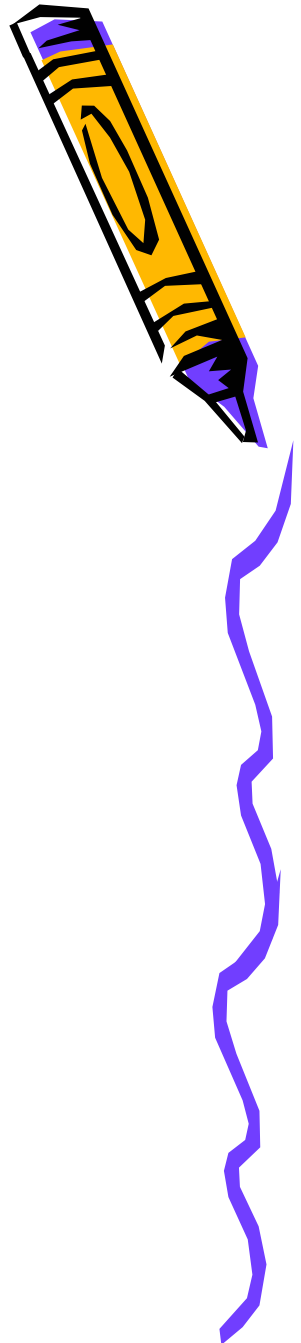


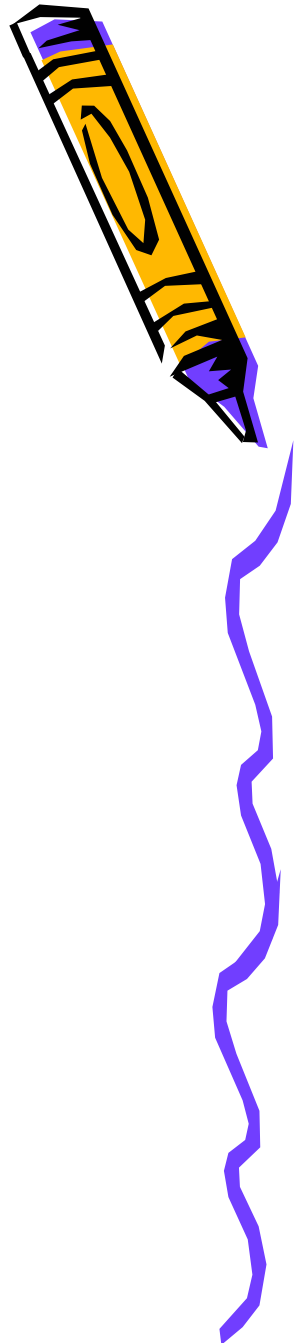
Adjuvante Therapie bei älteren Brustkrebspatientinnen

- Wer ist alt ?
- > 65 Jahre ?
- > 70 Jahre ?
- > 75 Jahre ?
- oder > 85 bzw jünger bei
signifikanter Komorbidität ?



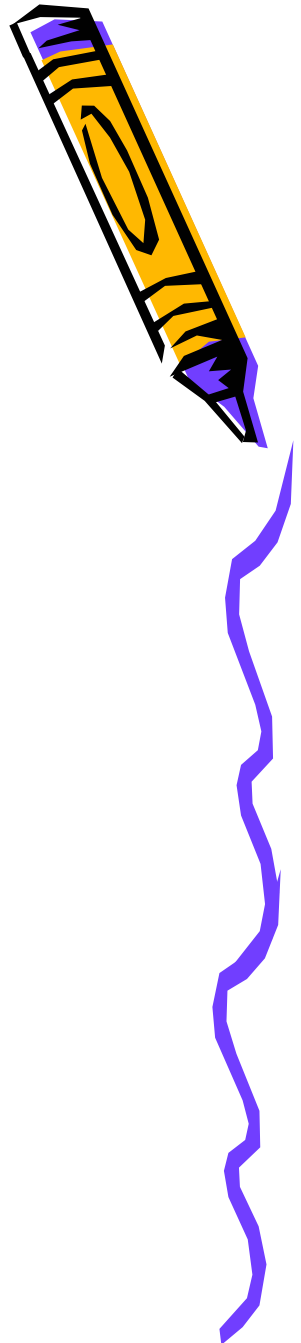
Wie lang ist die Lebenserwartung der Patientin ?

- z.b. mit 75 Jahren ?
- ...
- oder mit 85 Jahren ?
- ...

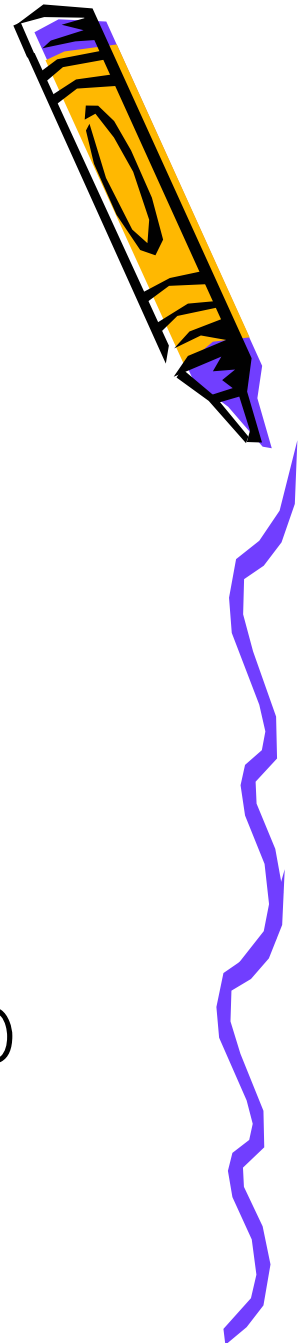


Wie beurteile ich die Belastbarkeit der Patientin für die geplante Therapie ?

- Charlson Comorbidity Index
- ECOG Skala
- Funktionstests (ADL/AIDL)
- Persönlicher Eindruck ?
- NCCN assessment



Woraus besteht eine adjuvante Therapie bei diesen Patientinnen ?



- Antihormonelle Therapie (TAM vrs Aromatasehemmstoff)
- Chemotherapie (Anthracyclin/Taxan/ CMF)
- Herzeptin
- Radiatio
- Alternative Therapieverfahren (Mistel, Vitamine/Spurenelemente)
- Begleitende Therapieverfahren (Lebensführung)



Tamoxifen for Early Breast Cancer

<u>Age</u>	<u>Recurrence</u>	<u>Mortality</u>
<50	45% (SD 8)	32% (SD 10)
50-59	37% (SD 6)	11% (SD 8)
60-69	54% (SD 5)	33% (SD 6)
>70	47% (SD 3)	34% (SD 13)

Tamoxifen for Early BC: An Overview of Randomized Trials

EBCTG; Lancet 1998; 351: 1451

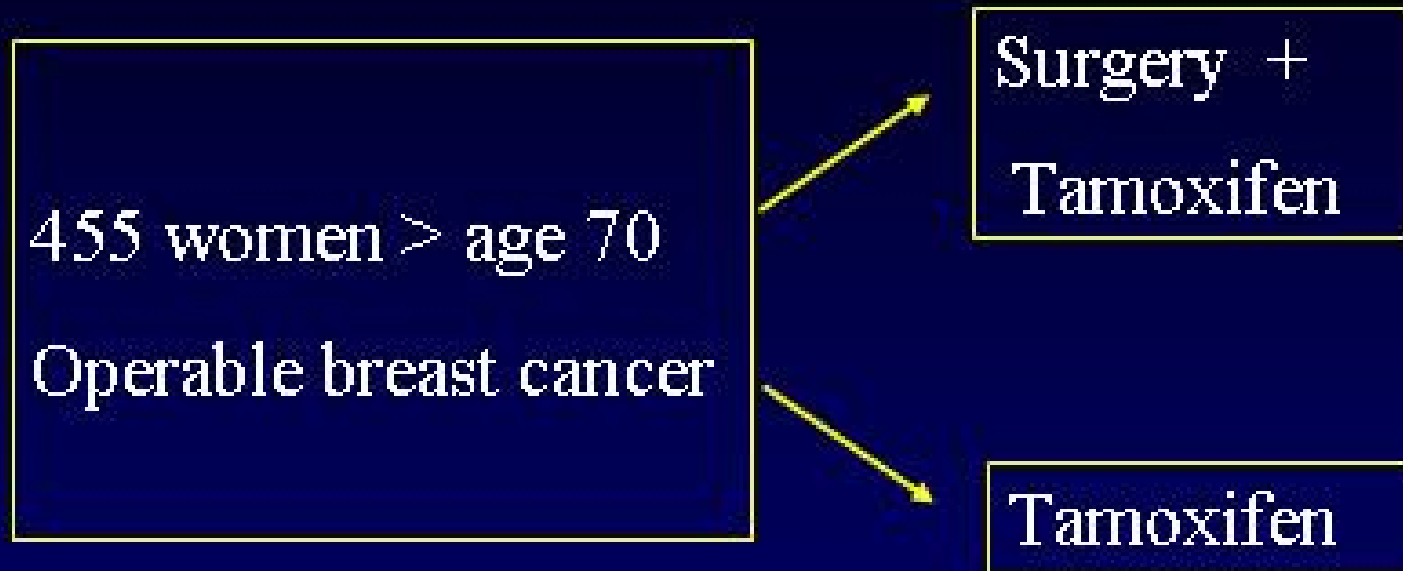
Key Aromatase Inhibitor Trials

All Favor AI Arm

Trial	Design	F/U	n	Δ DFS
ATAC	A v T v AT	5 yr	9366	2.5-3.0%
BIG 1-98	T v Let	~ 2 y	8028	~ 2%
IES	T>E v T	~ 3 yr	4742	~ 5%
ARNO	T>A v T	~ 3 yr	3214	3%
MA 17	L v Placebo	~ 4 yr	5187	~5%

No overall survival Δ except MA-17 N+

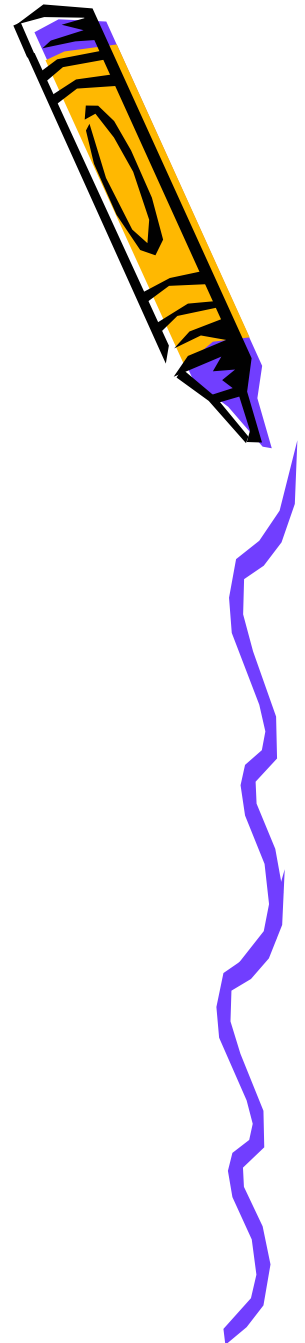
Breast Cancer in Women > 70: Surgery Improves Survival



Results: ↑ Breast Cancer Mortality with No Surgery

HR 1.68 (95%CI =1.15-2.47)

Antihormonelle Therapie Nebenwirkungen



- Tamoxifen: cave Thrombosen, Endometriumkarzinom
- Aromatasehemmstoffe: Cave Osteoporose, Gelenkbeschwerden
- Kognitive Funktion ?



Poly-Chemotherapy for Early Breast Cancer: Early Breast Cancer Trialists' Collaborative Group

➤ Only 1224 women > age 70

“These trials of chemotherapy involved too few women older than 70 years of age to be reliably informative as to whether it confers any net survival benefit among them.”

Poly-Chemotherapy for Early Breast Cancer

<u>Age</u>	<u>Recurrence</u>	<u>Mortality</u>
<40	40% (SD 6)	29% (SD 7)
40-49	36% (SD 4)	30% (SD 5)
50-59	23% (SD 3)	15% (SD 4)
60-69	13% (SD 3)	9% (SD 4)
≥70	12% (SD 11)	13% (SD 12)

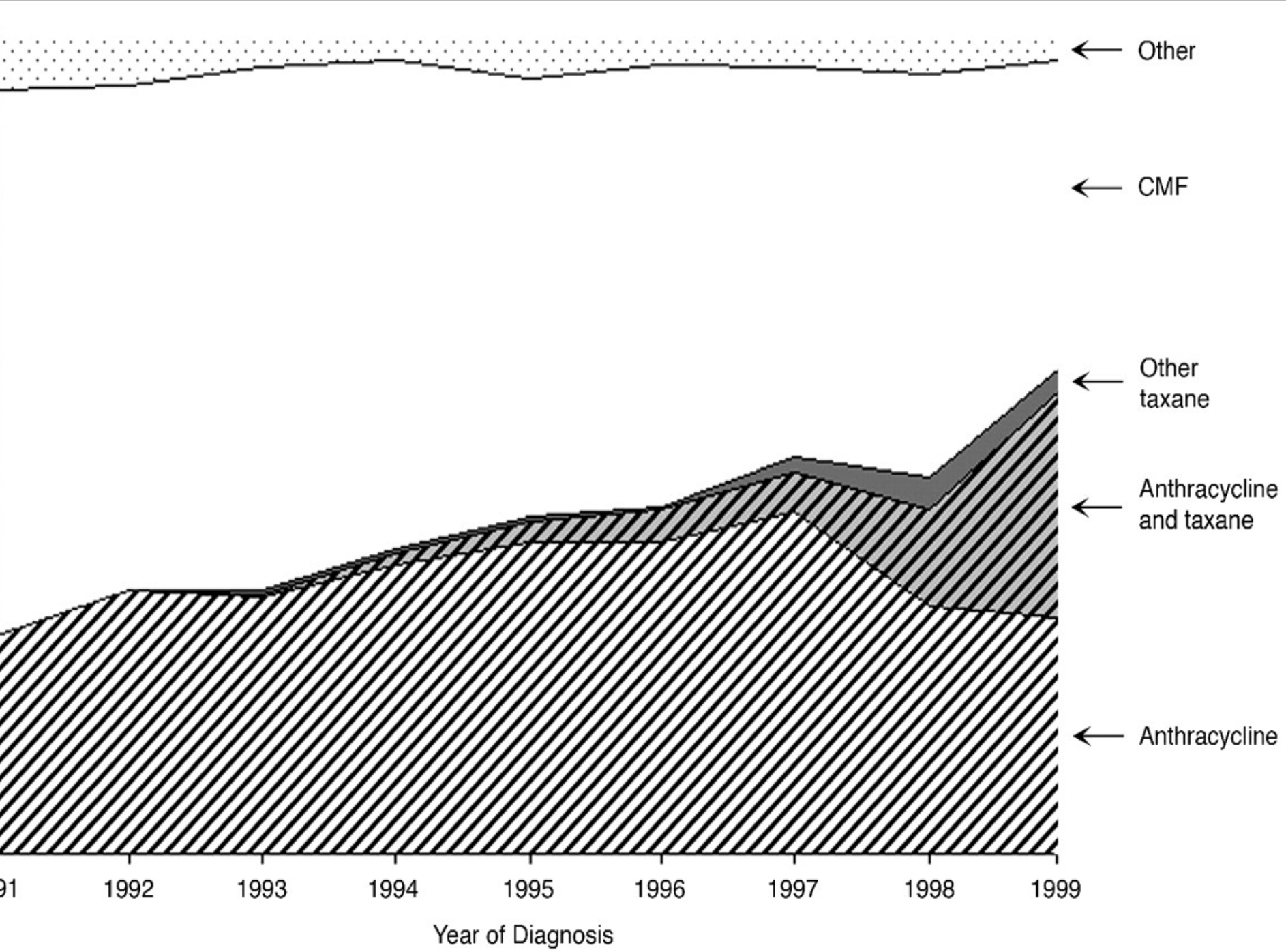
EBCTCG, Lancet 2005; 365: 1687-171

Giordano et al JCO 2006 use and outcomes of adjuvant chemotherapie in older women with breast cancer



- Medicare -linked- database - Alter > 65 J, Stadium I-III, zwischen 1991-1999, insgesamt 41,390 eingeschlossen, Chemotherapie erhielten 7,4% 1991 , 16,3 % 1999.
- Patientinnen mit lymphknotenpositiven, rezeptornegativen Mammakarzinomen profitierten signifikant (HR 0,72)





adjuvantonline.com

Berechnungsbeispiele

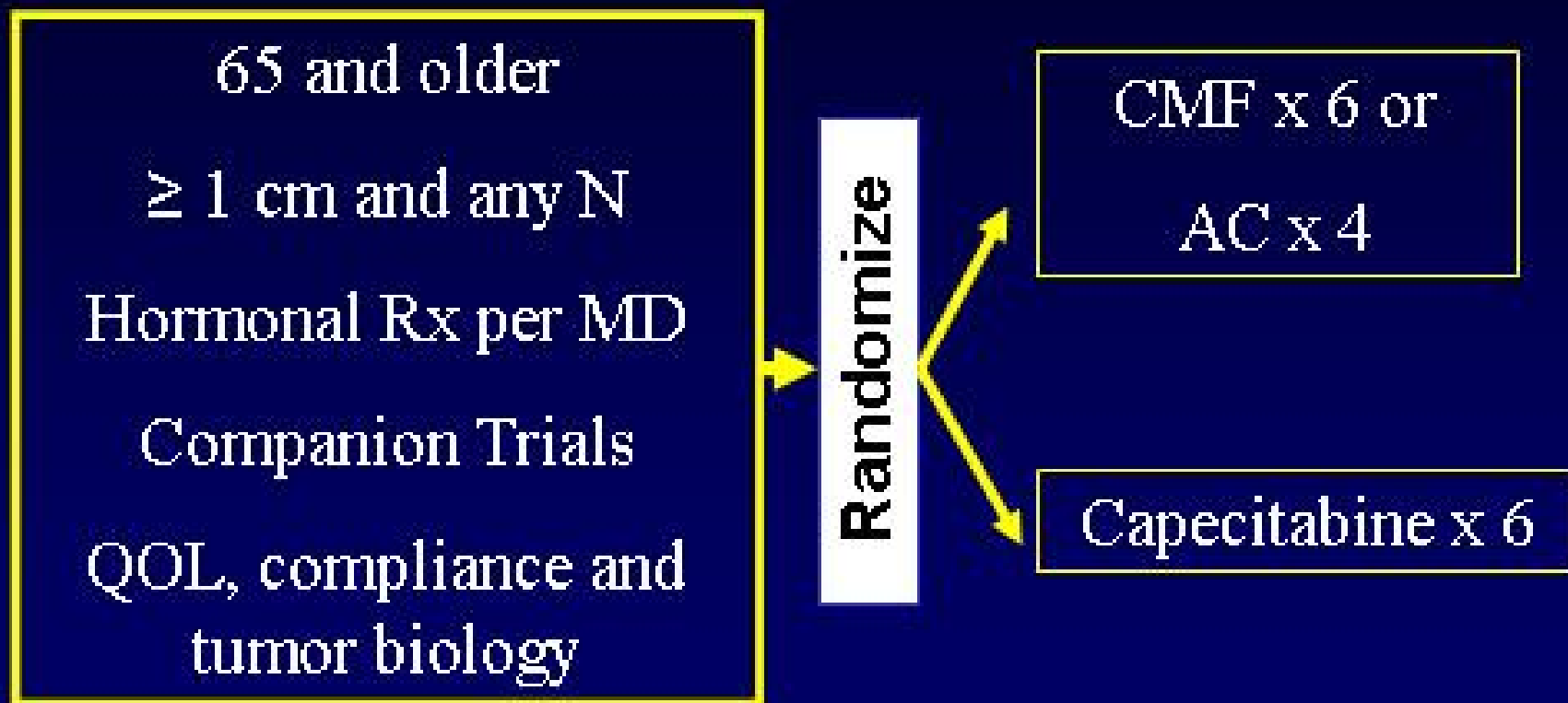


- 80 J, geringe Komorbidität, positive Hormonrezeptoren, G3, Tumorgröße 1-2 cm, Lymphknoten nicht betroffen : Ohne Therapie leben nach 10 Jahren 46,5 %, davon sind etwa 10% am Mammakarzinom verstorben, 43% aus anderen Gründen. Antihormonelle Therapie bringt 2,4 %, Chemo 2%
- 80 J, geringe Komorbidität, negative Hormonrezeptoren, G3, Tumorgröße 2-3 cm, Lymphknoten nicht betroffen : Benefit der Chemotherapie: 5%
- 80 J, altersentsprechende Komorbidität, negative Hormonrezeptoren, G3, Tumorgröße 2.3 cm, 1-3 Lymphknoten betroffen: Benefit der Chemotherapie 6%



Adjuvant Trial for Older Patients

CALGB-CTSU 49907



Equivalence = 5 year OS 60% CMF or CA vs > 52% capecitabine

Anthracycline Related Cardiac Dysfunction

- Associated with age, heart disease, radiation
- Characterized by global myocardial hypokinesis
- Manifested by decreased LVEF
- Onset of CHF may be acute or appear years after treatment
- Incidence 4% to >36%, potentially irreversible



Incidence* of a $\geq 10\%$ Decrease in Cardiac Function Relative to Baseline

Time (mo)	CEF			CMF		
	N	>20 %	10-20 %	N	>20 %	10-20 %
6	291	0.7	18.6	296	0.7	8.5
12	270	1.5	17.0	286	1.4	8.0
36	185	4.3	22.2	172	1.2	9.9
60	139	5.0	20.1	144	0.7	8.3

* expressed as percentages

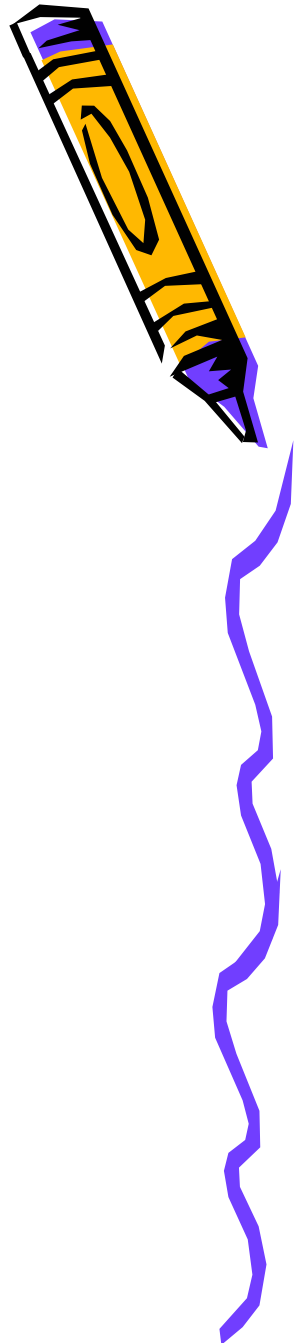
Cumulative Incidence of Cardiac Events After Paclitaxel*

	AC->T		AC->T->H		AC->TH->H	
	RT	No RT	RT	No RT	RT	No RT
After Paclitaxel	N=487	N=184	N=529	N=186	N=417	N=154
6 mo	0%	0%	1.3%	1.1%	1.4%	5.2%
1 yr	0%	0%	2.1%	1.7%	1.7%	5.9%
2 yrs	0%	0%	2.5%	2.9%	1.7%	5.9%
3 yrs	0%	0.8%	2.5%	2.9%	1.7%	5.9%
4 yrs	1.5%	0.8%	2.5%	2.9%	1.7%	5.9%

*Among those with satisfactory post AC LVEF, on study before 4/25/2004, and cardiac event & progression free at end of paclitaxel

Chemotherapie Nebenwirkungen

- Akuttoxizität : Haarverlust, Übelkeit, Kardiotoxizität, Verschlechterung des Allgemeinzustandes und kognitive Störungen, Polyneuropathie, Muskelschmerzen, Cystitis
- Langzeittoxizität: Kardiotoxizität, kognitive Störungen, Polyneuropathie, Sekundärneoplasien



ADJUVANT TRASTUZUMAB (T) TRIAL "BACKBONE" DESIGN

**Women with HER2
3+ (IHC) or FISH +
Disease**

Confirmed by central lab
or approved by ref. lab

Age ≥ 70

Uncontrolled HTA

~~Angina pectoris or arrhythmia
on medications~~

~~Hx of MI, CHF~~

~~Small node -
ER/PR + tumors~~

N=13,365

R
A
N
D
O
M
I
Z
E

Chemotherapy
No trastuzumab



Chemotherapy
and trastuzumab



Variables in
the 5 trials

- Type of chemotherapy
- Timing of T initiation
- Schedule of T administration
- Duration of T administration

ADJUVANT TRASTUZUMAB TRIALS :

Patient characteristics

SIMILARITIES

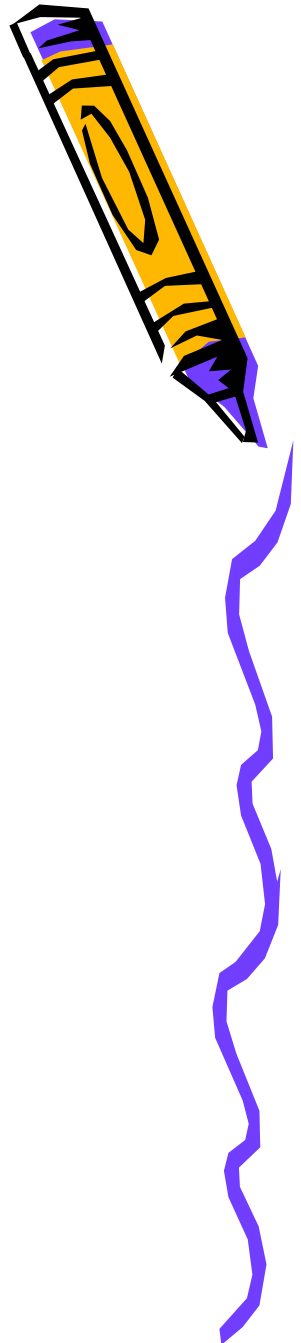
- **Median age** : **51-52 years**
 - **Proportion of grade 3 tumors** : **60-69 %**
 - **Planned endocrine therapy** : **46-54 %**
-

ADJUVANT TRASTUZUMAB TRIALS : KEY MESSAGES FOR DAILY PRACTICE (II)

- **Quality of HER-2 testing is essential for patient selection**
- **The benefit versus harm ratio of each adjuvant trastuzumab regimen needs to be evaluated for each individual woman; it remains unknown for women with cardiac risk factors, age about 70 and / or small (≤ 1 cm) node negative cancers**

Nebenwirkungen von Herzeptin

- Kardiotoxizität,
insbesondere in
Kombination mit
Anthrazyklinen, evtl
reversibel



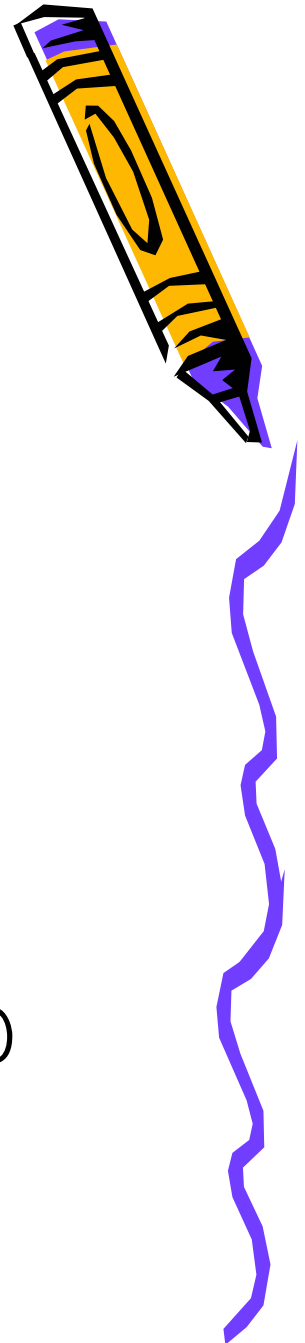
Radiotherapie



- Risikoabschätzung : Z.b.Tumorgröße > 3 cm ,
Lymphknotenbefall > 3 ?
- Dagegen Tumor kleiner als 2 cm,
Hormonrezeptorpositivität, Lymphknoten nicht
befallen: Minderung des Rezidivrisikos bei
Radiatio nach brusterhaltender Therapie etwa von
4 % auf 1% ? (Hughes et al 2004)
- Neue Therapieverfahren ?



Woraus besteht eine adjuvante Therapie bei diesen Patientinnen ?



- Antihormonelle Therapie (TAM vrs Aromatasehemmstoff)
- Chemotherapie (Anthracyclin/Taxan/ CMF)
- Herzeptin
- Radiatio
- Alternative Therapieverfahren (Mistel, Vitamine/Spurenelemente)
- Begleitende Therapieverfahren (Lebensführung)

