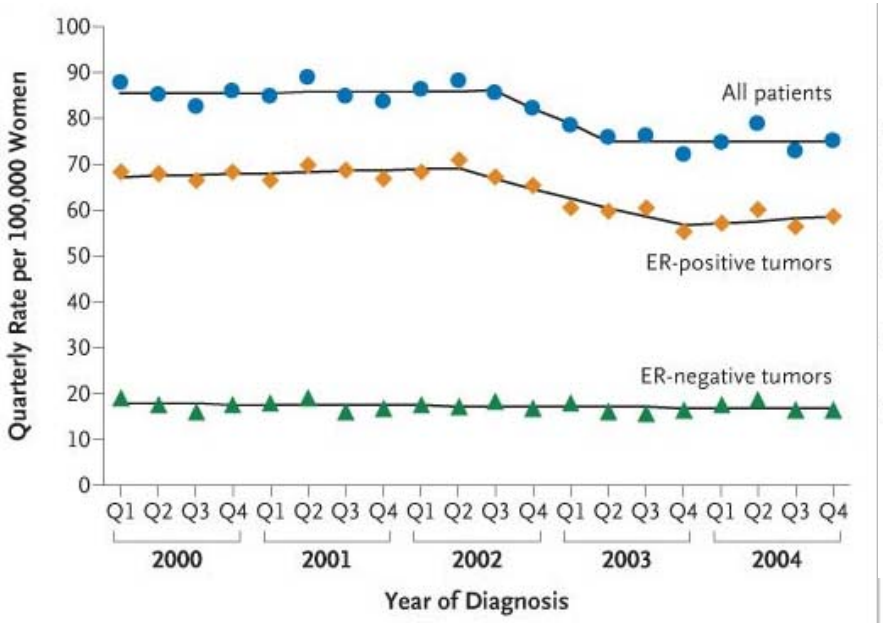
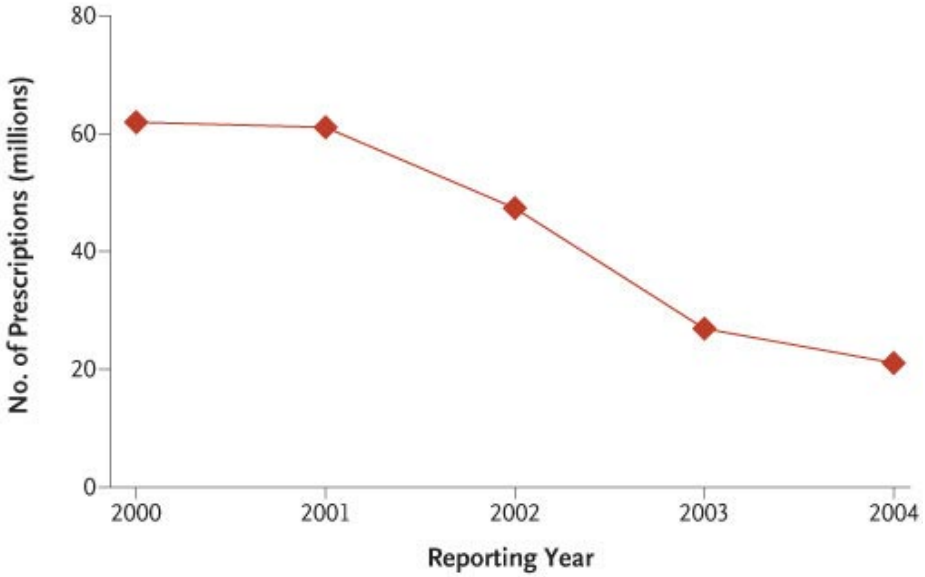
Brustkrebsinzidenz USA

SEER-Analyse

Brustkrebs-Inzidenz 50 – 69J



Verschreibung von HET



Inzidenzreduktion 2002 – 2003:
Alle 7%; ER+: 12%

Ravdin PM NEJM 356(16): 1670-1674 (2007)

Brustkrebsinzidenz USA

Mögliche Gründe für Reduktion ER+ Mammakarzinome

1. Reduktion der HET:
   - Verminderte Stimulation präexistenter Karzinome ?
   - Reduktion der Inzidenz ?

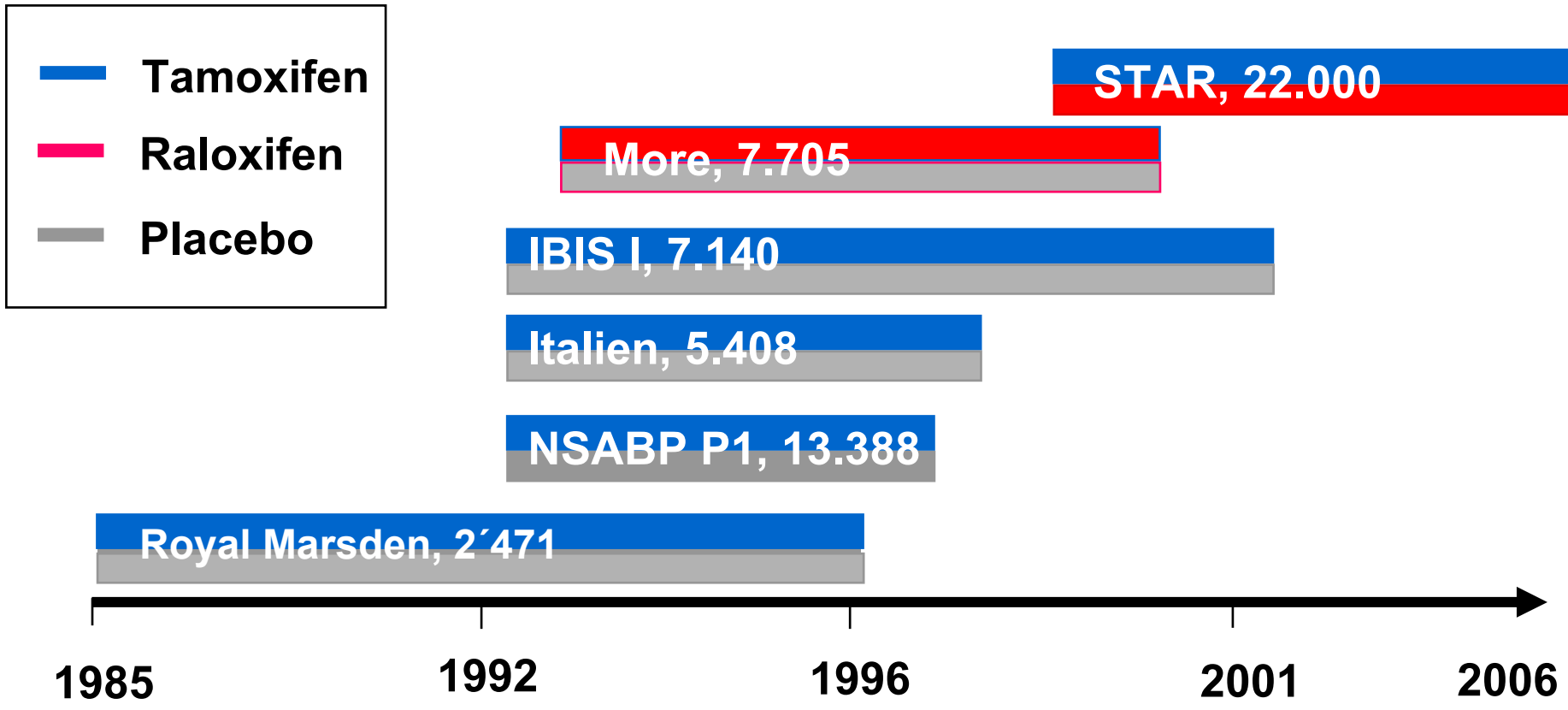
2. Reduktion der Mammographiehäufigkeit in der Altersgruppe 50 – 69 Jahre zwischen 2000 – 2003: 3,2%

3. Präventionseffekt durch Tamoxifen oder Raloxifen ?

Ravdin PM NEJM 356(16): 1670-1674 (2007)

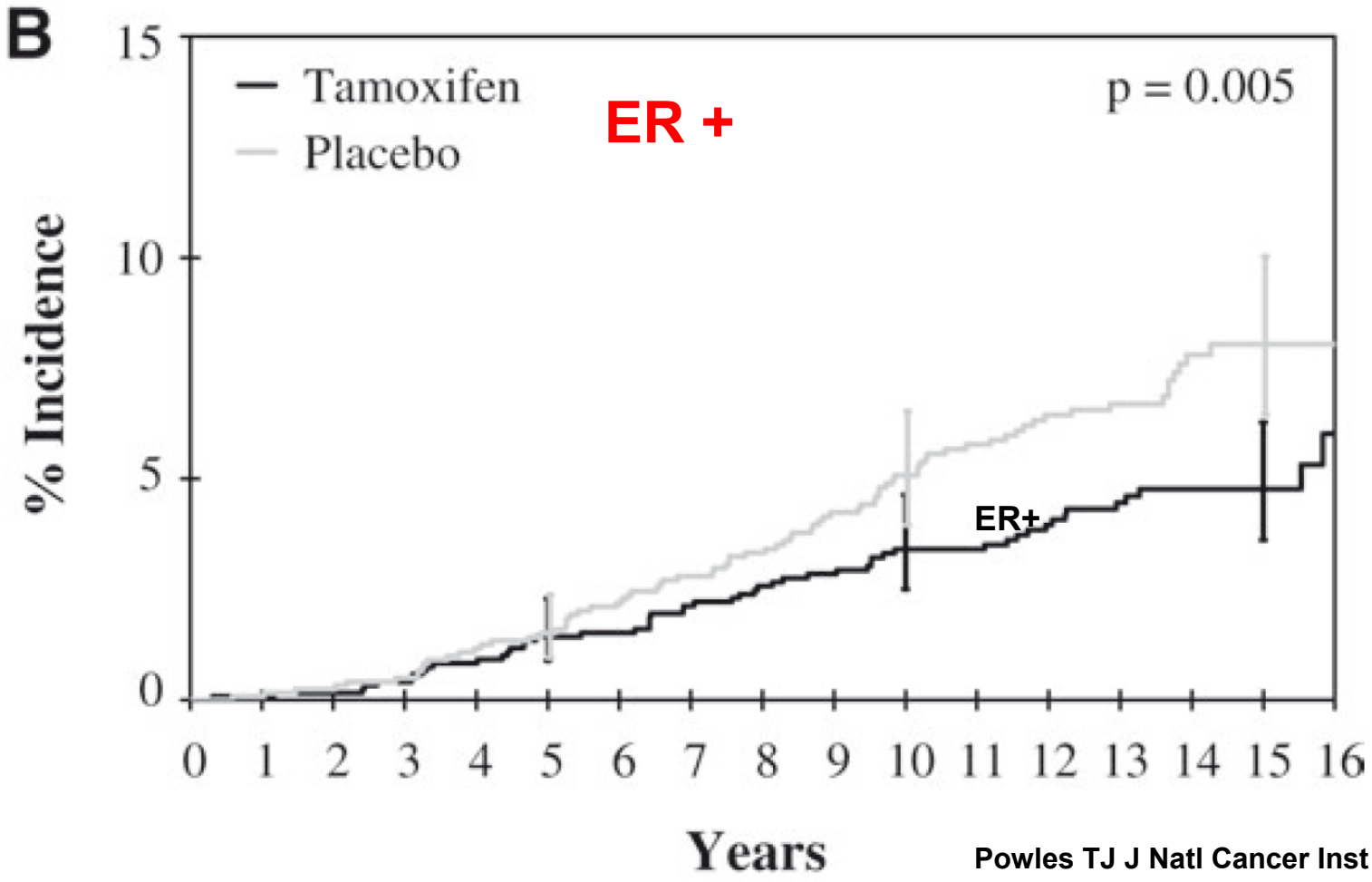
Brustkrebs: Update 2007

Präventionsstudien



Präventionsstudien: Royal Marsden (Tam vs Placebo)

Alter: 30 – 70 J., n = 2494, F-u: 20 Jahre;

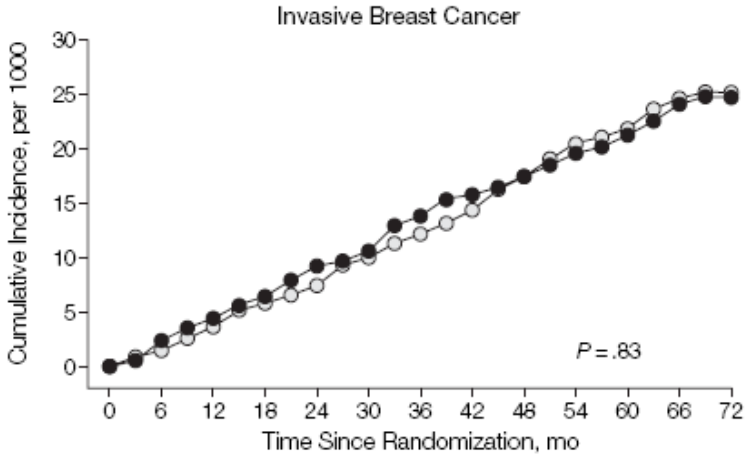


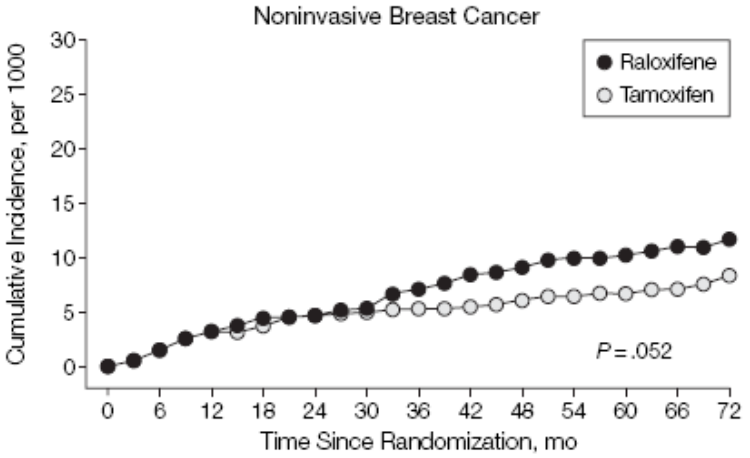
Powles TJ J Natl Cancer Inst 2007;99: 283 – 90

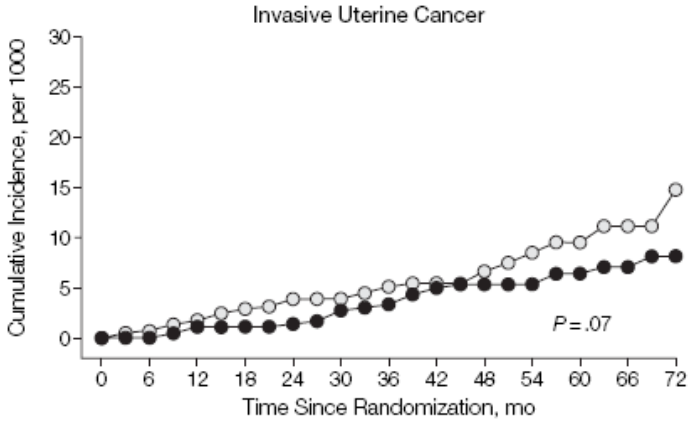
Brustkrebs

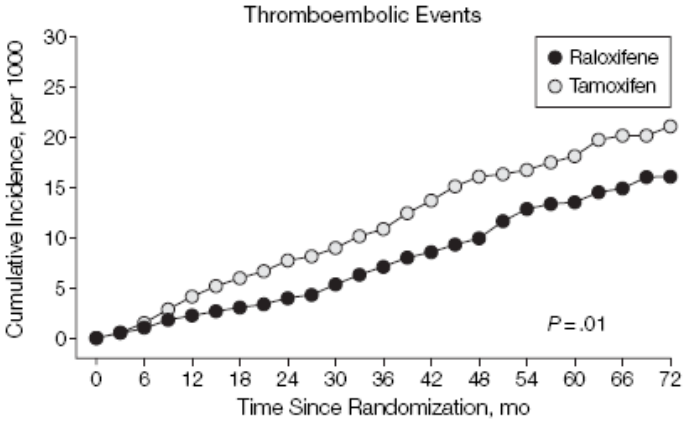
Präventionsstudien: STAR-Trial

Tam: n = 9.872; Ral: n = 9.875



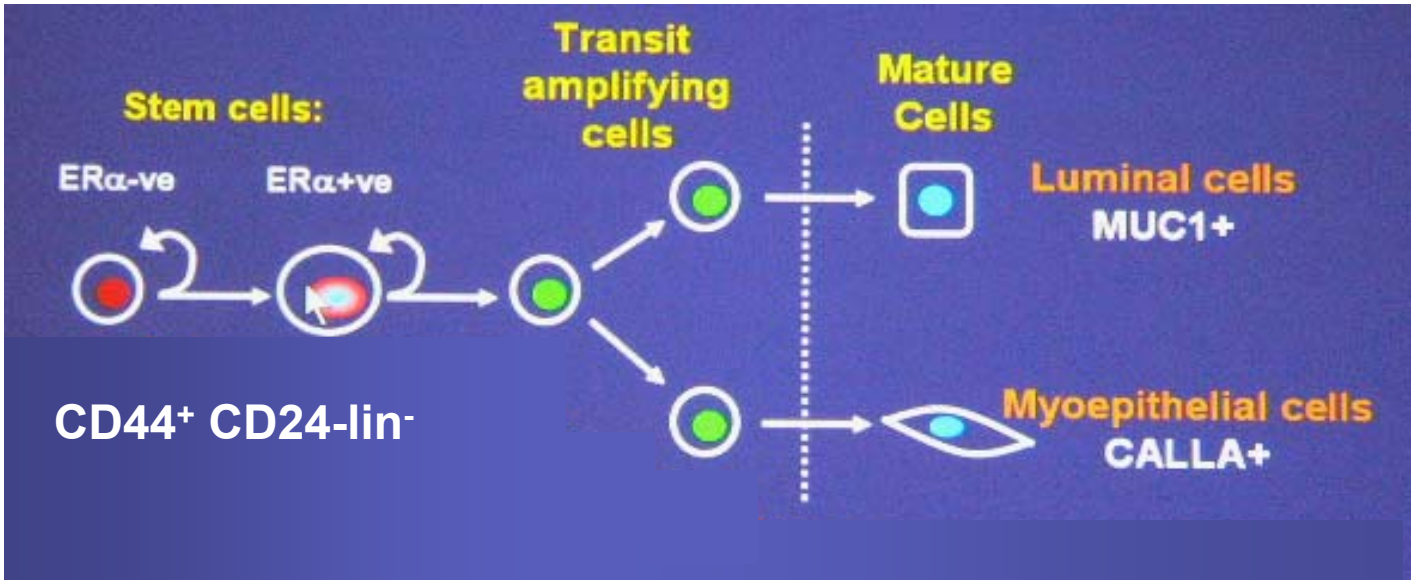


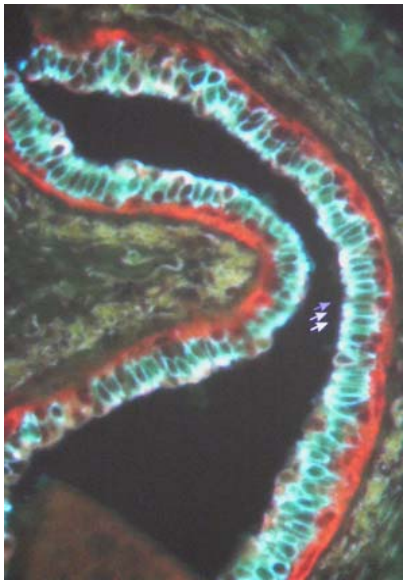


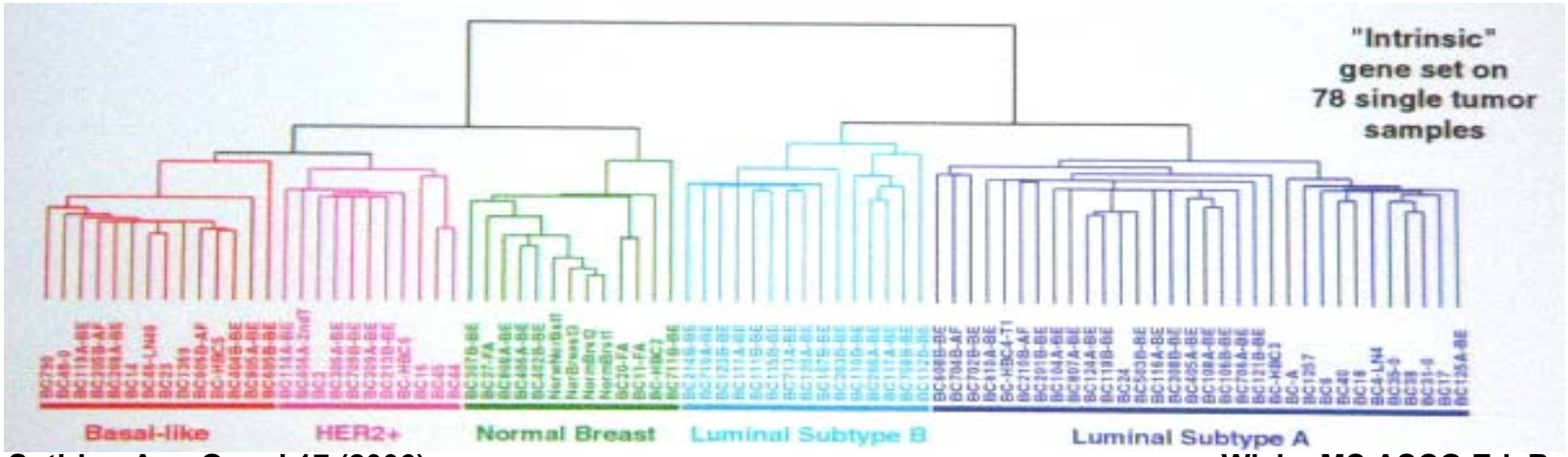


Vogel JAMA. 2006;295:2727-2741

Brustkrebs: Stammzellhypothese





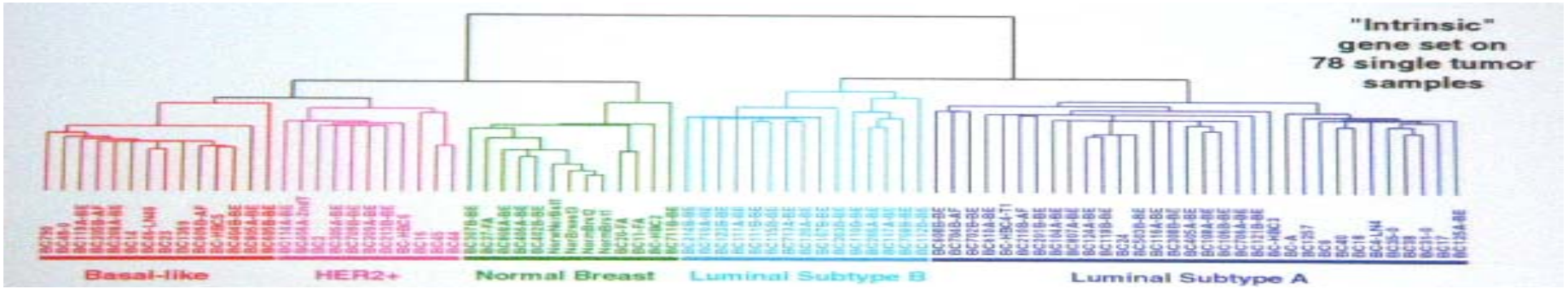


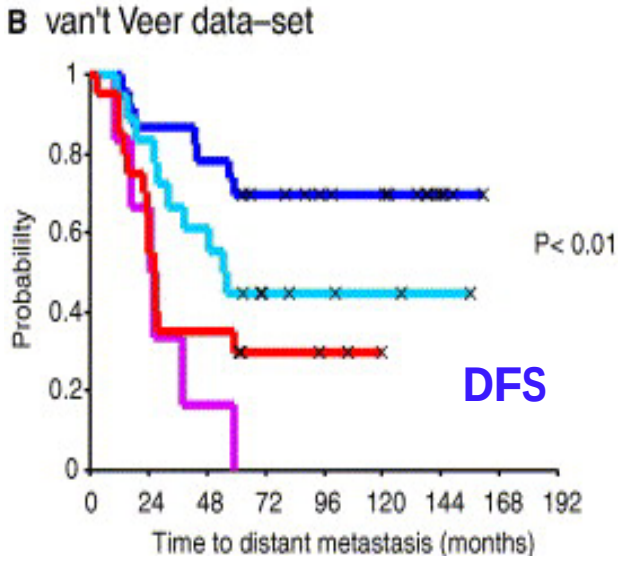
Sotiriou Ann Oncol 17 (2006)

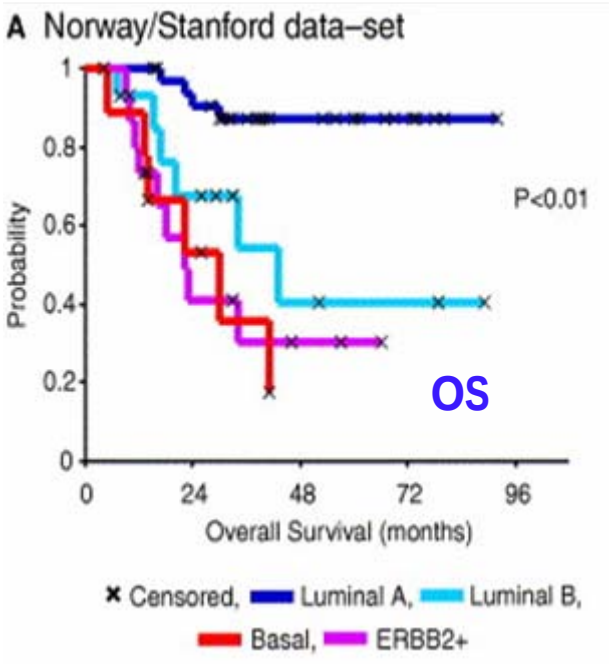
Wicha MS ASCO Ed. Book 8 (2007)

Brustkrebstherapie: spezifisch

BREAST CANCER SUBTYPES, AND SURVIVAL

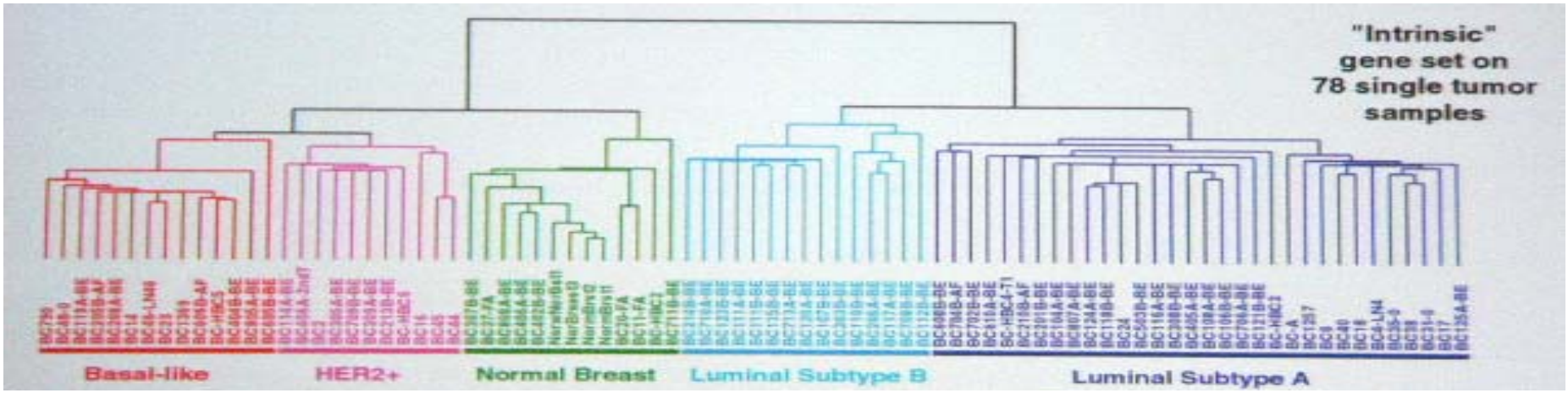






Brustkrebssubtypen

Genetische Profile



Basal-like BRCA	Basal-like spor.	HER-2 +	Luminal B	Luminal A
ER- / PR-	ER- / PgR-	ER- / PgR-	ER+ / PgR-	ER+ / PgR+
G3	G3	G3	G1,2	G1
Ki67: 50-60%	Ki67: 50-60%	Ki67: 40-50%	Ki67: 5-20%	Ki67: 5%
HER2 - / EGFR +	HER2 - / EGFR +	HER2 +	HER2 -	HER2 -
BRCA 1/2 pos	BRCA 1/2 neg			
P53 / cMYC ↑	P53 / cMYC ↑			

Brustkrebs: Adjuvante Situation
Prämenop., HR+: Chemo- vs Hormontherapie

Studie	Therapie	Selektion	Ergebnis (DFS)
ZEBRA (n=1.640)	CMF x 6 G x 2 J	N+, ER+/-	CMF = G (ER+)
IBCSG VIII (n=1.063)	CMF x 6 G x 2 J CMF x 6 → G 1,5 J	N-, ER+/-	CMF = G (ER+) CMF→G = G CMF→G = CMF
Scandinav. (n=732)	CMF x 9 OA (RT)	N+, ER+	CMF = OA
TABLE (n=600)	CMF x 6 Leuprorelin x 2 J	N+, ER+	CMF = L
GABG (n=771)	CMF x 3 Goserelin 2 J	N0, ER+	CMF = G
ABCSG (n=1034)	G 3J + **Tam** 5J CMF x 6	N+/-, ER+	G + Tam > CMF
GROCTA (n=244)	OA/G 2J + Tam 5J CMF x 6	N+/-, ER+	G + Tam = CMF
France (n=333)	OA + **Tam** 2J FAC x 6	N+, ER+	OA + Tam = FAC

Dellapasqua J Clin Oncol 23:1736-1750 (2005)

Adjuvante Situation: Lumnial A/B (HR+)

Prämenopause, HR positiv

EBCTCG: Stellenwert von GnRH-Gabe: 11 906 Frauen, 16 Studien

GnRH-A vs Chemotherapie:

Rückfall: (rel Risiko: +3.9%) p = ns; Tod: (rel Risiko: -6.7%) p = ns

GnRH-Zugabe zu Tam, Chemotherapie oder beidem:

Rückfall: (rel Risiko: -12.7%) p = 0.02; Tod: (rel Risiko: -15.1%) p = 0.03

GnRH-A + Tam vs Chemotherapie + Tam:

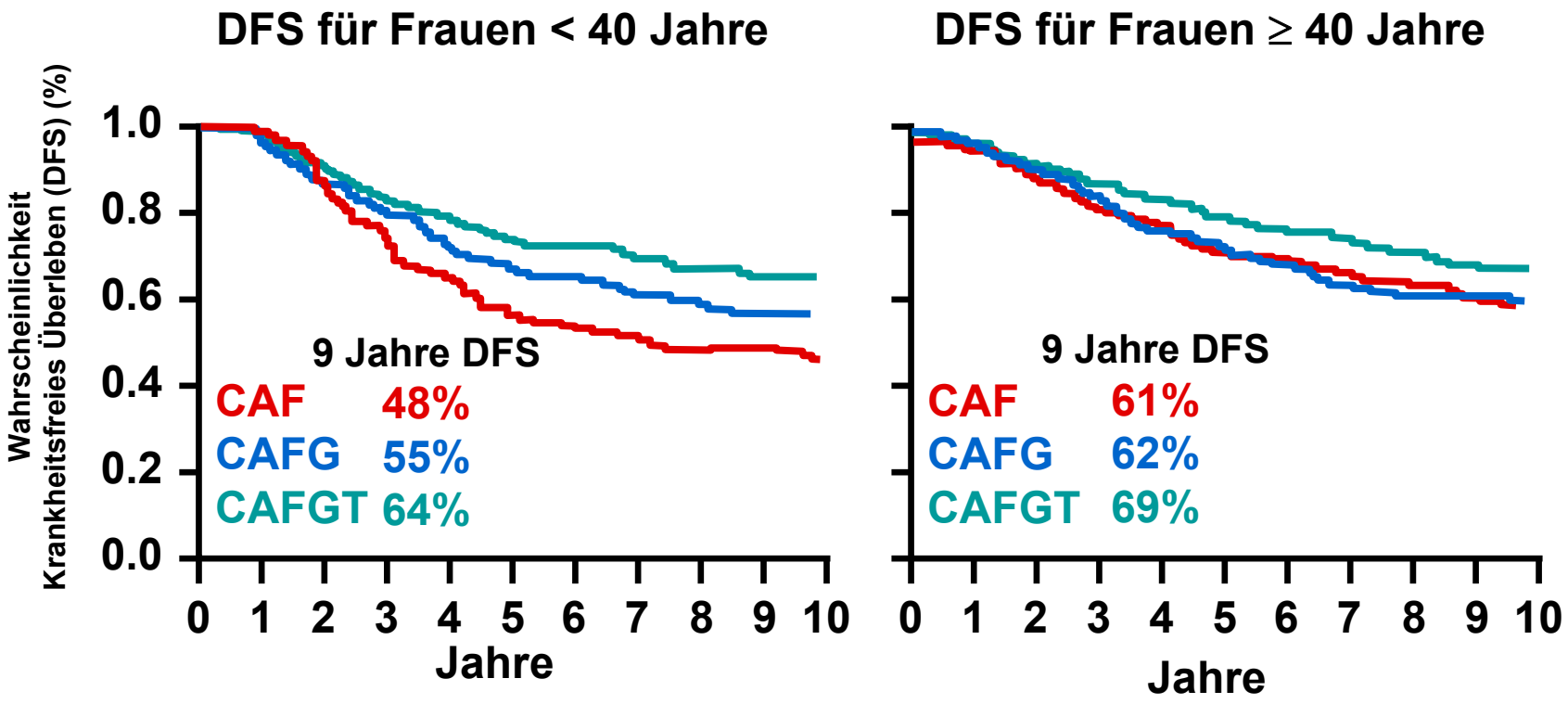
keine Studien

EBCTCG Lancet 369: 1711-1723 (2007)
Davidson Ed. Book 96-99 ASCO 2007

Hormonrezeptorpositive Karzinome

HR+, Prämenopause

CAF (n=494) vs CAF → GnRH (n=502) vs CAF → GnRH + Tamoxifen (n=507)



7.2.4 Davidson J Clin Oncol 23.(2005)

Adjuvante Situation, Luminal A/B (HR+)

Postmenop.: Aromatasehemmer vs Tamoxifen

Metaanalyse von 10 randomisierten Studien

Tam vs AI / up-front / switch

	Population	Pts (#RCTs)	RR (95% CI) FEM/REM	p
DFS	Overall	27,563 (10)	0.80 (0.76, 0.85)	<0.0001
	Up- Front	11,163 (2)	0.86 (0.80, 0.94)	0.0004
	Early Switch	8,776 (5)	0.76 (0.68, 0.84)	<0.0001
	Late Switch	7,624 (3)	0.67 (0.56, 0.80)	0.00001
OS	Overall	25,109 (8)	0.89 (0.82, 0.97)	0.01
	Up-Front	11,163 (2)	0.95 (0.86, 1.06)	0.41
	Early Switch	8,776 (4)	0.80 (0.69, 0.92)	0.003

Ciccarese Proc ASCO abstr. 539 (2007)

Letrozole (5y) vs Tamoxifen (5y)

BIG 1-98: follow-up 51 months

Variable	Letrozole (n = 2,463) No. of Patients	%	Tamoxifen (n = 2,459) No. of Patients	%	
Disease-free survival events; primary efficacy end point	352	14.3	418	17.0	Δ 2,7%
Local	19	0.8	38	1.6	
Contralateral breast	14	0.6	26	1.1	
Regional	13	0.5	11	0.5	
Distant	182	7.4	212	8.6	Δ 1,2%
Soft tissue	11	0.5	18	0.7	
Bone	83	3.4	88	3.6	
Viscera	88	3.6	106	4.3	
Second, nonbreast malignancy	63	2.6	82	3.3	
Death without prior cancer event	60	2.4	48	2.0	
Deaths; overall survival events	194	7.9	211	8.6	Δ 0,7%
Systemic failures; systemic disease-free survival events	331	13.4	374	15.2	

Coates AS JCO 25 (2007)

Brustkrebs: Adjuvante Situation

Postmenopause:Tam vs Switch AI (ARNO)

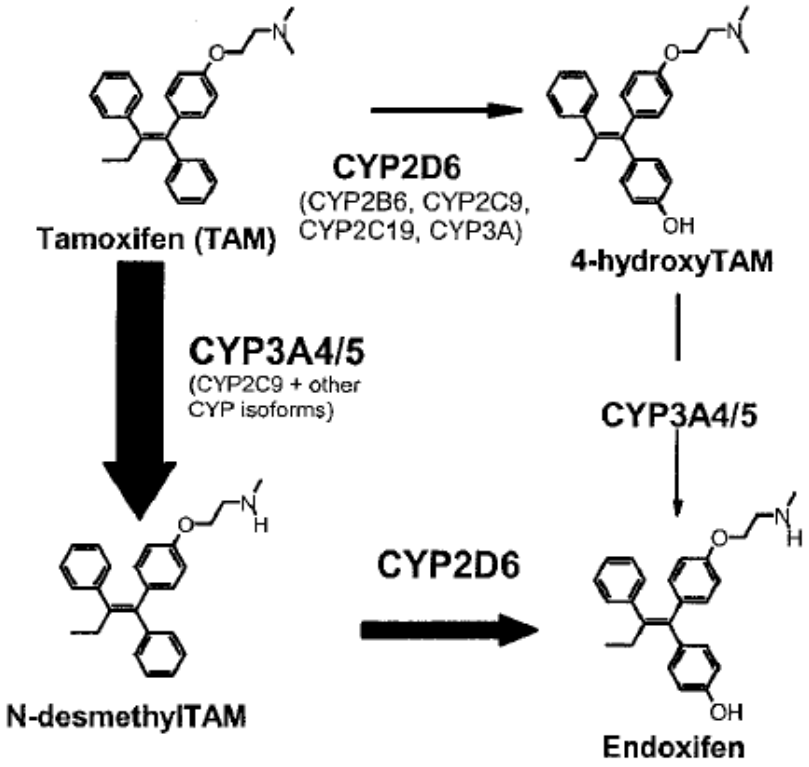
Event	Anastrozole (1 mg/d; n = 489) No.	%	Tamoxifen (20-30 mg/d; n = 490) No.	%	
Patients without an event	451	92.2	434	88.6	
Any recurrence*	36	7.4	47	9.6	Δ 2,2%
Local or distant recurrence	31	6.3	43	8.8	
Local recurrence	12	2.5	11	2.2	
Distant recurrence	27	5.5	33	6.7	Δ 1,2%
New contralateral breast cancer	7	1.4	5	1.0	
Deaths	15	3.1	28	5.7	Δ 2,6%
After recurrence	13	2.7	19	3.9	
In the absence of recurrence	2†	0.4	9‡	1.8	

Kaufmann JCO 25:2664-2670 (2007)

Gezielte Tumortherapie

Berücksichtigung pharmakogenetischer Zielstrukturen

Tamoxifen: CYP2D6 **extensive (72,1%) / intermediate (21,1%) / poor (6.8%) metabolizer**



Wirkstoffkonzentration = Wirksamkeit

BIG1-98: Tamoxifen vs Letrozol

5J. DFS
Letrozol: HR 0.84
Tamoxifen: HR 0.813

bei Pat. ohne CYP2D6 Mutationen könnte Tam AI überlegen sein

Punglia Proc ASCO abstr. 502 (2007)

Gezielte Therapie

Berücksichtigung pharmakogenetischer Zielstrukturen

Tamoxifen: CYP2D6

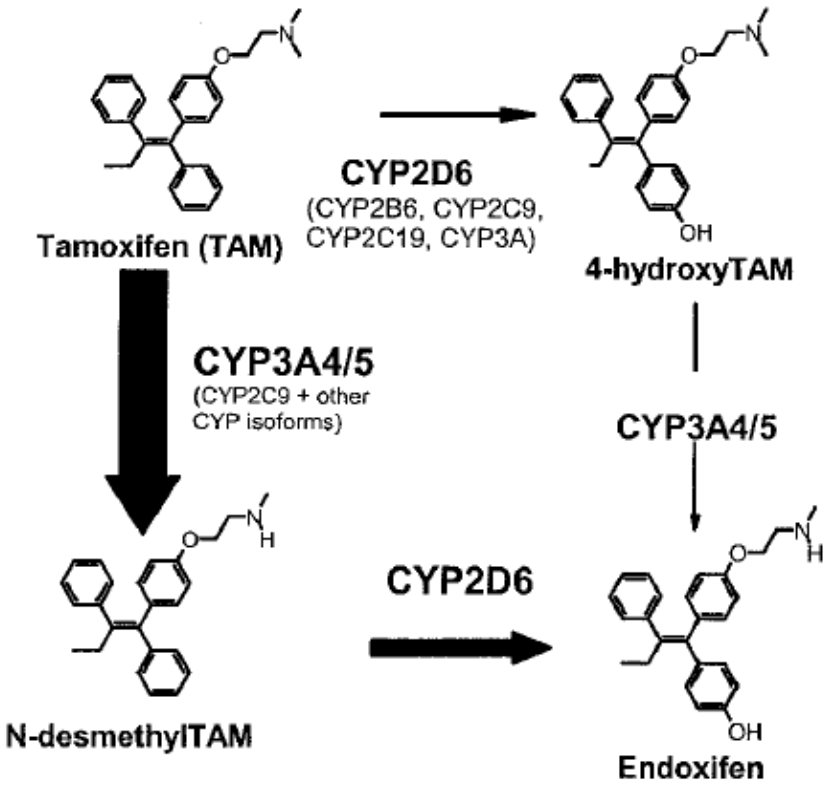
Outcome	*CYP2D6* genotypes: Wt/Wt or Wt/*10 No.	Wt/Wt or Wt/*10 %	*10/*10 No.	*10/*10 %	*P**
CR	0		0		.01860
PR	1		0		
SD ≥ 24 wk	8		6		
Clinical benefit	9	100	6	50	
SD < 24 wk	0		3		
PD	0		3		
No clinical benefit	0	0	6	50	
Total	9	100	12	100	

H-S Lim J Clin Oncol 25:3837-3845 (2007)

Adjuvante Situation: Lumnial A/B (HR+)

Single nucleotide polymorphism

Tamoxifen: CYP2D6



Antiarrhythmika	
Ajmalin	CYP2D6
Encainid	CYP2D6
Flecainid	CYP2D6
Mexiletin	CYP2D6
Propafenon	CYP2D6
Spartein	CYP2D6

Beta-Blocker	
Alprenolol	CYP2D6
Bufuralol	CYP2D6
Carvedilol	CYP2D6
Metoprolol	CYP2D6
Propranolol	CYP2D6
Timolol	CYP2D6

Antidepressiva, trizykl. ~	
Amitriptylin	CYP2D6
Clomipramin	CYP2D6
Desipramin	CYP2D6
Imipramin	CYP2D6
Nortriptylin	CYP2D6

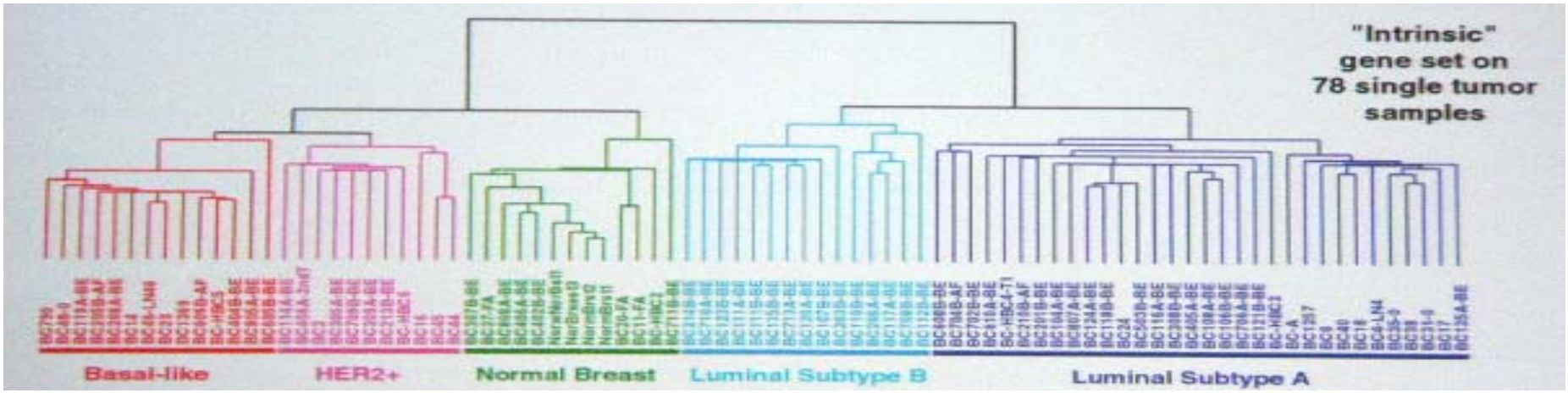
Antidepressiva, tetrazykl. ~	
Maprotilin	CYP2D6

Antidepressiva, andere ~	
Fluoxetin	CYP2D6
Paroxetin	CYP2D6

Neuroleptika	
Clozapin	CYP2D6
Haloperidol	CYP2D6
Perphenazin	CYP2D6
Remoxiprid	CYP2D6
Thioridazin	CYP2D6
Trifluperidol	CYP2D6

Brustkrebssubtypen

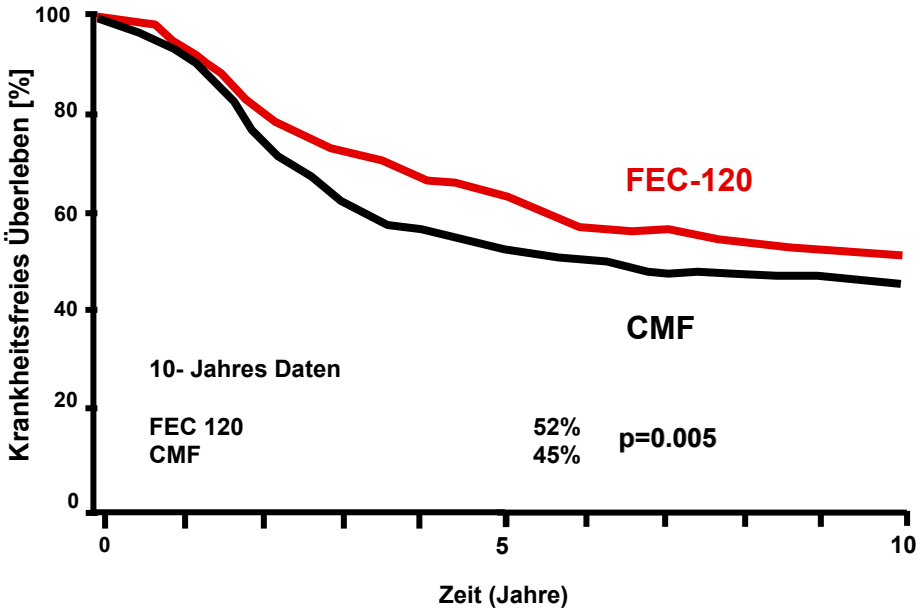
Genetische Profile



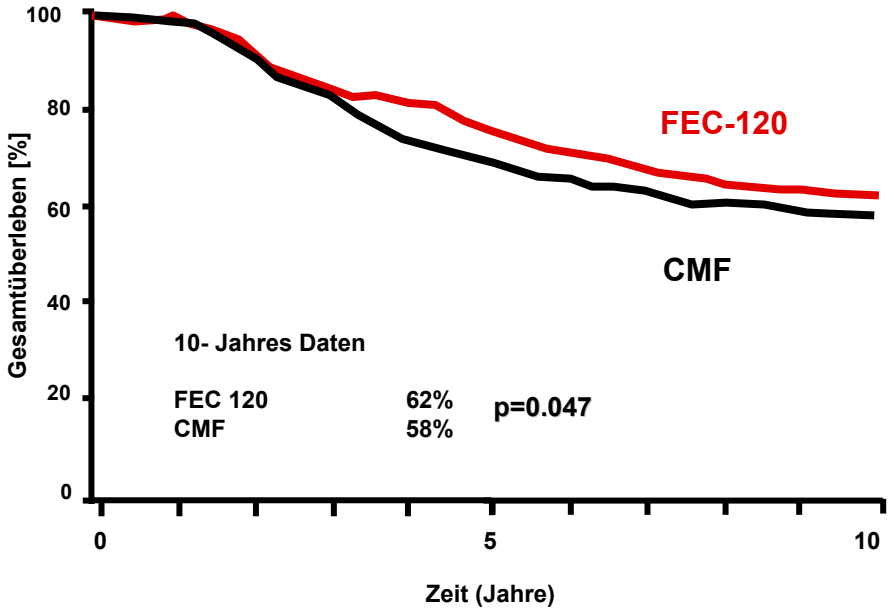
HER-2 +	Luminal B	Luminal A
ER- / PgR-	ER+ / PgR-	ER+ / PgR+
G3	G1,2	G1
Ki67: 40-50%	Ki67: 5-20%	Ki67: 5%
HER2 +	HER2 -	HER2 -

Pre(peri)menopausal Patients
FEC-120 vs CMF, N+ (n=710)

Krankheitsfreies Überleben



Gesamtüberleben



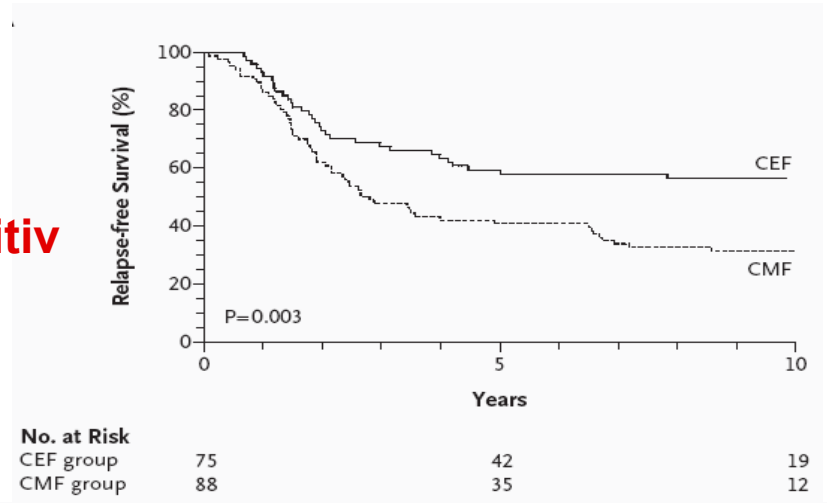
Levine et al. *San Antonio 2002,* Abstr. 17

Genetische Profile: HER2 positiv

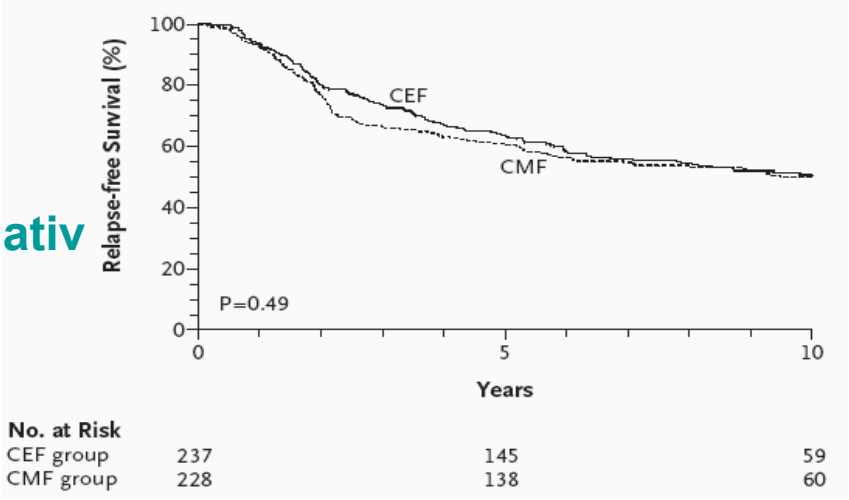
spezifische Therapie

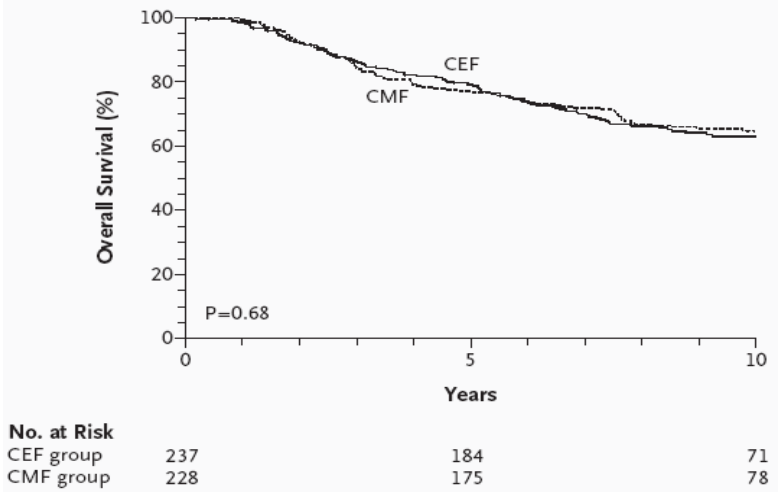
Adjuvant N+: FEC-120 vs CMF

HER2:
FISH positiv



HER2:
FISH negativ

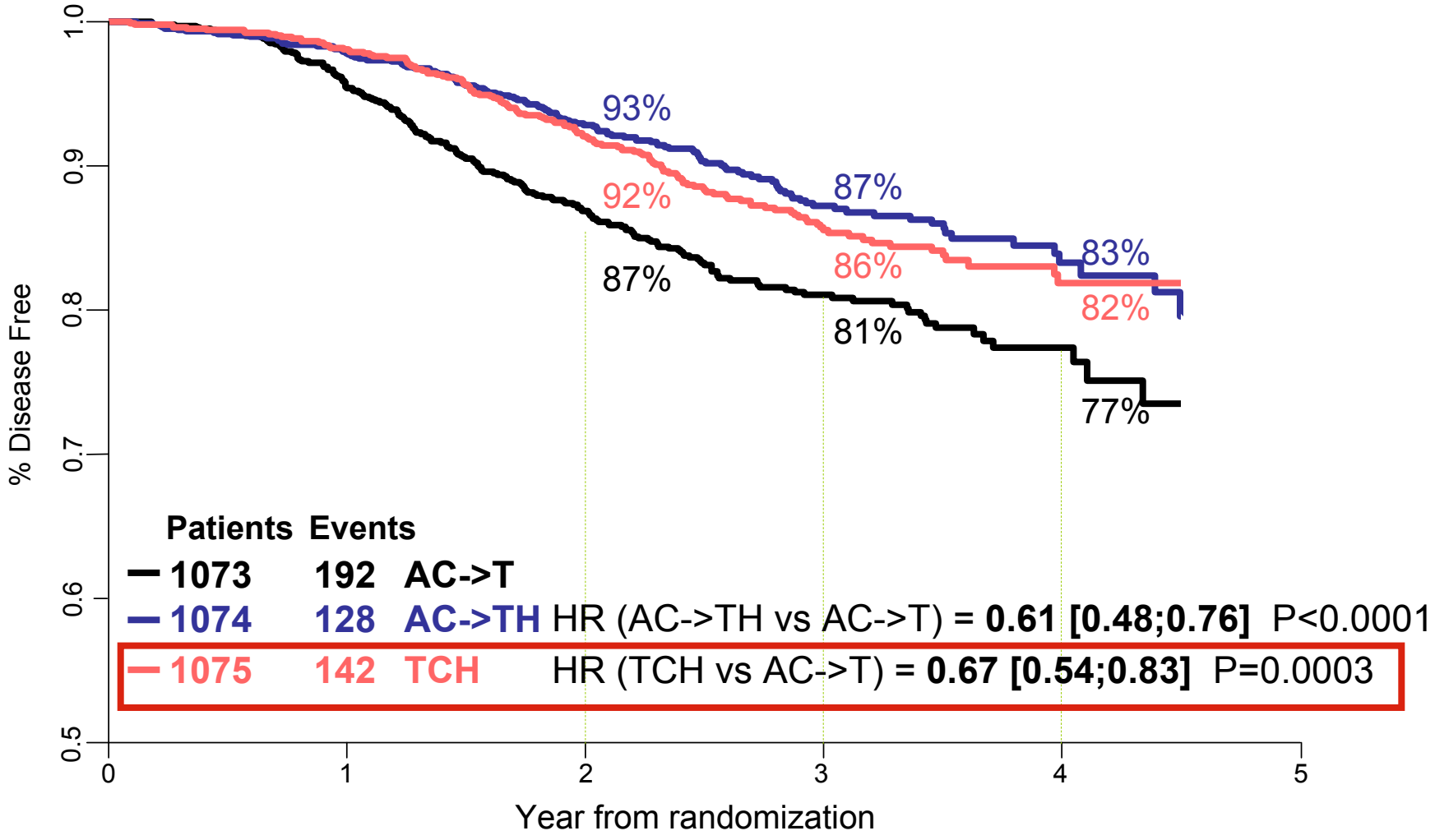




Pritchard KI NEJM; 354:2103-11 (2006)

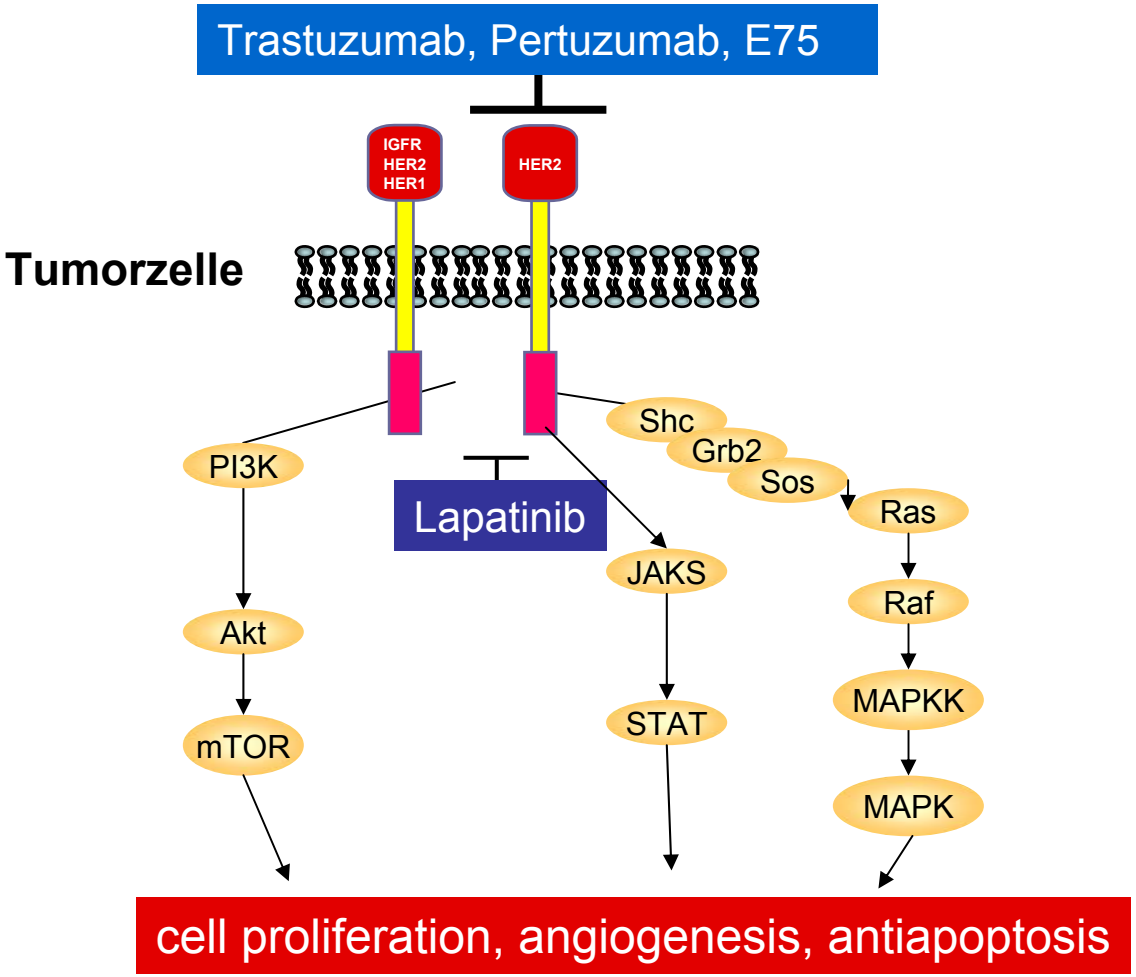
Genetische Profile: HER2 positiv

BCIRG 006: DFS



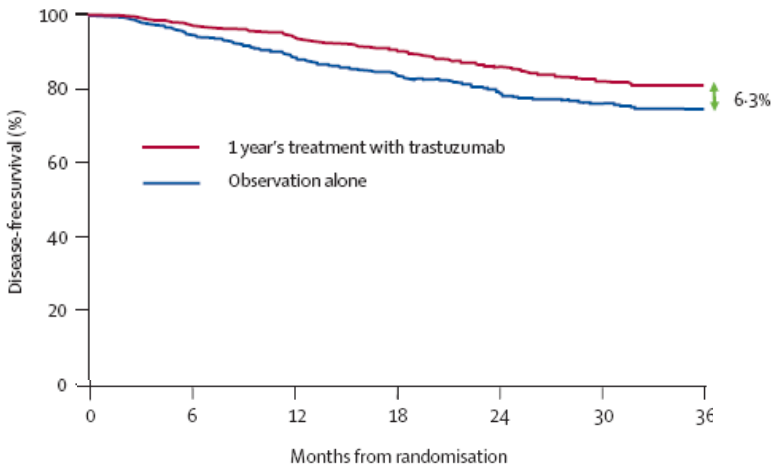
Wachstumsfaktorrezeptoren

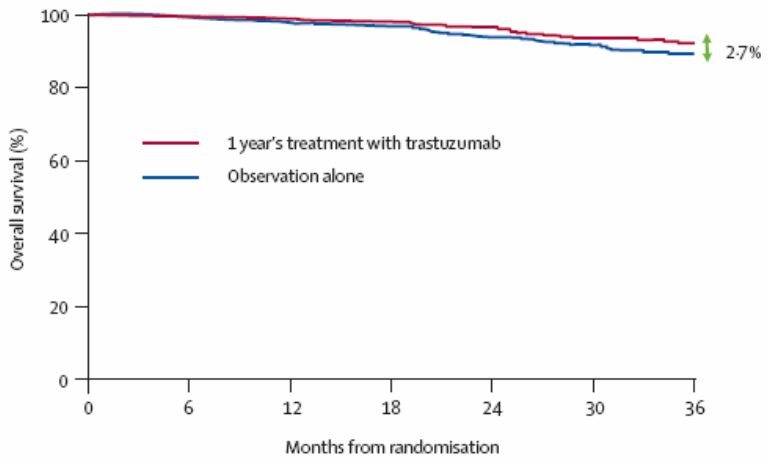
Blockademöglichkeiten



Genetische Profile: HER2 positiv

HERA (follow-up 2y)



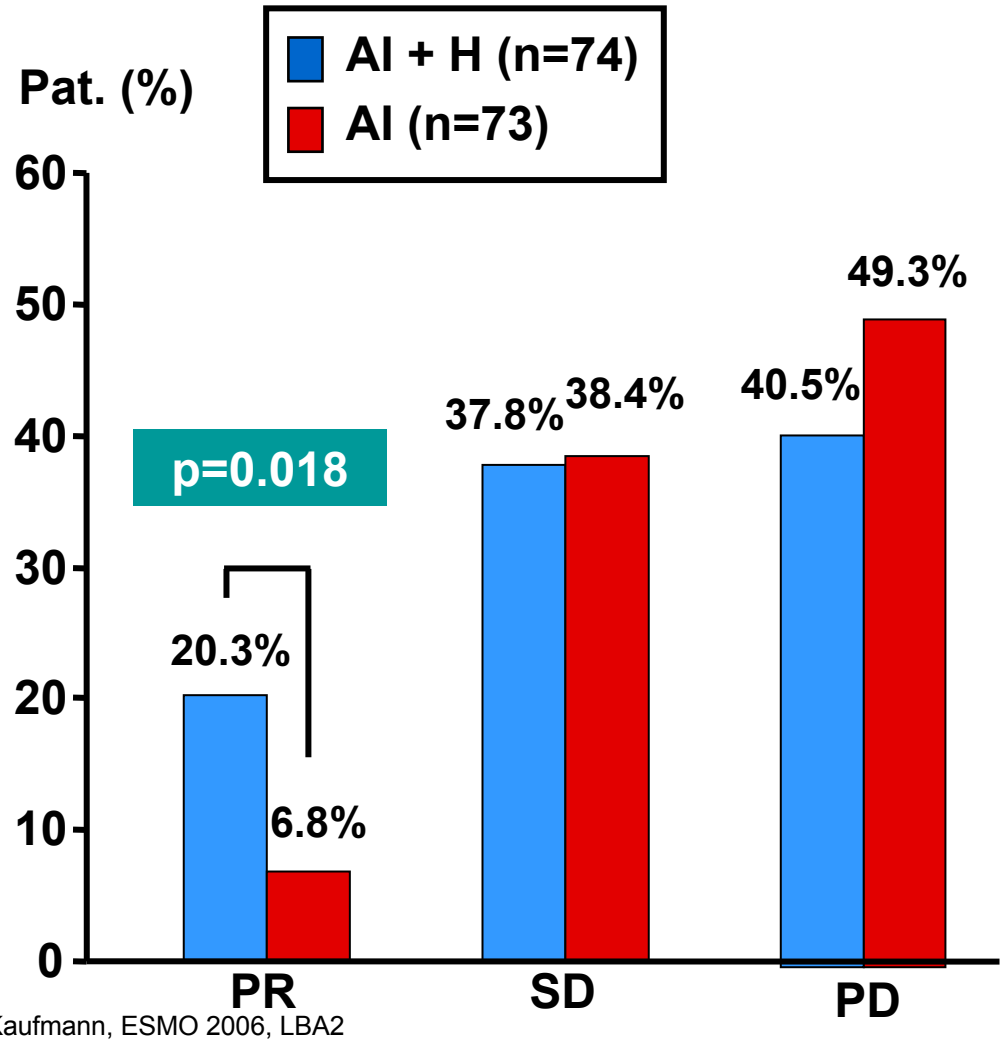


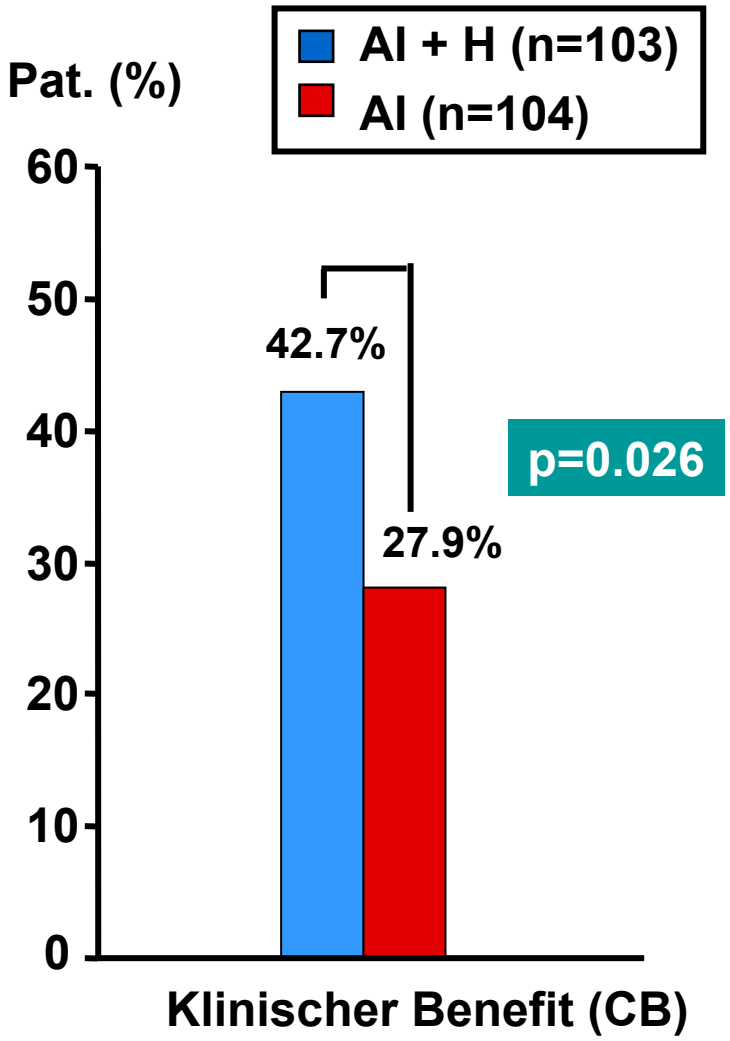
	Observation group (n=1698)	1-year trastuzumab group (n=1703)	
Number of events	321 (19%)	218 (13%)	
Deaths	90 (5%)	59 (3%)	Δ 2%
Distant event	233 (14%)	152 (9%)	Δ 5%
Central nervous system	22 (1%)	26 (2%)	
Locoregional event	68 (4%)	45 (3%)	
Contralateral breast cancer	9 (0·5%)	7 (0·4%)	
Second non-breast malignant disease	8 (0·5%)	6 (0·4%)	

Smith I Lancet 2007; 369: 29–36

Kombination gezielter Therapien

TANDEM-Studie: Objektives Ansprechen





B. Kaufmann, ESMO 2006, LBA2

HER2+ HR+: Situation bei Fernmetastasierung

TANDEM-Studie: AI vs AI + Trastuzumab

Results	*A (104)*	*A + H (103)*	*p*
TTP	2.4 month	4.8 months	0.0007
OS	23.9 months	28.5 months	0.325
(70% X over)			
PR	6.8%	20.3%	
Clinical Benefit	27.9%	42%	0.026

In patients with central lab confirmation of positive hormone receptor results:

	A (73)	*A + H(77)*	*p*
PFS	3.8 months	5.6 months	0.006

Patients without Liver metastases did somewhat better than the entire group

	A (75)	*A + H (70)*	*p*
PFS	3.8 mos	7.7 months	0.0006
OS	32.1 months	41.3 months	0.04

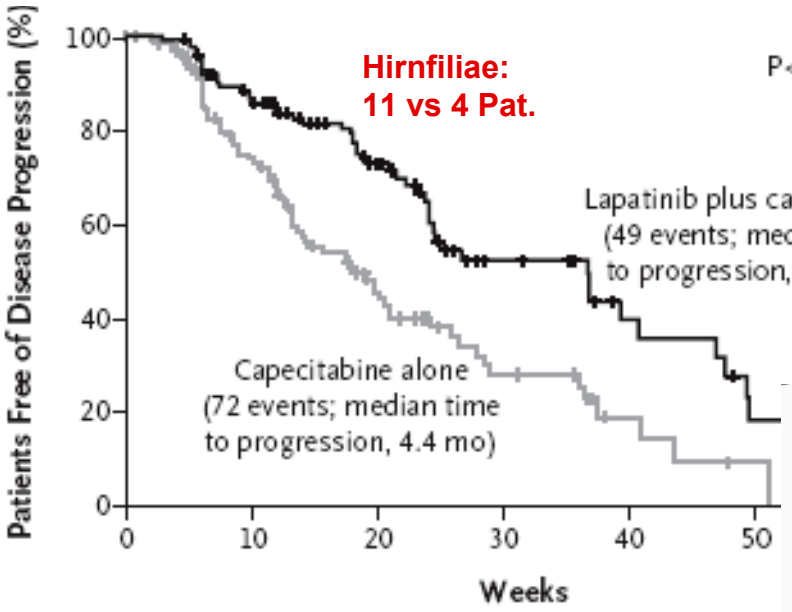
About 15% of patients in the A + H arm had no progression for at least 2 years and therefore further chemotherapy could be post-poned for that interval.

Mackey JR et al, SABCS 2006, abstr # 03

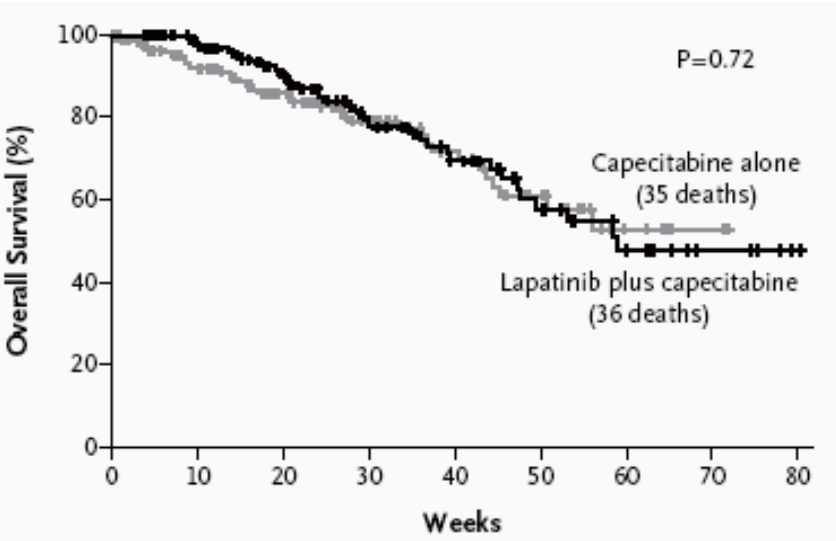
HER2+: Situation bei Fernmetastasierung

Tyrosinkinaseinhibitoren

Lapatinib bei Her2 pos. vorbeh. Mamma-Ca



No. at Risk						
Lapatinib plus capecitabine	163	96	52	21	10	4
Capecitabine alone	161	78	33	14	4	1



No. at Risk									
Lapatinib plus capecitabine	163	129	100	58	39	23	13	5	1
Capecitabine alone	161	122	85	61	35	22	6	2	0

Geyer Ch.E. N Engl J Med 2006;355:2733-43

Genetische Profile: HER2 positiv

Risikofaktoren für Hirnmetastasen

Multivariate Analyse

Variable	HR	95% CI	*P*
HER-2 overexpression	3.55	1.45 to 8.72	.006
Tumor size > 2 cm	2.76	1.23 to 6.19	.013
≥ 1 positive nodes	—	—	NS
Grade 2 or 3 disease	—	—	NS
ER positive	0.32	0.15 to 0.65	.002
PR positive	—	—	NS

Gabos Z J Clin Oncol 24:5658-5663 (2006)

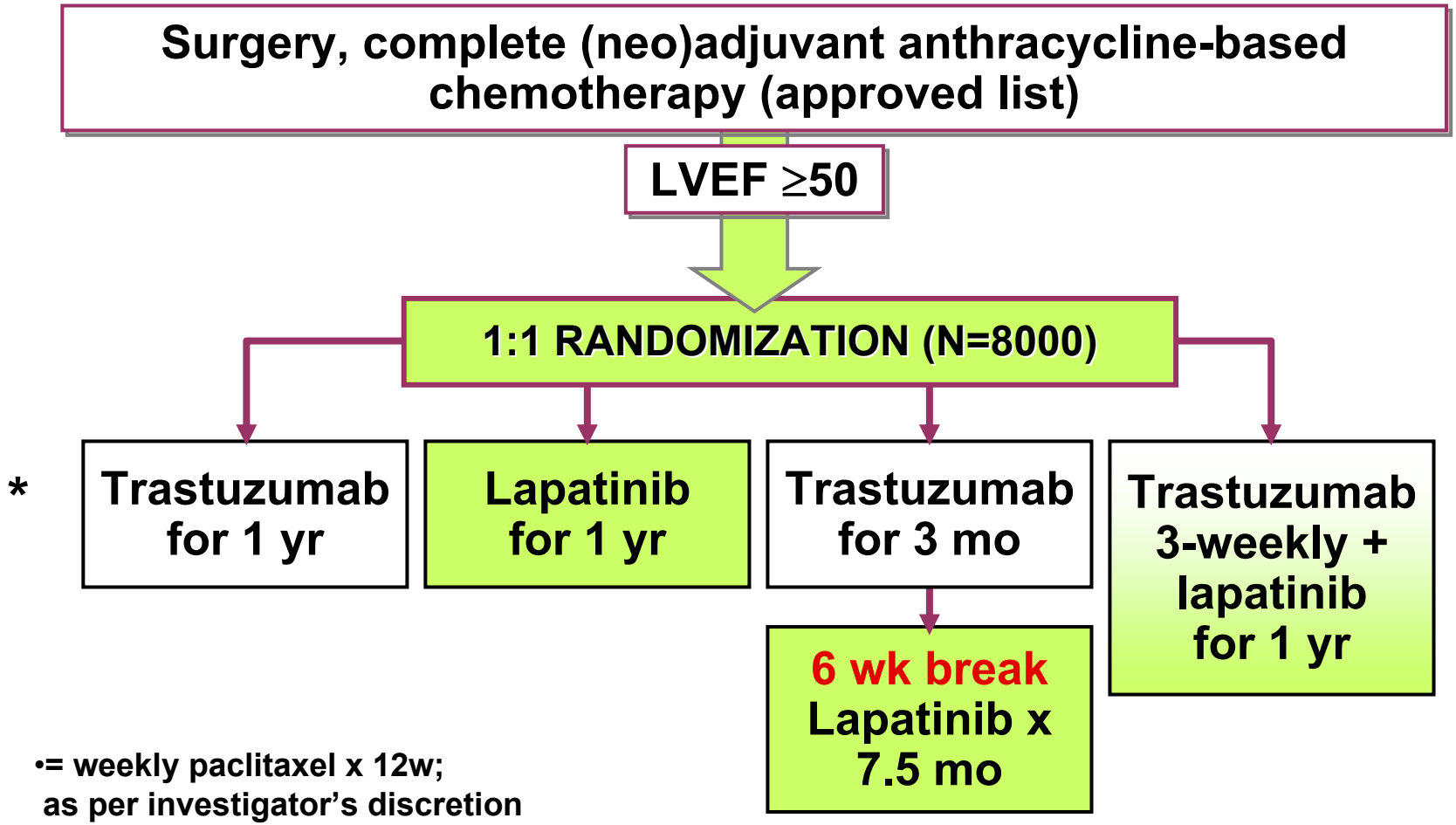
Genetische Profile: HER2 pos.
Lapatinb

- 39 Pat. Hirnmetastasen (HER2 pos.) unter Trastuzumab
- Dosis: 2x 750mg/m² /d Lapatinib für 4 Wochen (+)

- Ergebnis: **ZNS-Ansprechen:**
  PR 2 (158 d, 347 d)
  MR 1
  SD (>= 16 Wo.): 5
  Kein ZNS-Ansprechen:
  PR 4
  ohne ZNS-Progress:
  23 Pat.: 8 Wo., 8Pat.: 16 Wo., 4Pat.: 24 Wo.

Lin ASCO 2006 abstr. 503

Brustkrebs: (Neo)Adjuvante Situation, HER2 pos. ALTTO-Studie



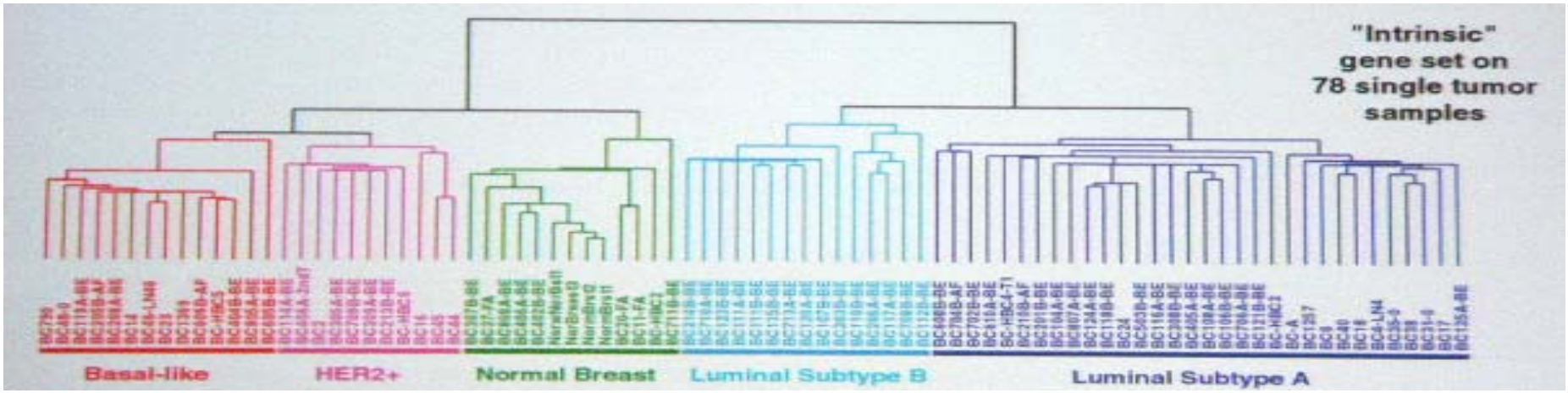
•= weekly paclitaxel x 12w;
as per investigator's discretion

Lapatinib-Problematik

- Toxizität von HER1 und HER2-Hemmern (Herz, Haut, Schleimhäute, Fatigue,…)
- Resorption zusammen mit Mahlzeiten ↑
- Bei gleichzeitiger Anwendung von **CYP3A4-Hemmstoffen** (z. B. Grapefruitsaft, Cimetidin, Erythromycin, Verapamil) kann deren Abbau verlangsamt und damit **Wirkungen und Nebenwirkungen verstärkt** werden.
- **CYP3A4-Induktoren,** wie (Carbamazepin, Phenytoin, Rifampicin, Barbiturate, Johanniskraut) beschleunigen hingegen den Abbau dieser Substrate und können **Wirkungen** und Nebenwirkungen **vermindern**.

Brustkrebssubtypen

Genetische Profile



Basal-like BRCA	Basal-like spor.	HER-2 +	Luminal B	Luminal A
ER- / PR-	ER- / PgR-	ER- / PgR-	ER+ / PgR-	ER+ / PgR+
G3	G3	G3	G1,2	G1
Ki67: 50-60%	Ki67: 50-60%	Ki67: 40-50%	Ki67: 5-20%	Ki67: 5%
HER2 - / EGFR +	HER2 - / EGFR +	HER2 +	HER2 -	HER2 -
BRCA 1/2 pos	BRCA 1/2 neg			
P53 / cMYC ↑	P53 / cMYC ↑			

Genetische Profile: basal-like (triple neg)

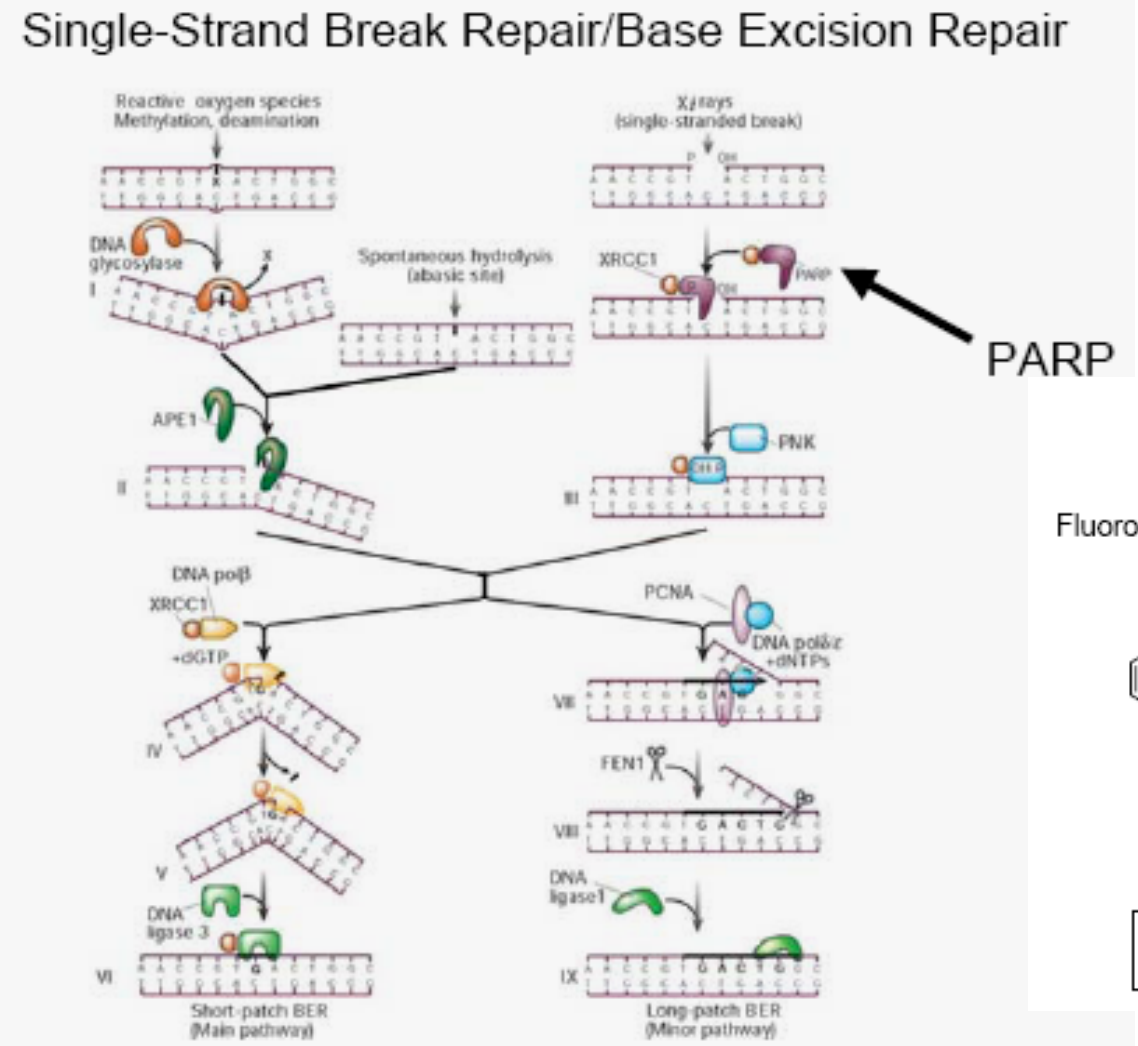
Triple-negativ vs non-tn ; neoadjuvant, retrospektiv

- n = 1.143 pts (MD Anderson)
- n = 258 (23%) triple negativ
- triple negativ: pCR: 63 / 257 (**25%**)
- non-tn: pCR: 99 / 888 (**11%**) **p = 0.0082**
- triple negativ: 5J OAS: **66%**
- non-tn: 5J OAS: **83%** **p < 0.0001**

Liedtke abstr. 10519 ASCO 2007)

Gene Profiling: basal like (triple neg)

Triple-negativ: BRCA1 positiv

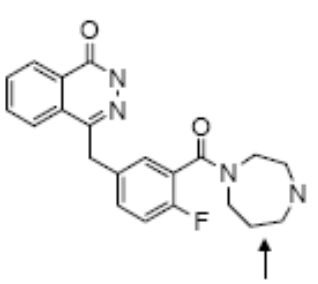


PARP

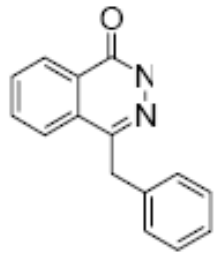
Poly (ADP-ribose) polymerase (PARP)

PARP Inhibitors

Fluorophenylphthalazine skeleton



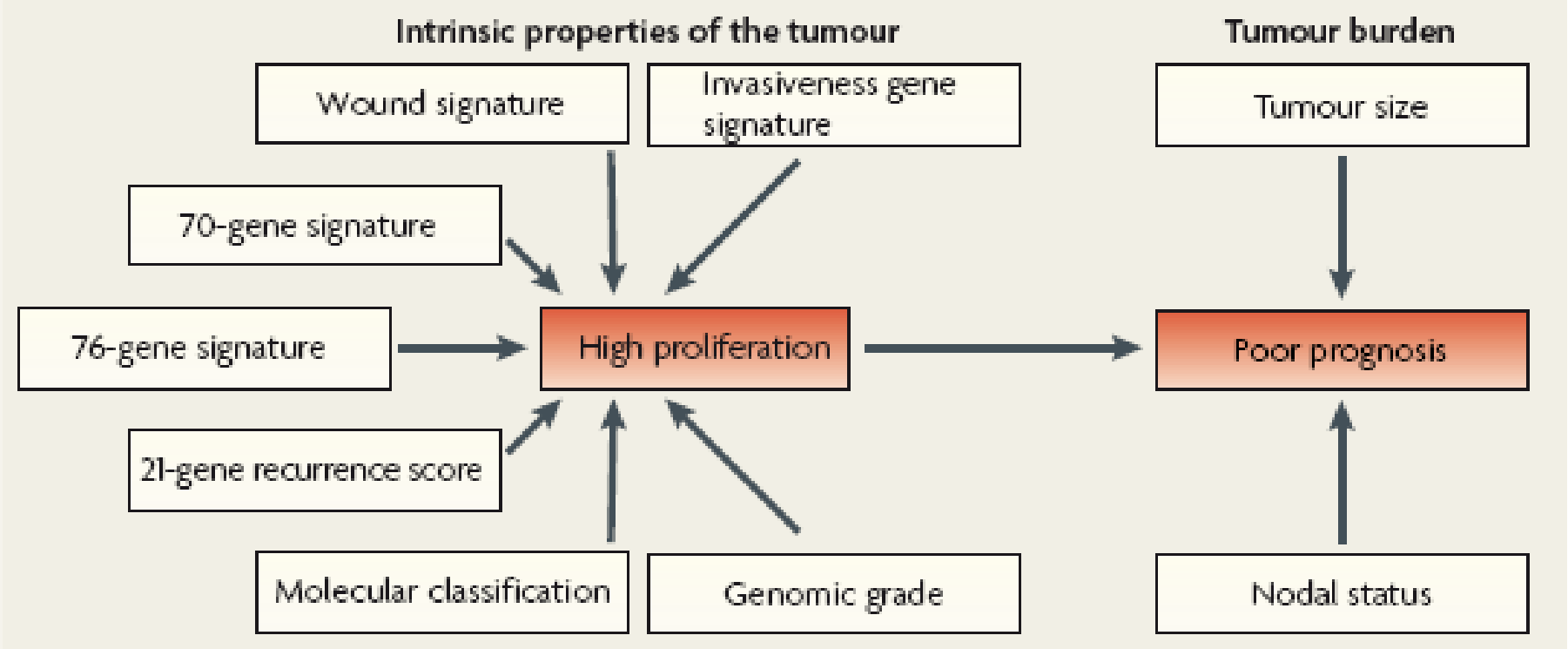
Piperazine



KU-0058948	KU-0051529
PARP-1 IC_{50} = 3.4nM	PARP-1 IC_{50} = 730nM

Yap abstr. 3529 ASCO 2007

Studien auf der Basis genetischer Profile



Stiriou & Piccart Nature 7: 545 (2007)

N0-Situation: Wer benötigt Chemotherapie?

Onkotype DX 21 Gene Recurrence Score (RS) Assay

Datenbasis: NASBP B-14 und B-20

16 Onkogene und 5 Referenzgene von 3 Studien

Proliferation
- Ki67
- Stx15
- Survivin
- Cyclin B1
- MYBL2

Invasion
- Stromolysin 3
- Cathepsin L2

HER2
- GRB7
- HER2

Östrogen
- ER
- PR
- Bcl2
- Scube2

GSTM1

BAG1

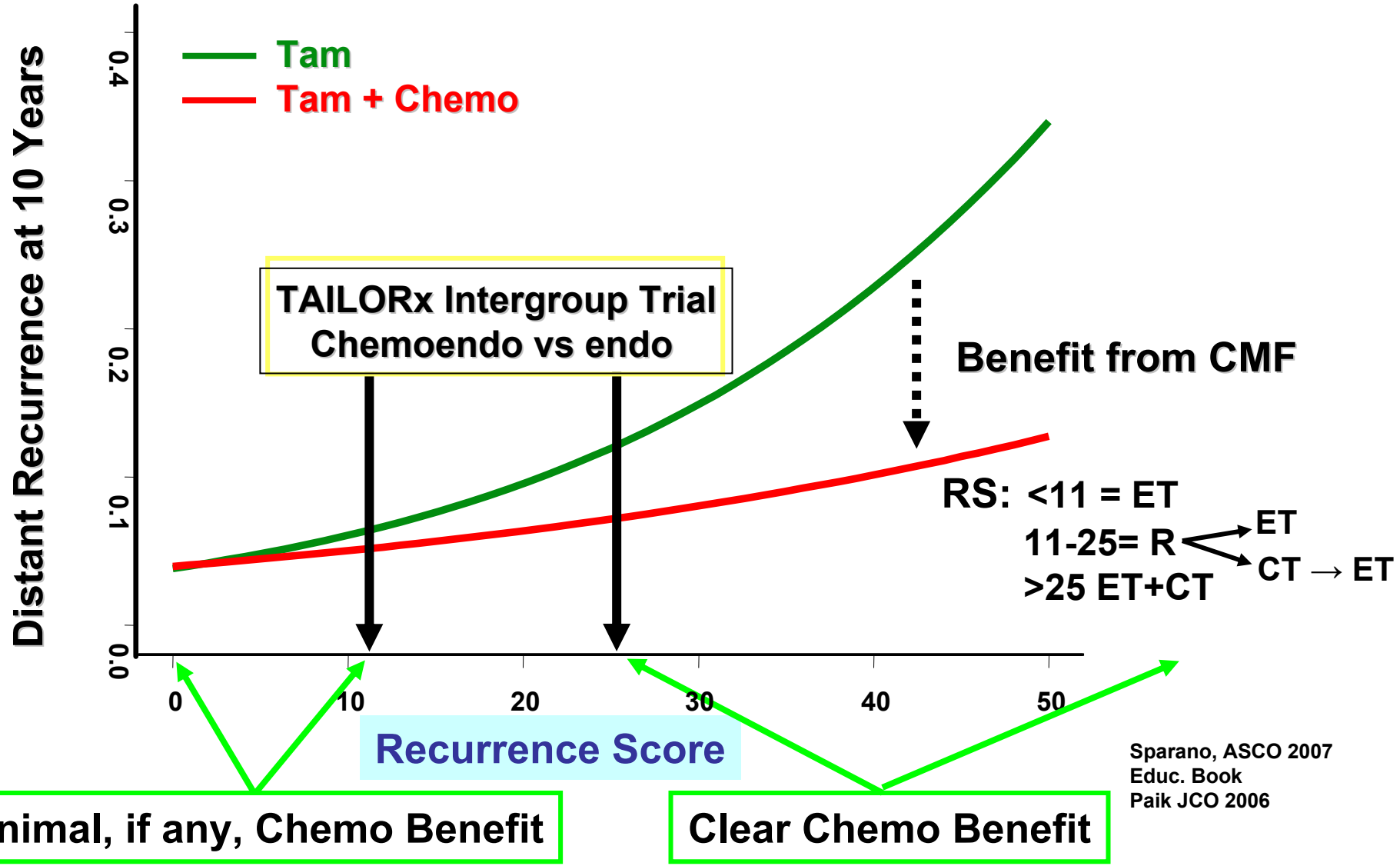
CD86

Kategoie	RS 0-100
Low Risk	RS <18
Int Risk	RS >= 18 und <31
High Risk	RS >=31

Paik, SA 2004

Oncotype Dx 21

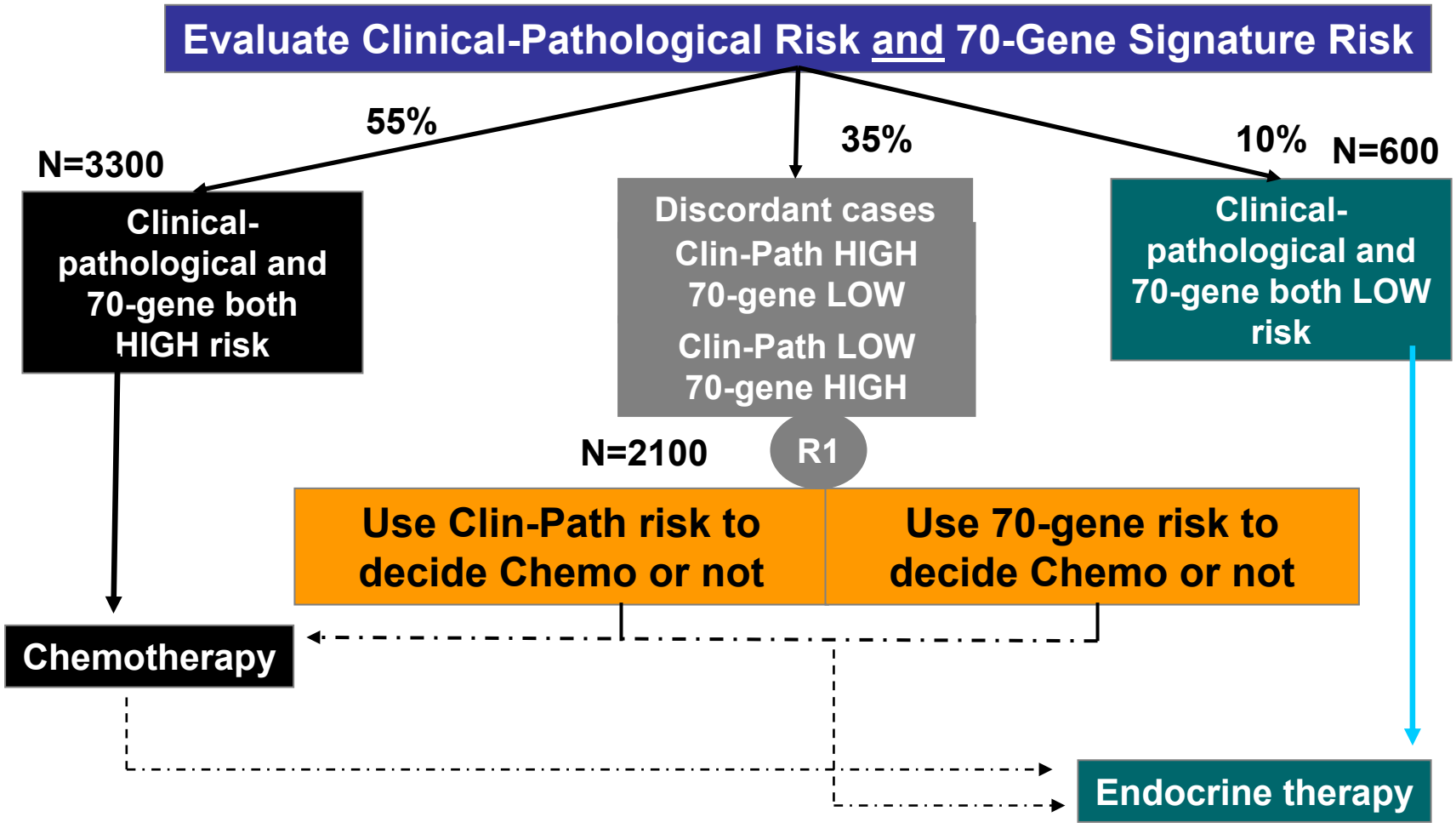
Predictive in NSABP B-20 and Informs TAILORx



Sparano, ASCO 2007
Educ. Book
Paik JCO 2006

EORTC-BIG MINDACT

6,000 Women with Node-Negative Breast Cancer



Potential CT sparing in 20-28% pts

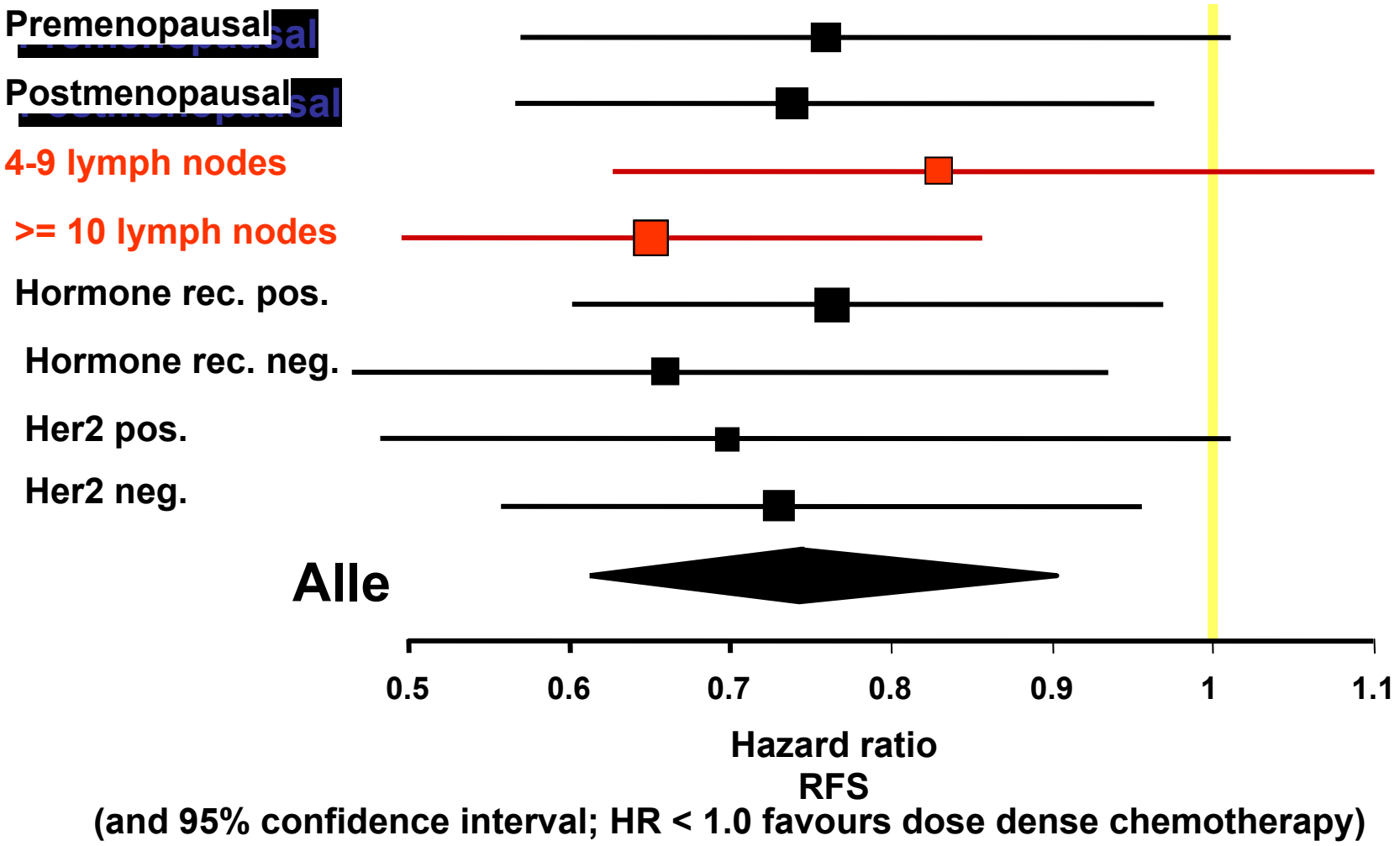
Adjuvante Situation
Dosisdichte, Lk-Zahl und Therapieerfolg

Surgery				
Breast conservation	107	0.75	0.42 to 1.34	0.34
Mastectomy	237	0.74	0.53 to 1.03	0.08
Nodal status				
5-9 positive nodes	91	0.92	0.51 to 1.68	0.80
≥ 10 positive nodes	253	0.73	0.52 to 1.02	0.06
Tumor size, cm				
< 2	104	1.23	0.72 to 2.12	0.44
2-5	175	0.51	0.34 to 0.78	< 0.01
> 5	63	1.10	0.57 to 2.11	0.78
Tumor grade				
1 and 2	140	0.79	0.50 to 1.26	0.32
3	201	0.79	0.54 to 1.14	0.21

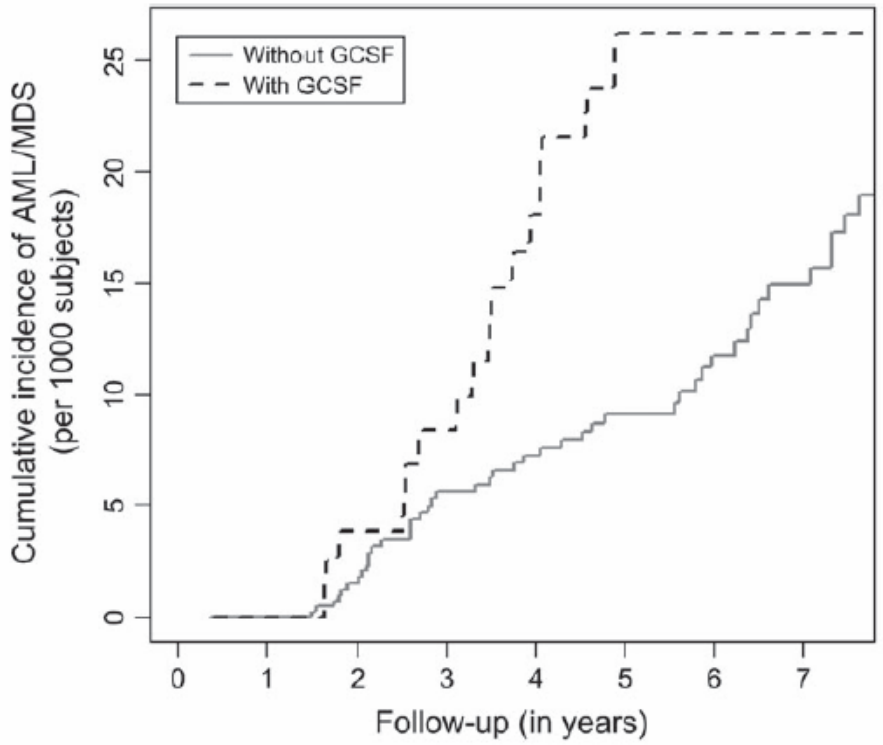
fu: 5,8 Jahre

IBCSG J Clin Oncol 24:370-378 (2006)

Dose-dense (3x) E150→T225→C2500 vs (4x) E90+P175+C600 in ≥4 + LN



AML/MDS nach G-CSF



No. of Pts at risk								
With GCSF	906	857	726	646	587	378	243	156
Without GCSF	4604	4339	3668	3213	2930	2302	1751	1359

		GCSF			Without GCSF	
Years	N	Incidence (per 1000)	95% CI	N	Incidence (per 1000)	95%CI
4	587	18.0	(7.8-28.1)	2930	7.2	(4.4-10.0)
7	156	26.2	(13.2-39.0)	1359	14.9	(10.0-19.8)

Hershman D J Natl Cancer Inst 2007;99: 196 – 205

Erythropoetin:

Erhöhtes Thromboserisiko

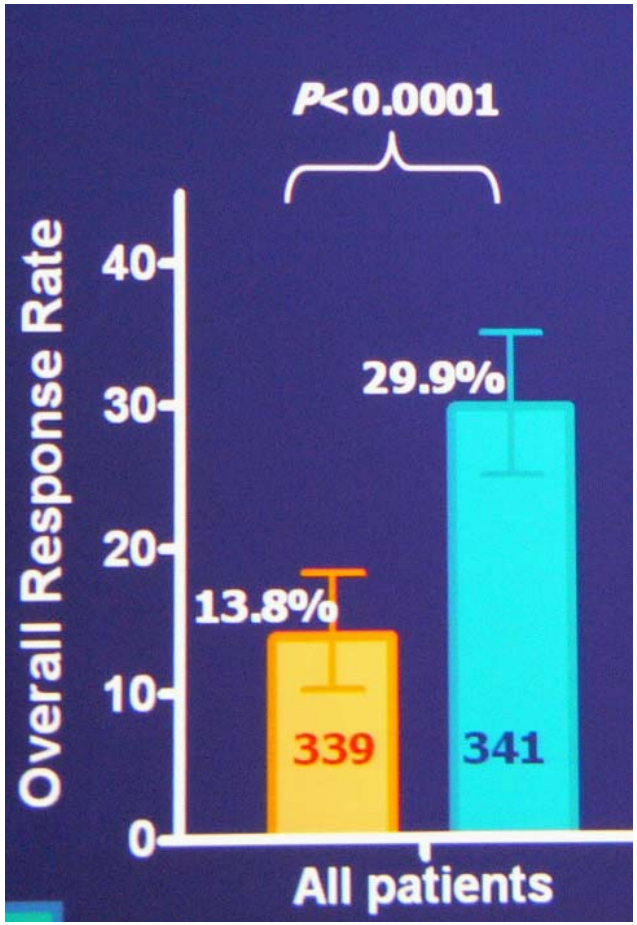
Beschleunigte Progression und Verkürzung des Überlebens
- Brustkrebs
- HNO-Tumore
- NSCLC

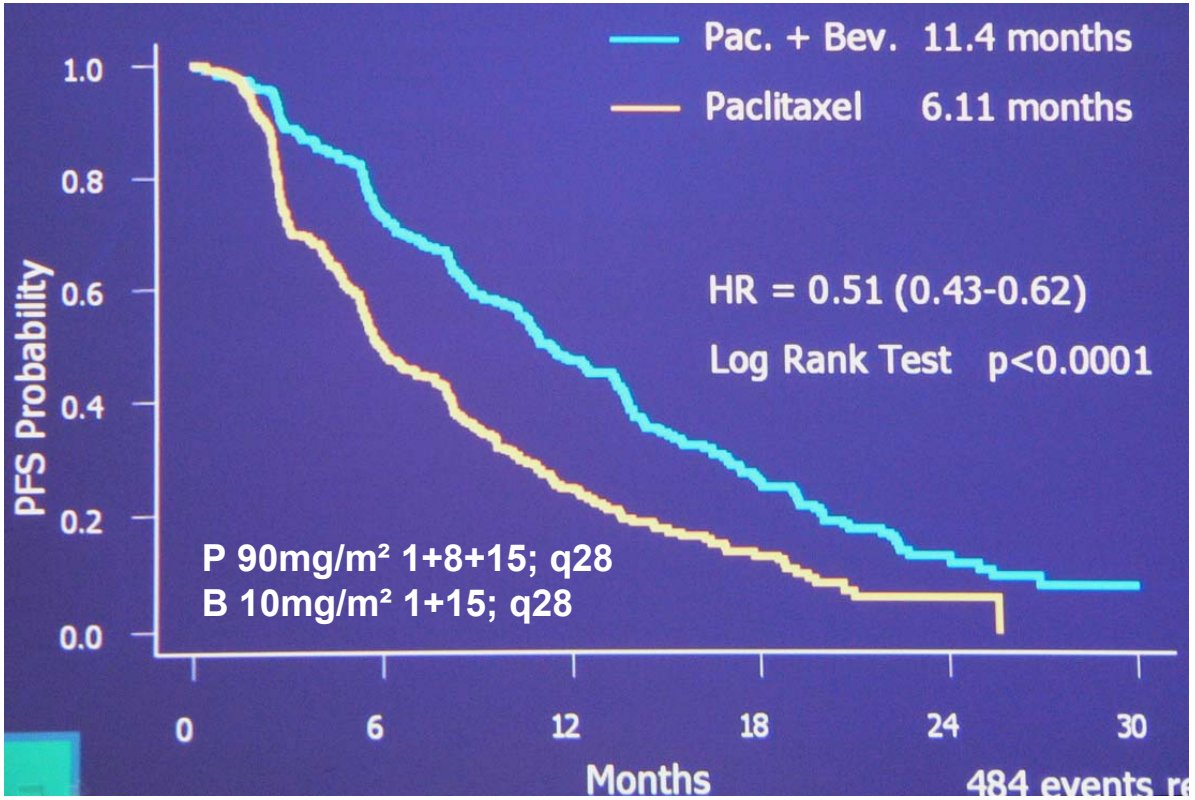
Zelluläre Erythropoetin-Rezeptoren
- Adenokarzinome (Brustkrebs)
- Plattenepithelkarzinome (HNO, NSCLC)

Steinbrook NEJM 356(24), 2448-2451 (2007)

Metastasierte Situation

Paclitaxel ± Bevacizumab

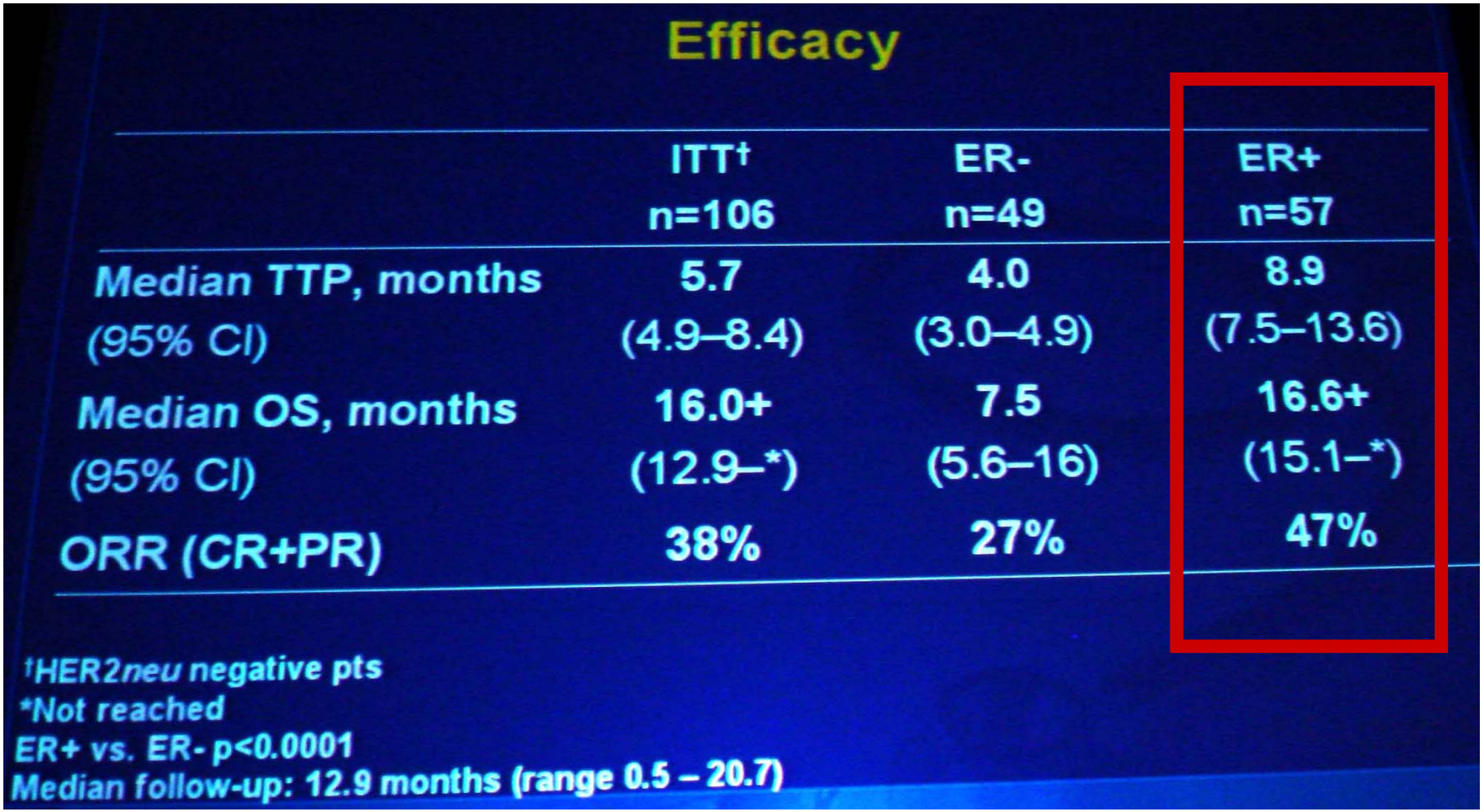




Miller, SABCS 2005

Metastasierte Situation

Paclitaxel ± Bevacizumab



Sledge ASCO (2007)

Phase II Trial of Trastuzumab + Bevacizumab as First-Line Treatment of Patients With HER2-Amplification

Overexpression of HER2 is associated with increased levels of VEGF in breast cancer

Patients with HER2-amplified breast cancer N=50

→ **Trastuzumab (4mg/kg loading dose, then 2 mg/kg qw) + Bevacizumab (10 mg/kg q2w)**

→ **ORR (WHO criteria)**

46% all PR

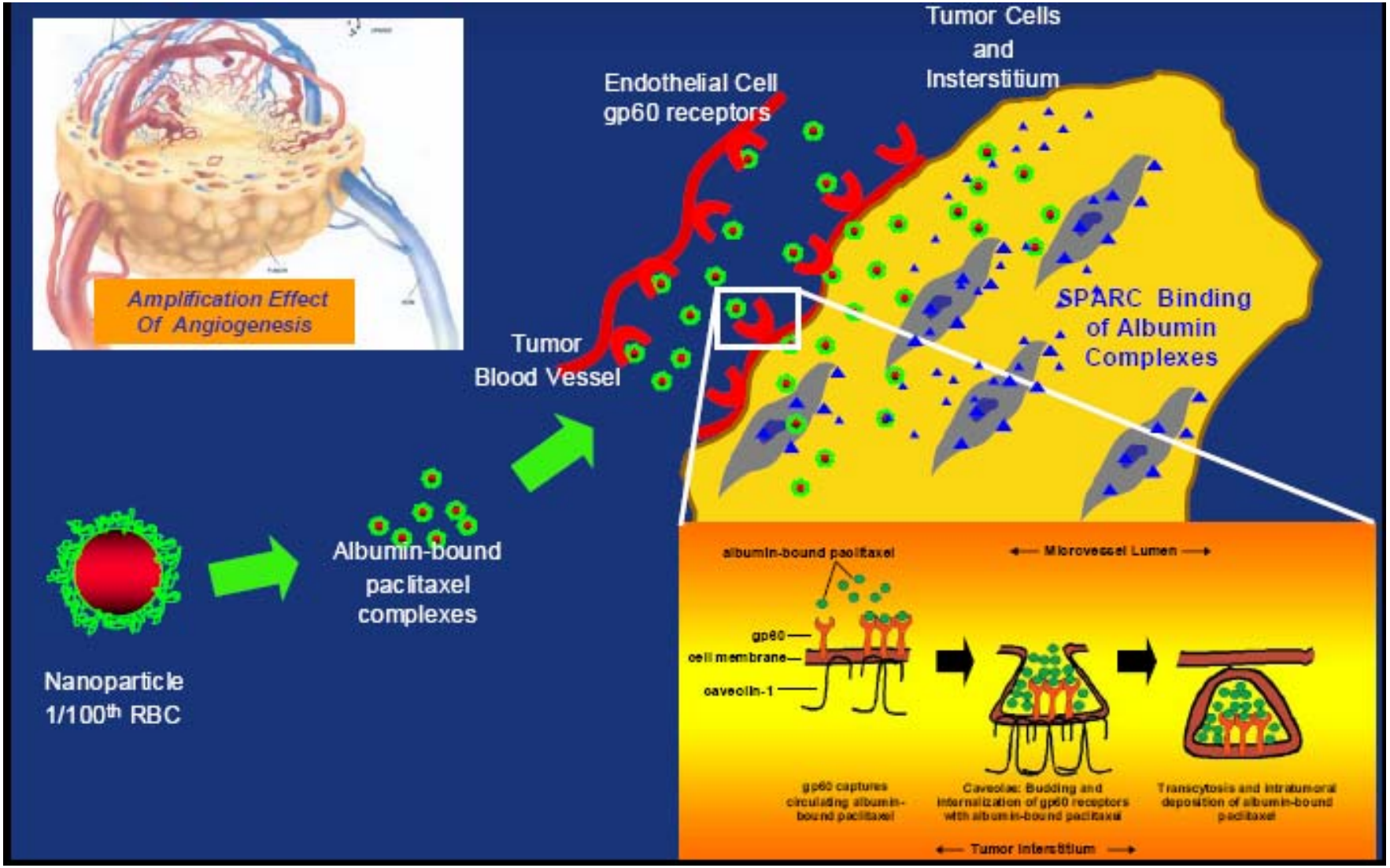
32% SD

- **Grade 1/2 AEs**
  - Fever/chills/headache (50%)
  - Hypertension (21%), epistaxis (21%)
- **Grade 3/4 AEs**
  - Hypertension (18%)
  - Proteinuria (4%), dyspnea (4%), left ventricular dysfunction (4%)

Pegram et al. SABCS 2006. Abstract 301.

Metastasierte Situation

nab-Technologie: nab-Paclitaxel



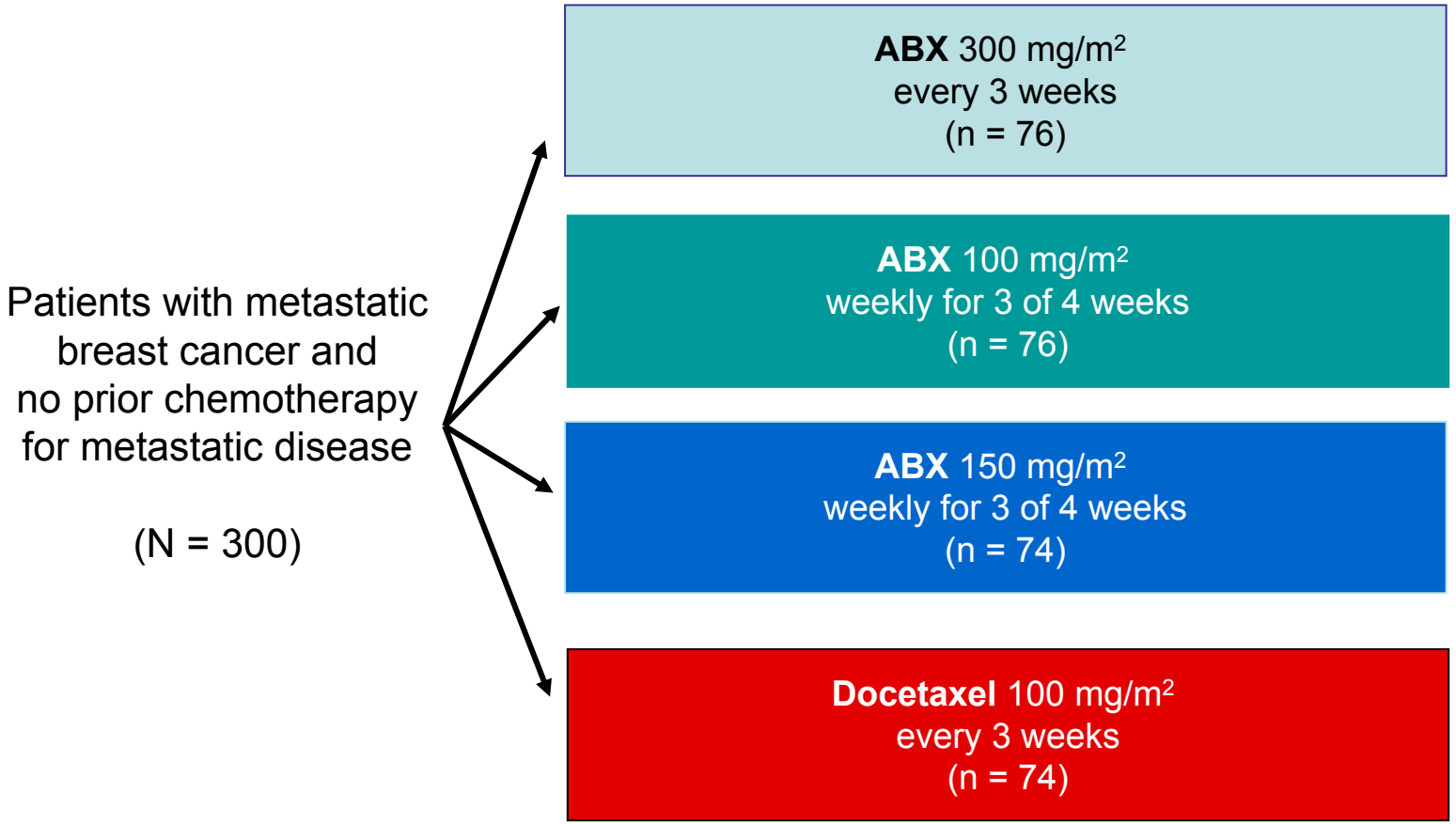
nab-Technologie

ABI-007 (260 mg/m²) vs Paclitaxel (175mg/m²)

Response	ABI-007 (260 mg/m²) No. of Patients/Total No. of Patients	%	95% CI (%)	Standard Paclitaxel (175 mg/m²) No. of Patients/Total No. of Patients	%	95% CI (%)	*P*
Complete and partial response							
All patients	76/229	33	27.09 to 39.29	42/225	19	13.58 to 23.76	.001
First-line therapy	41/97	42	32.44 to 52.10	24/89	27	17.75 to 36.19	.029
Second-line or greater therapy	35/132	27	18.98 to 34.05	18/136	13	7.54 to 18.93	.006
Prior anthracycline therapy							
Adjuvant and/or metastatic	60/176	34	27.09 to 41.09	32/175	18	12.56 to 24.01	.002
Metastatic only	31/115	27	18.85 to 35.07	18/130	14	7.91 to 19.78	.010
Dominant metastatic organ site							
Visceral	59/176	34	26.55 to 40.50	34/182	19	13.02 to 24.34	.002
Nonvisceral	17/50	34	20.87 to 47.13	8/43	19	6.97 to 30.24	NS
Age, years							
< 65	68/199	34	27.58 to 40.76	36/193	19	13.16 to 24.15	< .001
≥ 65	8/30	27	10.84 to 42.49	6/32	19	5.23 to 32.27	NS

Gradishar J Clin Oncol 23:7794-7803 (2005)

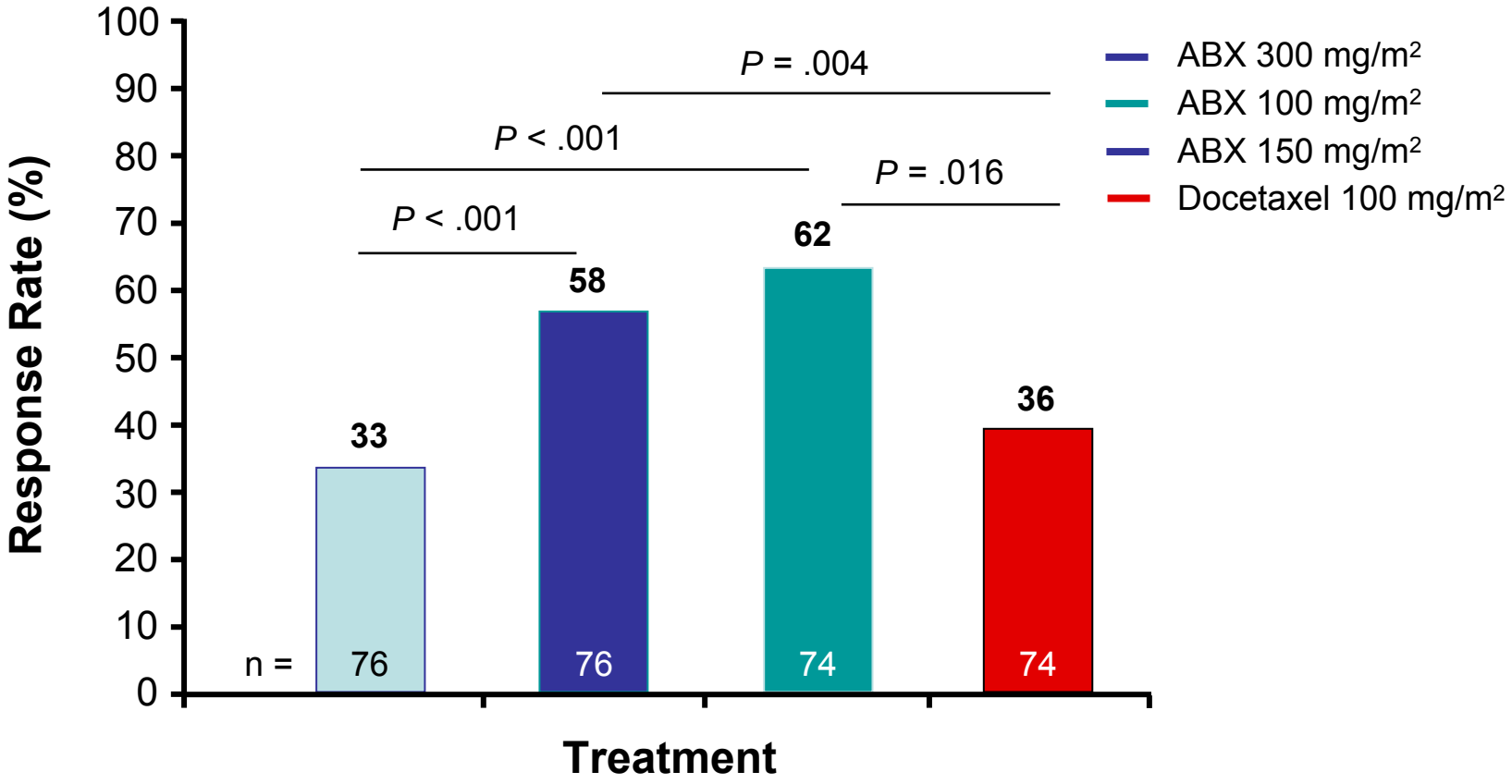
nab-Technologie
Randomisierte Phase II Studie



Gradishar W, et al. SABCS 2006. Abstract 46.

nab-Technologie

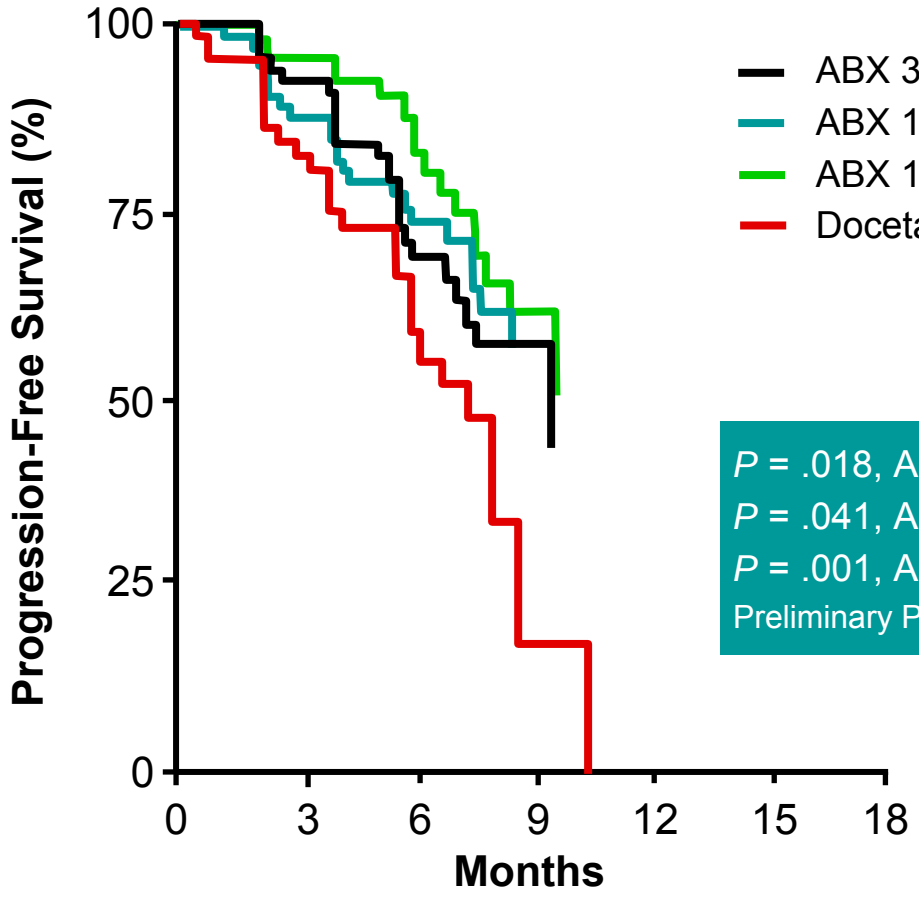
Randomisierte Phase II Studie



Gradishar W, et al. SABCS 2006. Abstract 46.

nab-Technologie

Randomisierte Phase II Studie



P = .018, ABX 300 mg/m² vs docetaxel
P = .041, ABX 100 mg/m² vs docetaxel
P = .001, ABX 150 mg/m² vs docetaxel
Preliminary PFS analysis (33% of potential events)

Gradishar W, et al. SABCS 2006. Abstract 46.

Stomatitis / Mukositis

Treatment Arm	p vs Doc	p vs (B)	Grade (%)			
			I	II	III	IV
nPac 300 mg/m^2 q3w (A)	<0.001	0.56	3			
nPac 100 mg/m^2 weekly (B)	<0.001		1			
nPac 150 mg/m^2 weekly (C)	<0.001	0.32				
Doc 100 mg/m^2 q3w (D)			**8**	**12**		

Gradishar W, et al. SABCS 2006. Abstract 46

Mamma-Ca: Update 2007
Zusammenfassung

- Mamma-Ca-Inzidenzabnahme in den USA: Grund: Rückgang von HRT?
- Tam reduziert Inzidenz von HR-pos. Mamma-Ca (20J.-Ergebnisse)
  Ral und Tam etwa gleich wirksam
- Stammzellkonzept:
  unterschiedlich proliferierende Mamma-Ca-Subgruppen (Ki67: 5 - >60%)
  Luminal A (ER+/PR+) / B (ER+/PR-),
  HER2,
  Basal-like (triple-neg),
- **Luminal A / B** (HR+)
  - HR+: Prämenopause: GnRH + (Tam / Chemo) = sign. Ergebnisverbesserung
  - HR+: Postmenopause: AI besser als Tam
    Cyp 2D6 extensive Metabolisierer: Tam besser als AI ?

Mamma-Ca: Update 2007
Zusammenfassung

- **HER 2+:**
  - Anthrazykline / Carboplatin + Taxane = gut wirksam
  - Trastuzumab: 1J. adjuvant: 2J-Ergebnisse: unverändert
  - HER2+ / HR+: AI + Trastuzmab wirksam (aber besser Chemo + Trast.)
  - HER2+ = vermehrt cerebrale Metast.
    Lapatinib bei Hirnfilliae begrenzt wirksam
    Lapatinib wirksam nach Trastuzumab + Chemo (Anthr + Taxane)
    Lapatinib-Wirkung beeinflusst durch Nahrungsaufnahme (↑), Grapefruit-Saft, Johanniskraut, Cyp 3A4, Carbamacepin ↓, Ketokonazol↑
- **Basal-like:**
  - Hohe proliferative Aktivität, hohe pCR-Quoten aber häufig Rezidive
  - Chemotherapie: Alkylantien, Platinderivate, Taxane, HD (?), PARP-I

Mamma-Ca: Update 2007

Zusammenfassung

- Individuelle Prognose-Einstufung
  durch Gen-Profiling besser ?
  - TailorX – Studie (Gen-Chip: OnkoType)
  - MINDACT – Studie (Gen-Chip: MammaPrint)
- Ln↑ → dosisdicht (HD)
- Bevacizumab verbessert 1st line Ergebnisse von Taxol
- Bevacizumab bei ER+ und HER 2 pos. besonders wirksam?
- nab-Technologie Bsp.: nab-Paclitaxel

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Universitätsmedizin Berlin

Mamma-Ca: Therapeutische Chancen

K. Possinger