

**ENDOCRINE RESPONSIVENESS
AND TAILORING ADJUVANT
THERAPY FOR POSTMENOPAUSAL
LYMPH NODE NEGATIVE BREAST
CANCER: A RANDOMIZED TRIAL**

International Breast Cancer Study Group
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In the past...

- IBCSG Trial VI: 3 courses of classical CMF are similar to 6 in terms of DFS and OS for premenopausal N+ breast cancer



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In the past...

- IBCSG Trial VII: 3 courses of classical CMF added to Tam improve DFS compared with Tam alone for postmenopausal N+ breast cancer



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IBCSG IX: Aims of the study

Compare

- 3 courses of chemotherapy (classical CMF) followed by Tamoxifen up to 5 years
- Tamoxifen alone for 5 years
 - DFS
 - patterns of relapse
 - overall survival
 - quality of life

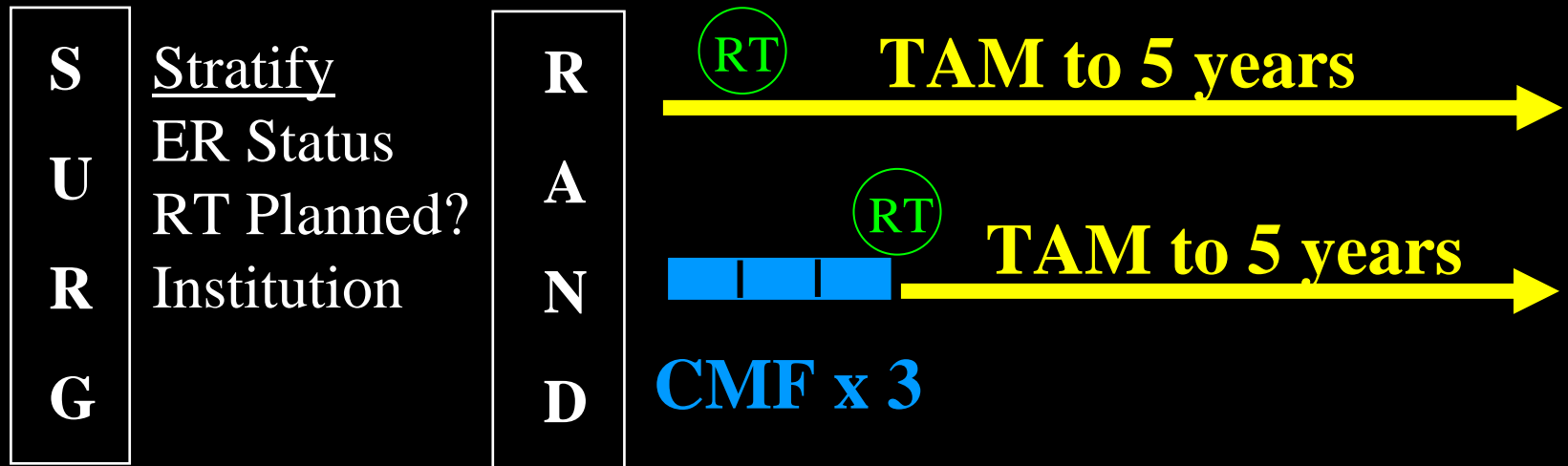


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Trial IBCSG IX

Postmenopausal Node Negative



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Inclusion criteria

- Postmenopausal
- Unilateral operable breast cancer
- Node negative
- Receptor status determined
- Adequate organ function
- No prior or concomitant malignancy



Patient characteristics

- From October 1988 to August 1999
 - **1715 patients randomized**
 - **1669 patients (97%) eligible**
 - Ineligibility: Premenopausal status, incorrect stage (in situ only, T4 or N+), inadequate surgery (involved margins without re-excision), previous malignancy



Patient characteristics

	Tam	CMF→Tam
Age median	61	60
ER-	22%	23%
ER+	73%	72%
ER?	4%	4%



Patient Characteristics

	Tam	CMF→Tam
Mx	49%	50%
Breast cons.	51%	50%
Tumor ≤ 1 cm	11%	13%
Tumor 1.1-2.0cm	47%	47%
Tumor > 2 cm	39%	37%
Tumor unknown	3%	3%



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Toxicity

- 2 CMF-related deaths (0.2%)
 - cardiac failure and infection (CMF-related)
- 3 Tamoxifen-related deaths (0.2%)
 - PE, MI, probable CVA



Sites of first failure

Median follow-up = 6 years

	Tam	CMF→Tam	Total
Soft tissue	5.5%	3.7%	4.8%
Bone \pm soft	2.0%	1.9%	2.0%
Viscera	5.6%	4.9%	5.2%
2 nd tumor (all)	4.2%	4.0%	4.1%
† \emptyset relapse	2.3%	2.3%	2.3%
	19.6%	16.8%	18.2%



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Sites of first failure—ER-

Median follow-up = 6 years

	Tam	CMF→Tam	Total
Soft tissue	7.8%	5.8%	6.7%
Bone ± soft	1.1%	1.0%	1.0%
Viscera	12.1%	7.3%	9.7%
2 nd tumor (all)	5.8%	1.5%	3.6%
† ∅ relapse	3.2%	1.6%	2.4%
	30.0%	17.2%	23.6%



Sites of first failure—ER+

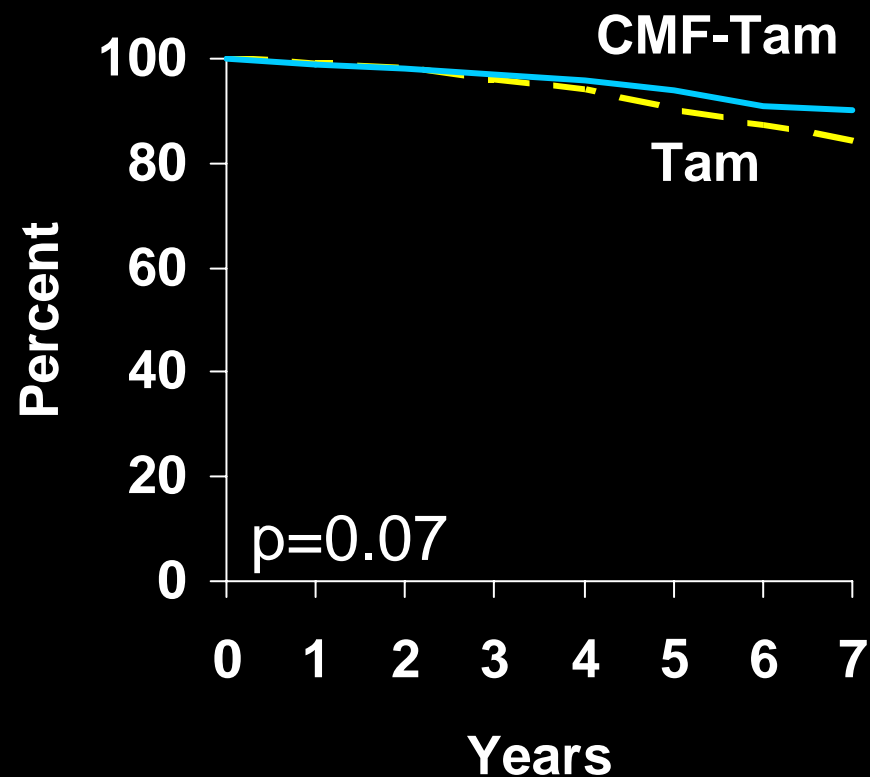
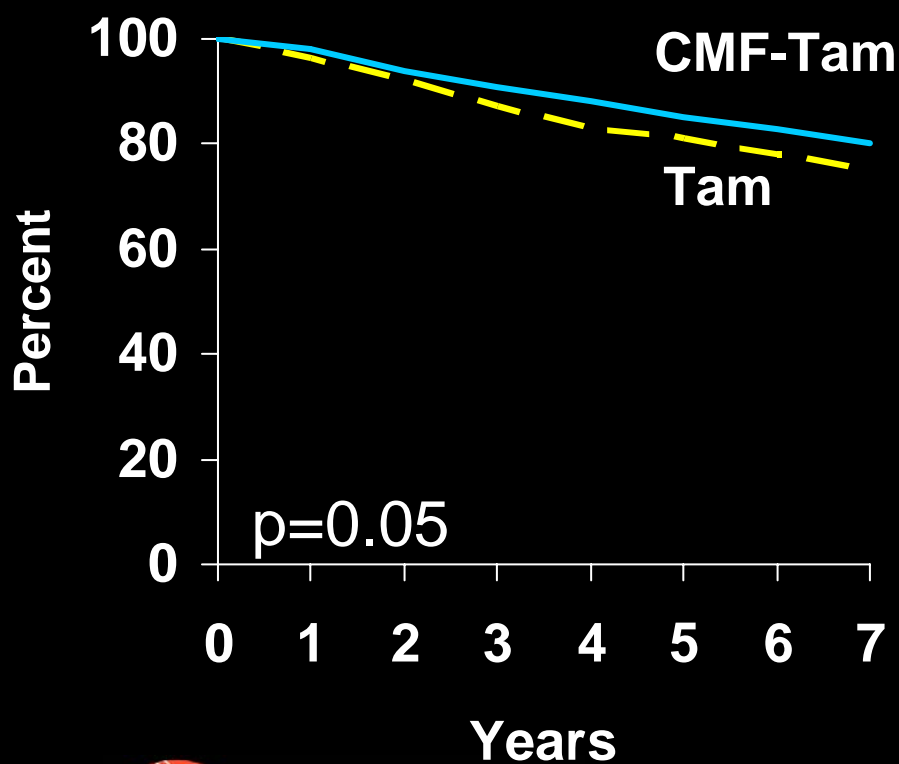
Median follow-up = 6 years

	Tam	CMF→Tam	Total
Soft tissue	4.7%	3.0%	3.8%
Bone \pm soft	2.1%	2.4%	2.2%
Viscera	3.5%	4.4%	3.9%
2 nd tumor (all)	3.7%	4.8%	4.1%
† \emptyset relapse	2.1%	2.4%	2.2%
	16.3%	17.0%	16.6%



All Patients (n=1669)

DFS OS



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DFS and OS according to ER

Prospective stratification by ER-status.

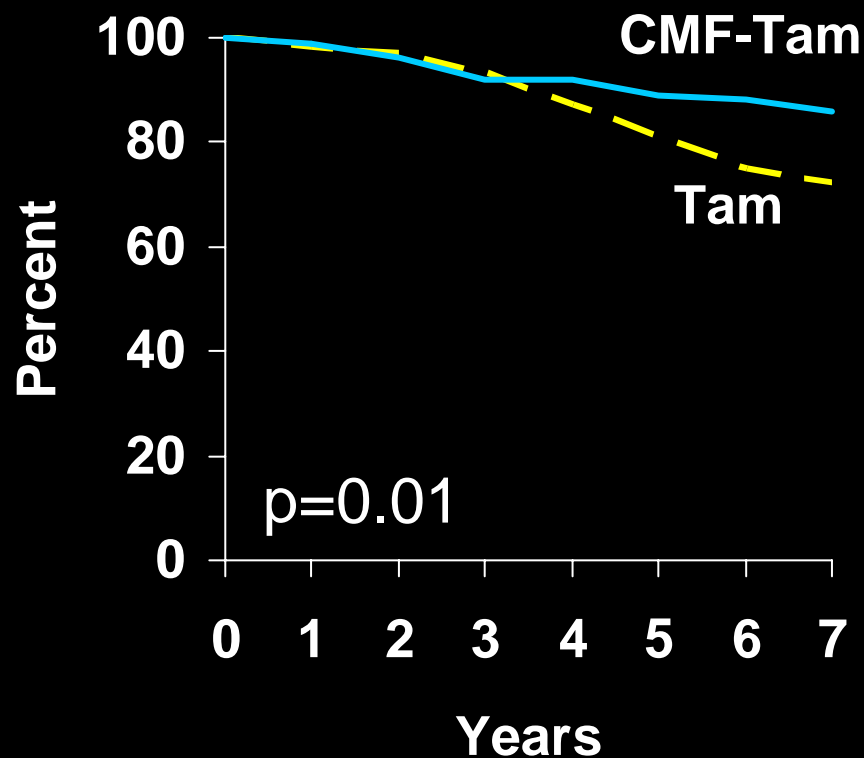
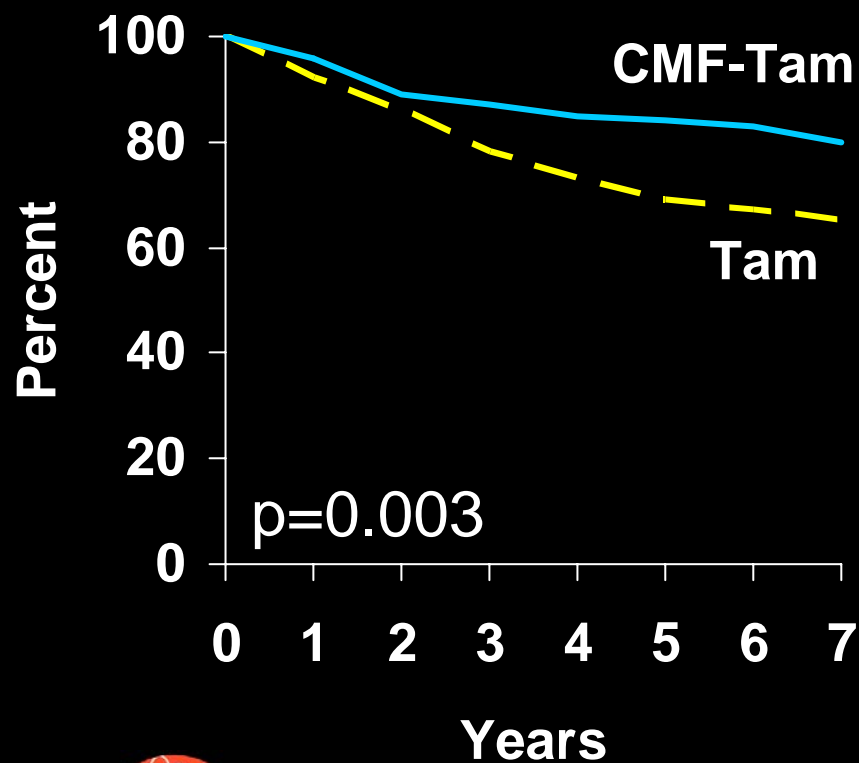
Outcome for CMF → Tam vs. Tam was significantly different according to ER.

- DFS ($p=.01$, test for interaction)
- OS ($p=.07$, test for interaction)



ER Negative (n=382)

DFS OS

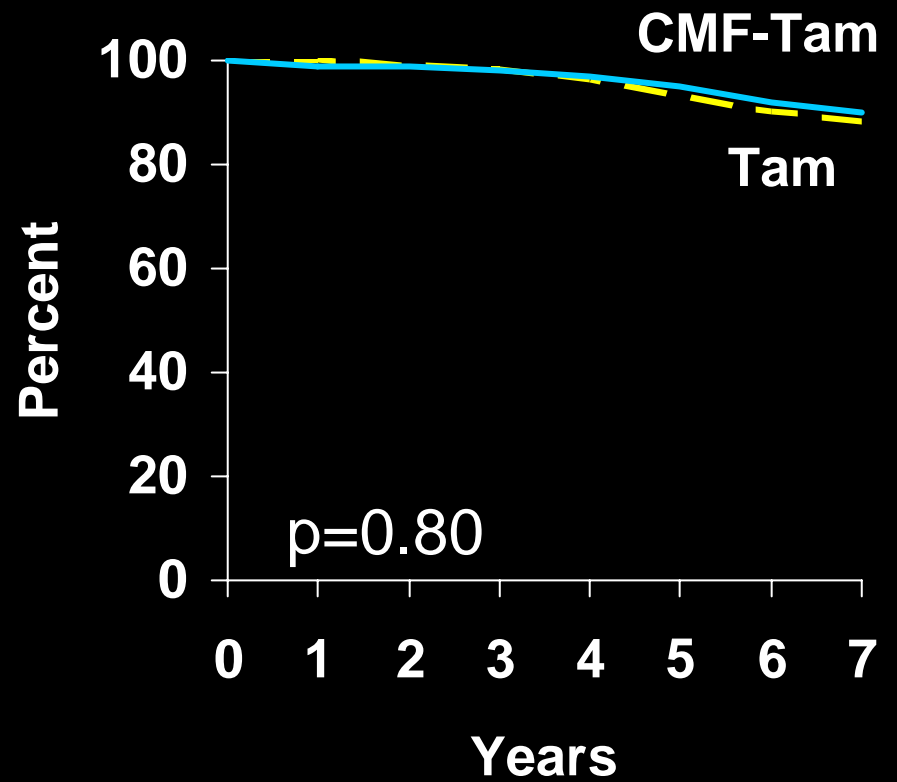
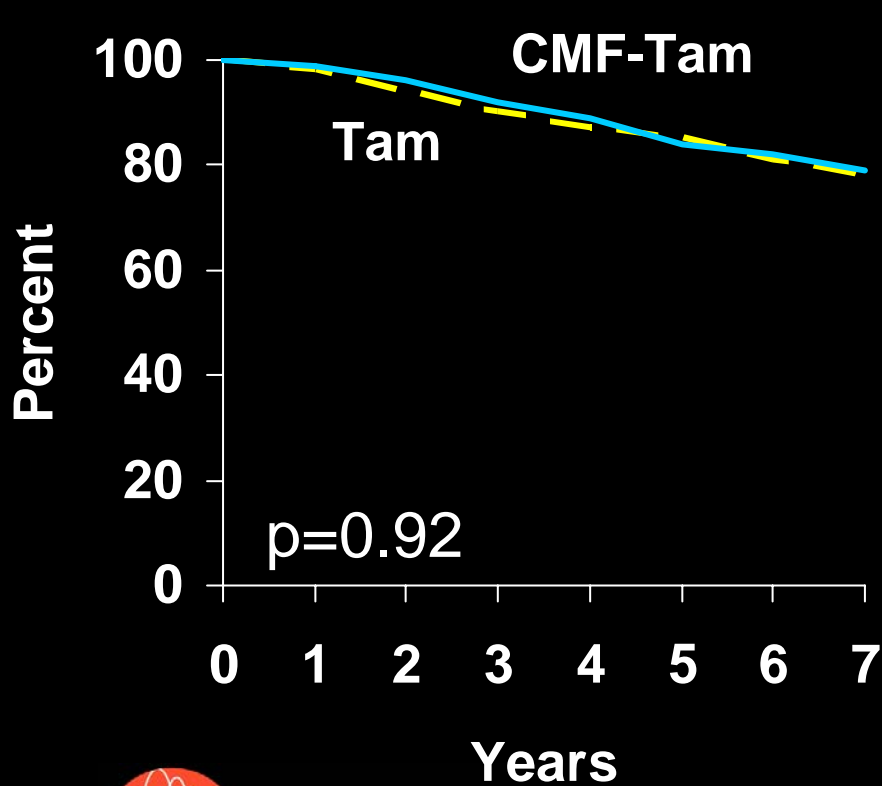


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ER Positive (n=1217)

DFS OS



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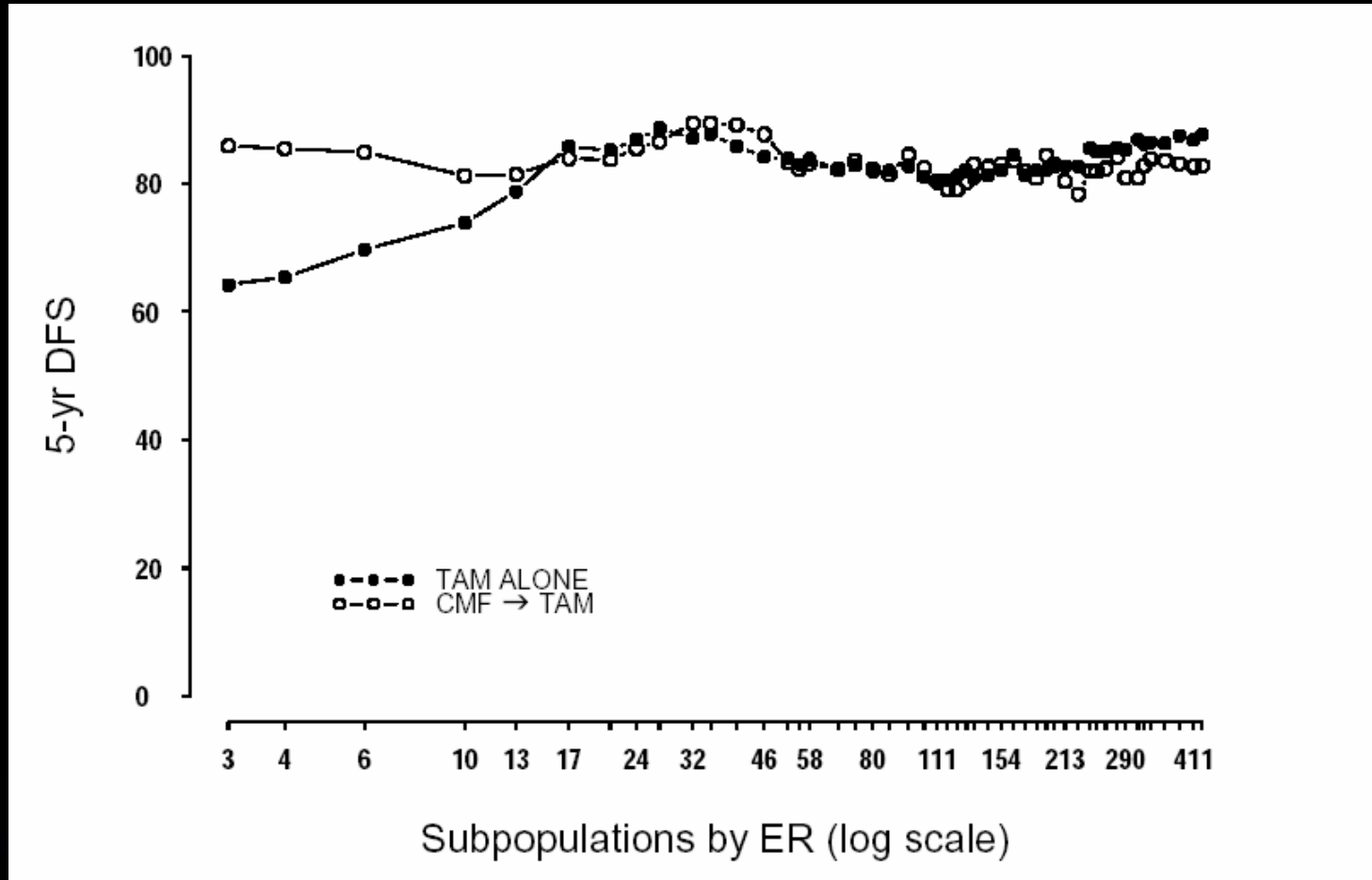
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DFS and OS according to ER

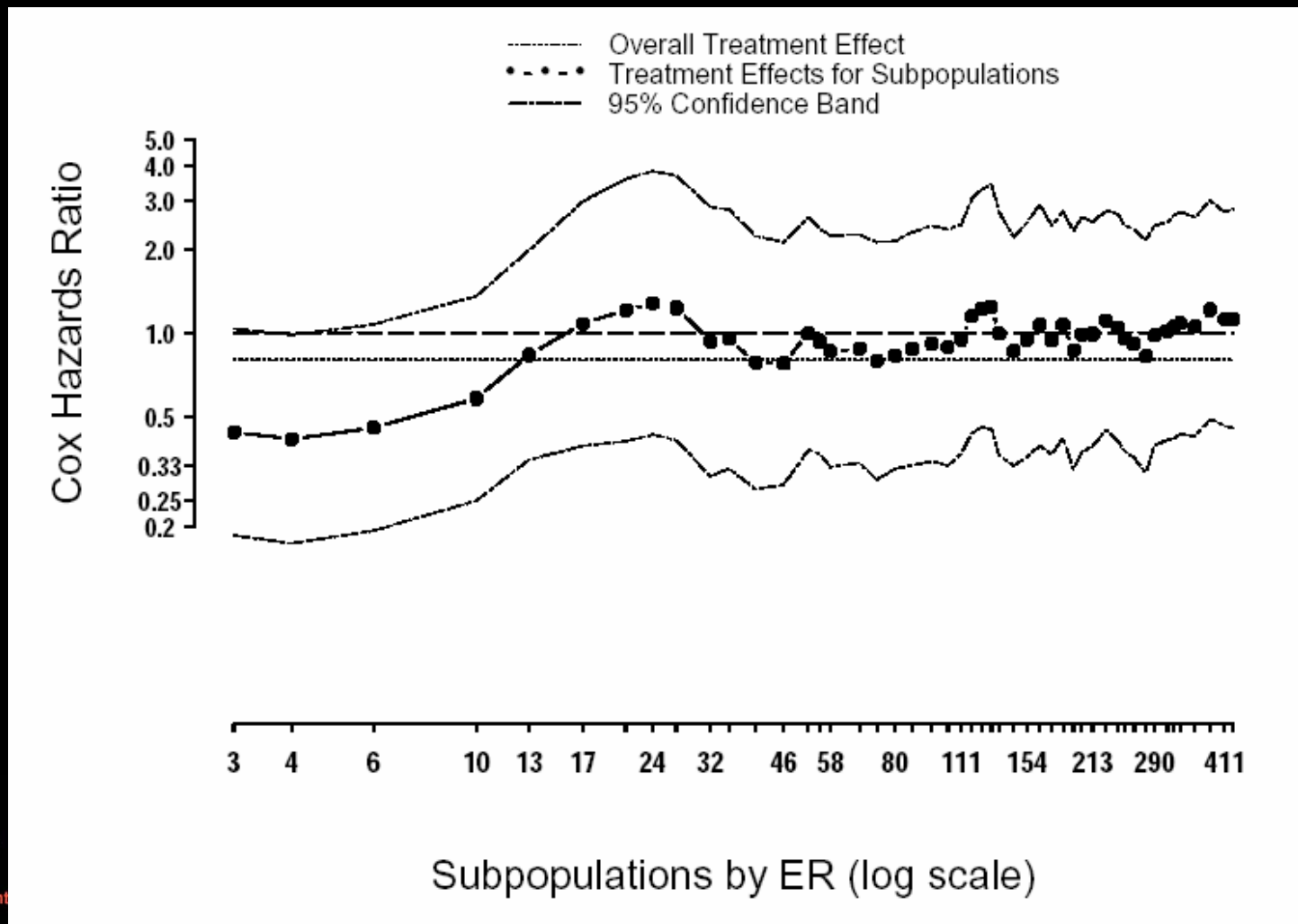
	Tam	CMF→TAM
5-year DFS		
ER Negative	69%	84%
ER Positive	85%	84%
5-year OS		
ER Negative	81%	89%
ER Positive	93%	95%



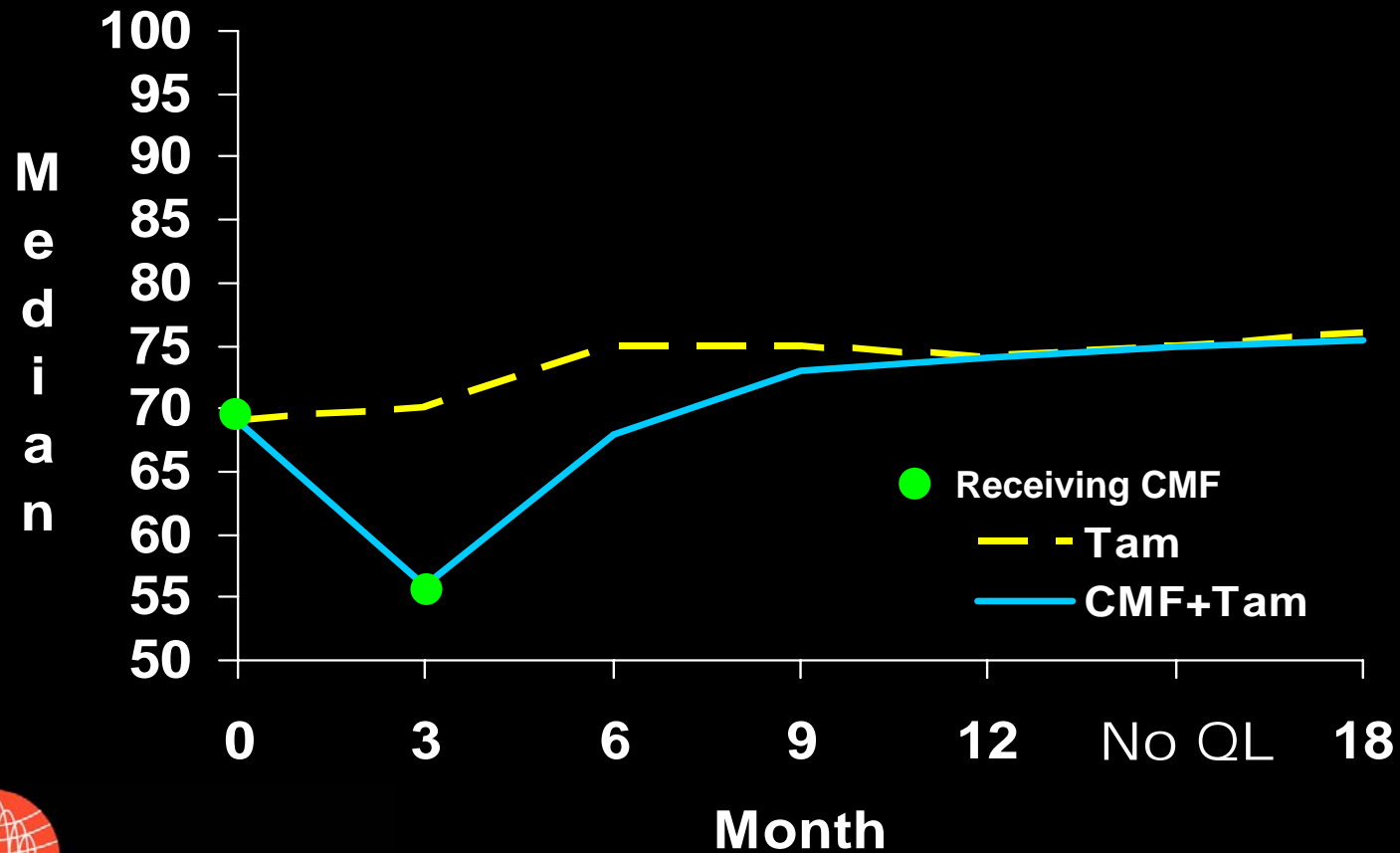
Subpopulation Treatment Effect Pattern Plot (STEPP)--DFS



Subpopulation Treatment Effect Pattern Plot (STEPP)--RR



Median Tiredness by Treatment (excluding failures)



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Conclusions

- For postm. patients with N- disease:
 - Substantial benefit from adjuvant CT if tumor is ER- (endocrine non-responsive)
 - No benefit from chemo-endocrine vs. endocrine alone for ER+ (endocrine responsive)





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