

Ösophagus-Karzinom:

Adenokarzinom versus Plattenepithelkarzinom

Vorgehen bei lokal fortgeschrittenen Tumoren

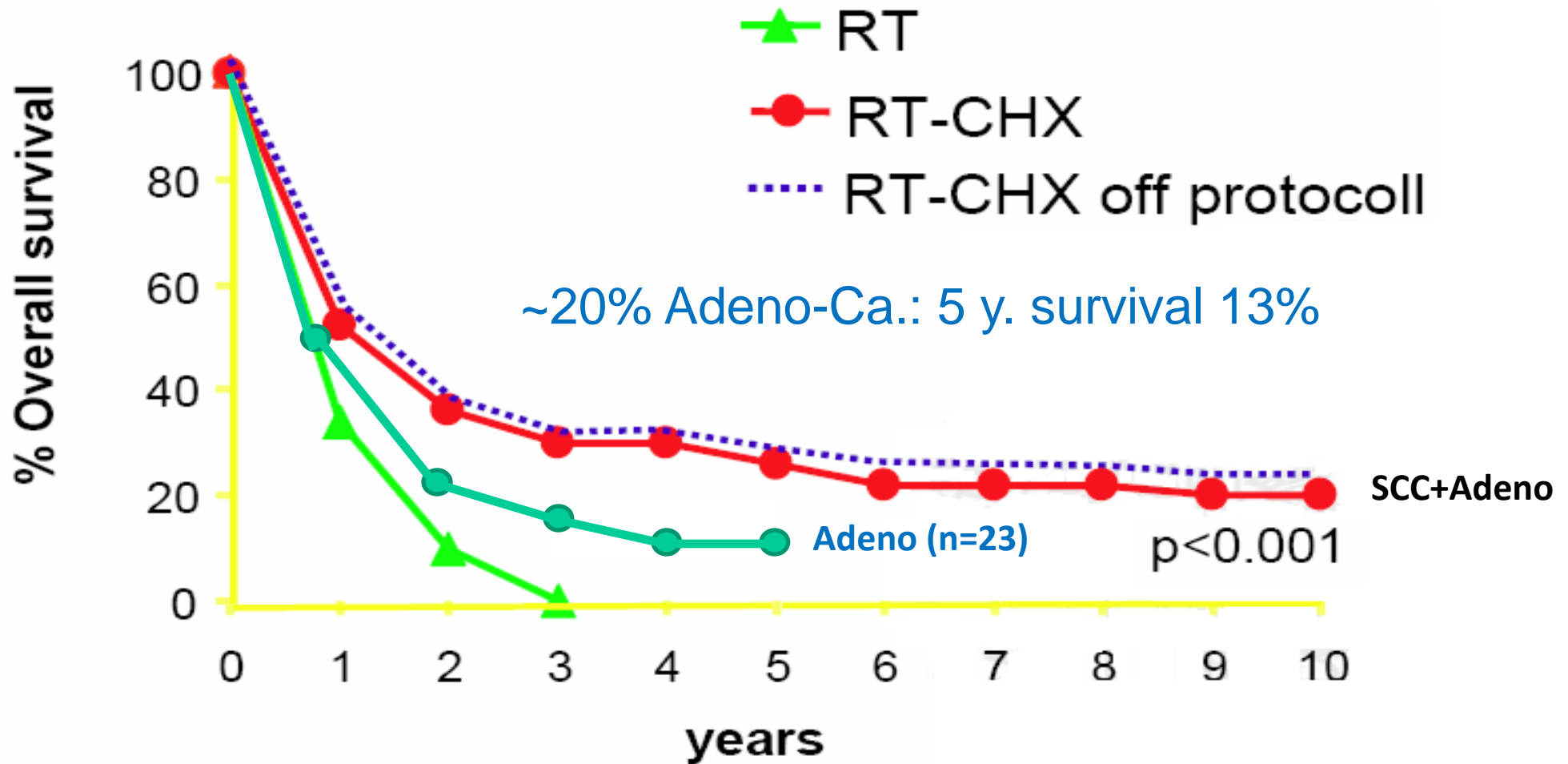
- aus strahlentherapeutischer Sicht



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Radiotherapy vs. Chemoradiation in non surgical treated esophageal cancer



Herskovic et al. NEJM 1992

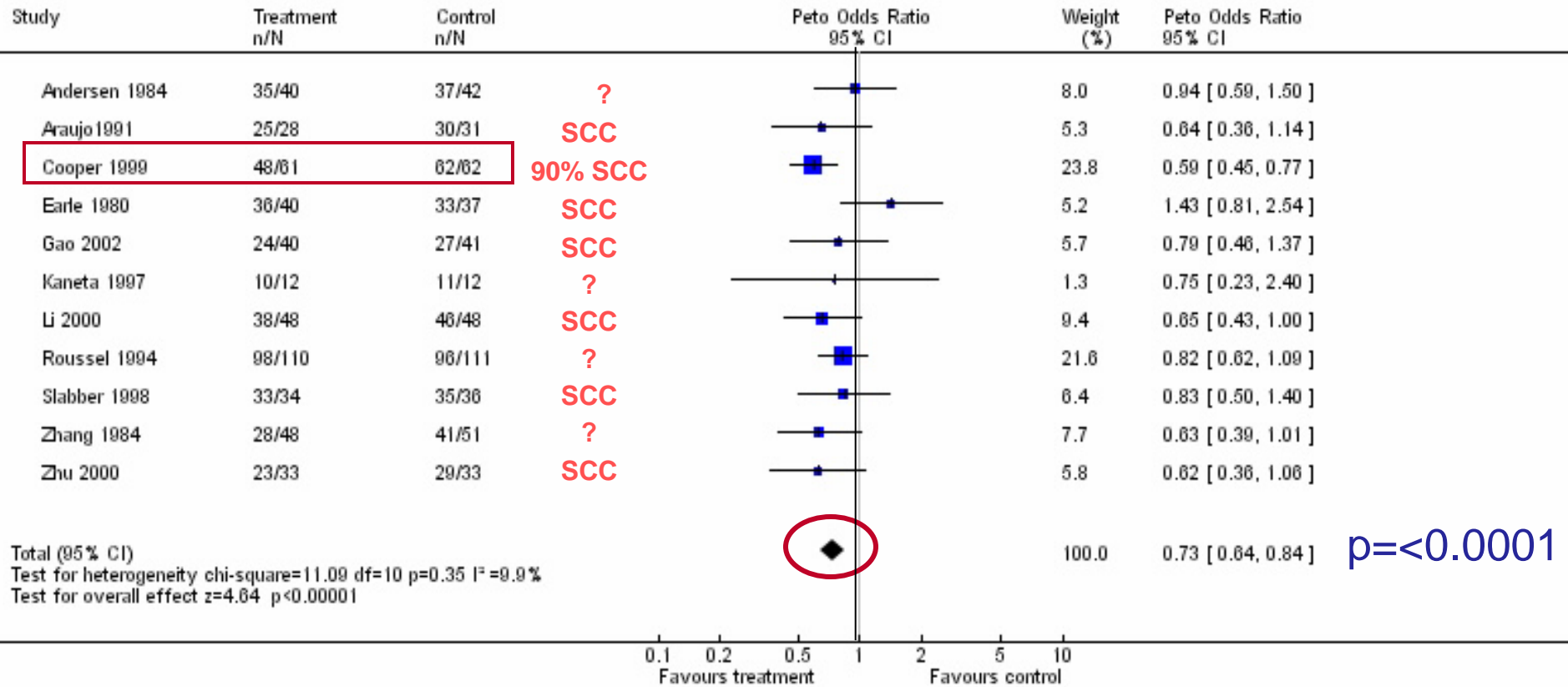
Update: Cooper et al. JAMA 1999

Esophageal Cancer -Radiochemotherapy

Radiation and Chemotherapy -- concomitant

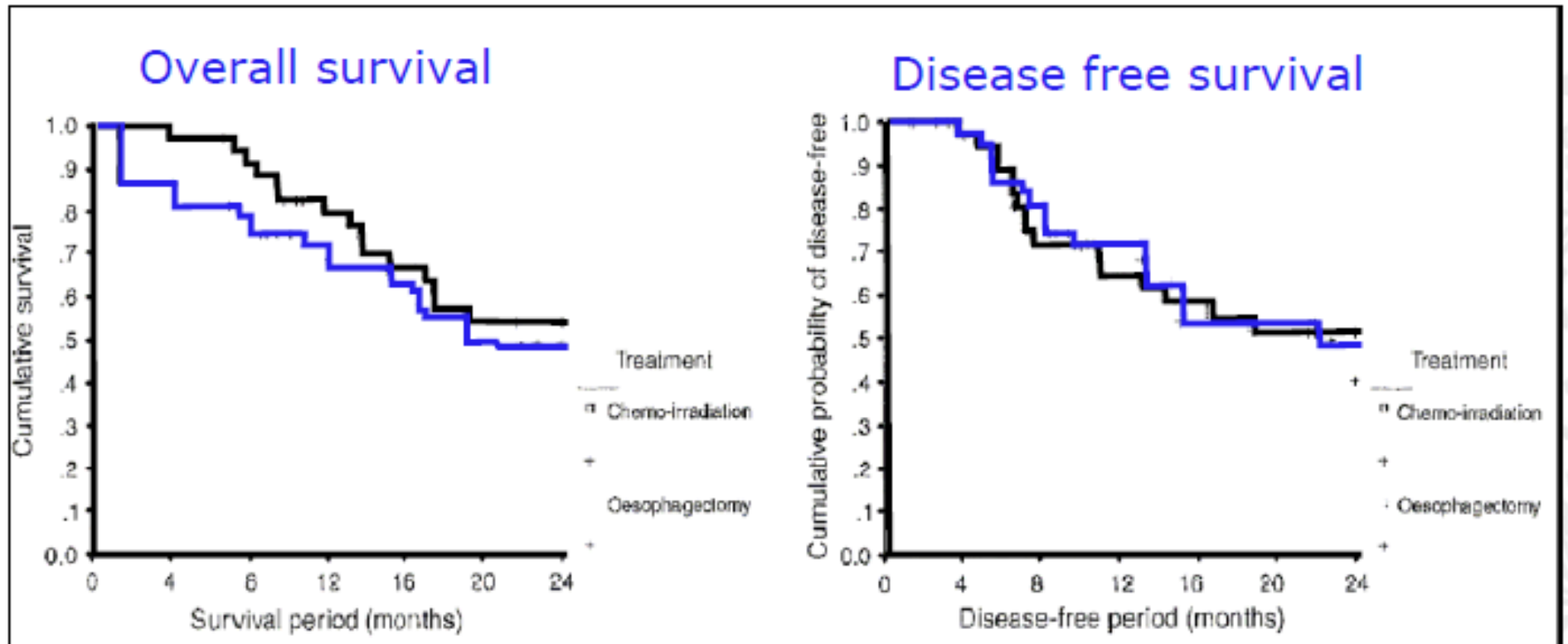
Overall survival -- concomitant treatment

Outcome: 01 HR OAS (concomitant)



Esophageal-Ca. (SCC): RT-CHX vs. Surgery

Randomized trial n=80 (Hong Kong)



Chiu et al. J Gastro Intest Surg 2006

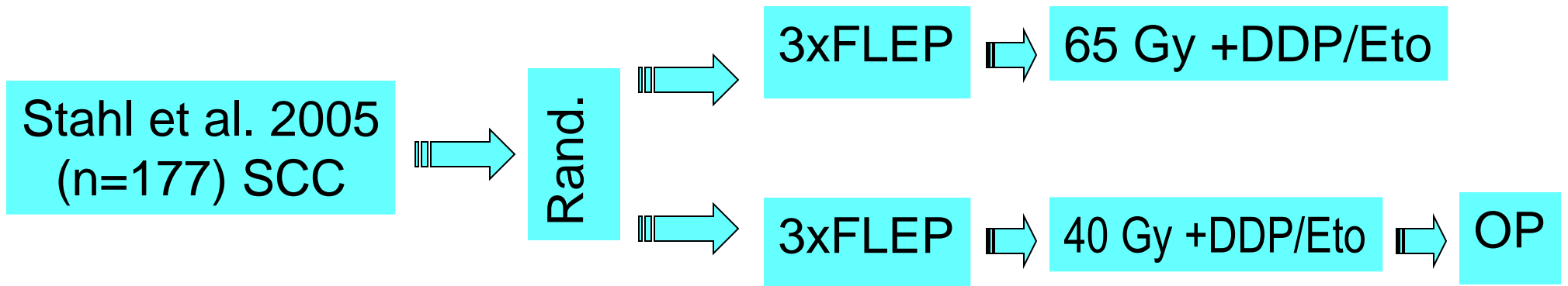
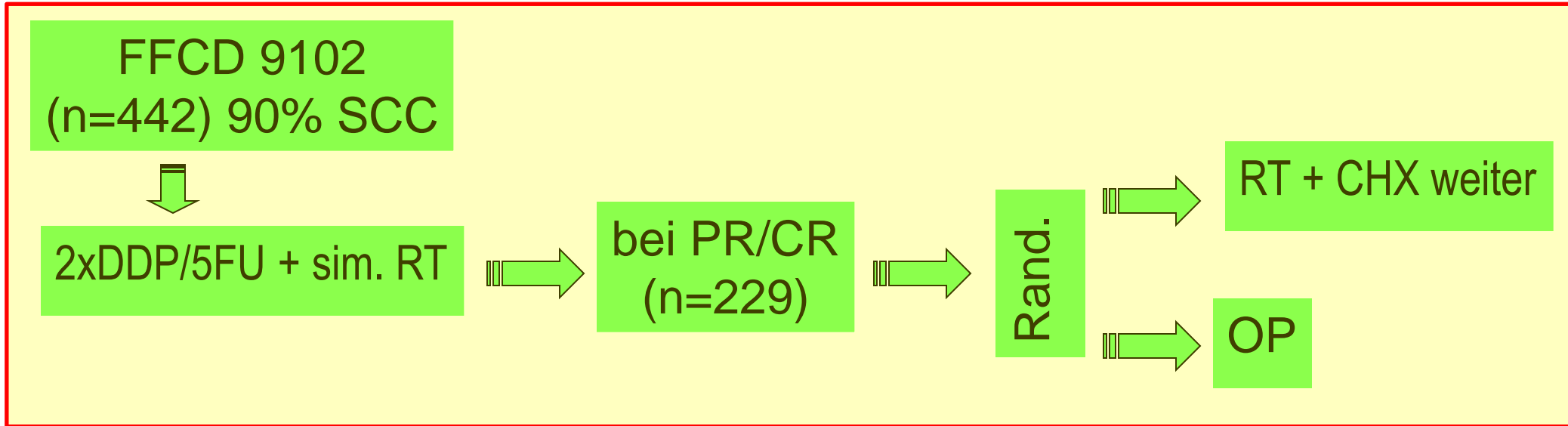
Esophageal-Ca.: patterns of recurrence OP vs. RT

first event	surgery	radiotherapy
local / regional	25-35%	40-60%*
distant	50-70%	10-60%

- *
 - approximately 40% persistent tumors after RT
 - in case of CR after RT only 15-25% locoregional recurrences
 - 15-20% of locoregional recurrences > 5 cm from primary lesion

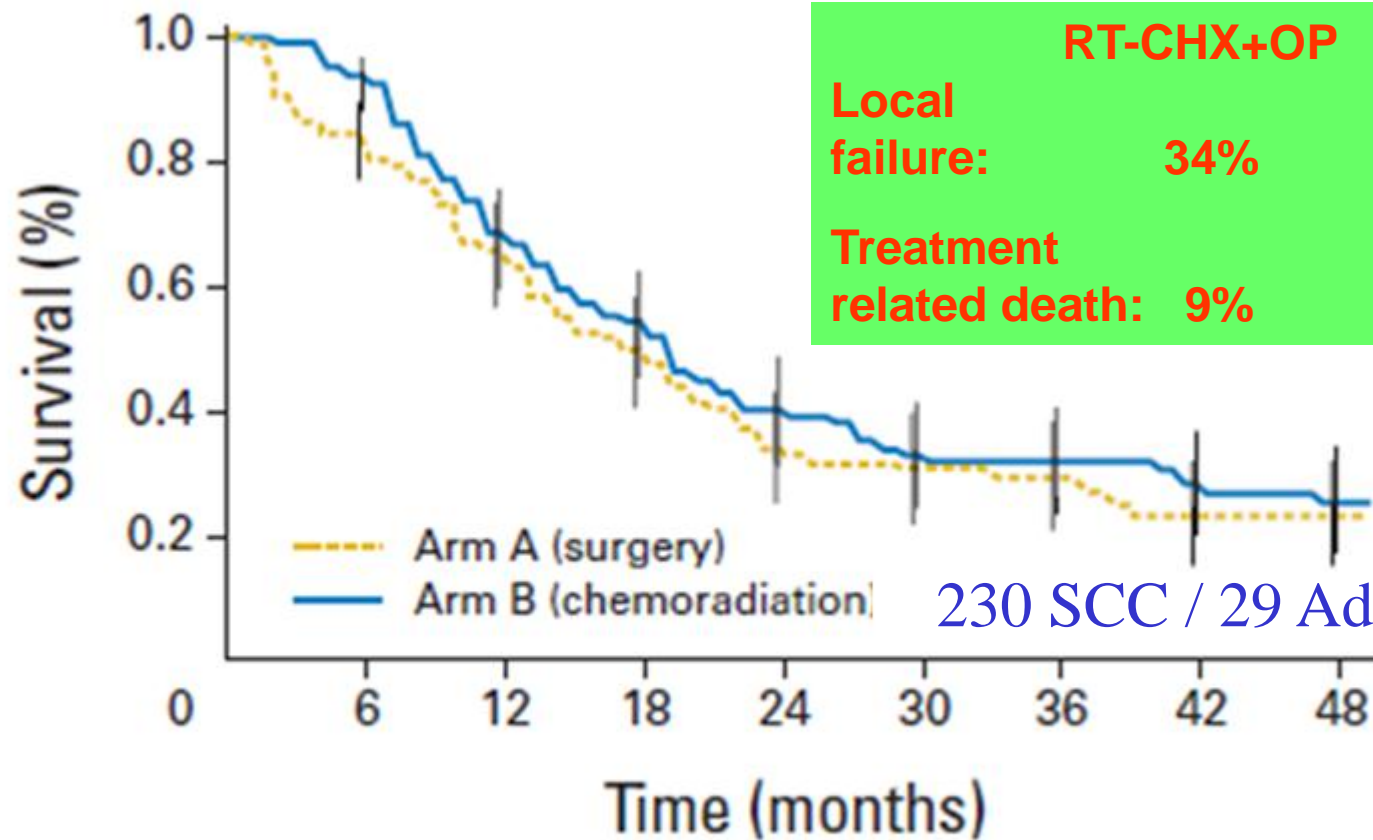
Ösophagus-Ca: Random. Studien zum Stellenwert der Chirurgie

CHX+RT+OP vs. RT+CHX



Ösophagus-Ca: Random. Studien zum Stellenwert der Chirurgie

Plattenepithel- und Adeno-Ca.: CHX+RT+OP vs. RT+CHX



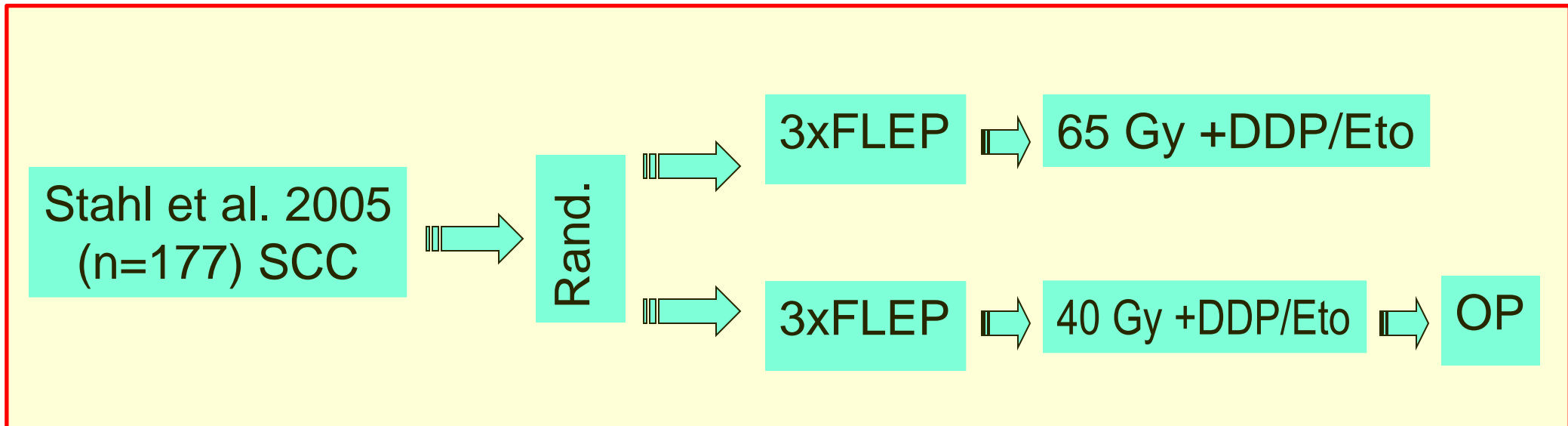
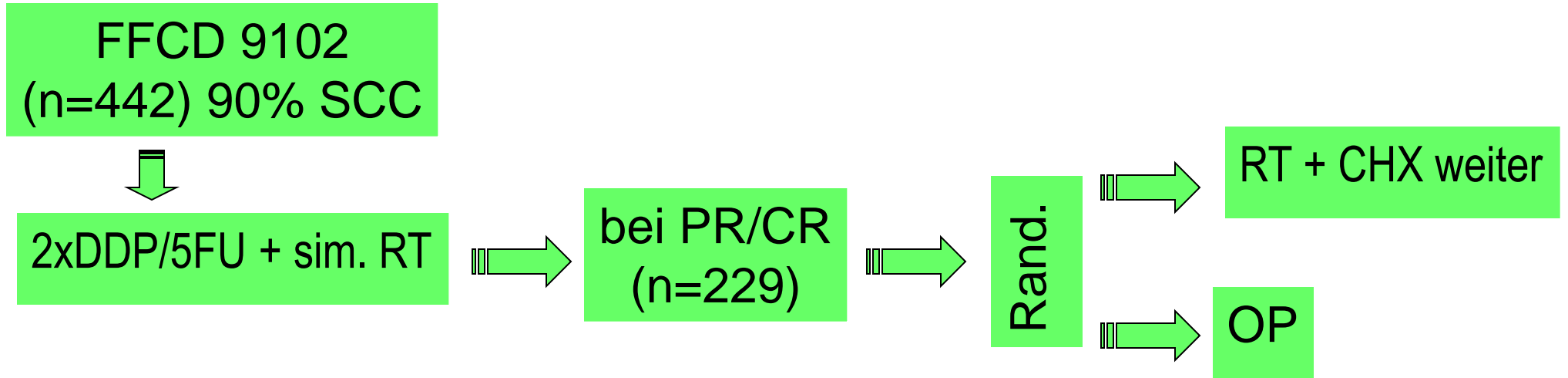
	RT-CHX+OP	RT-CHX	p
Local failure:	34%	43%	0.0014
Treatment related death:	9%	1%	<0.005

230 SCC / 29 Adeno-Ca.

Patients at risk	0	6	12	18	24	30	36	42	48
Arm A (surgery)	129	108	79	51	31	25	23	17	13
Arm B (chemoradiation)	130	122	84	61	40	29	25	21	14

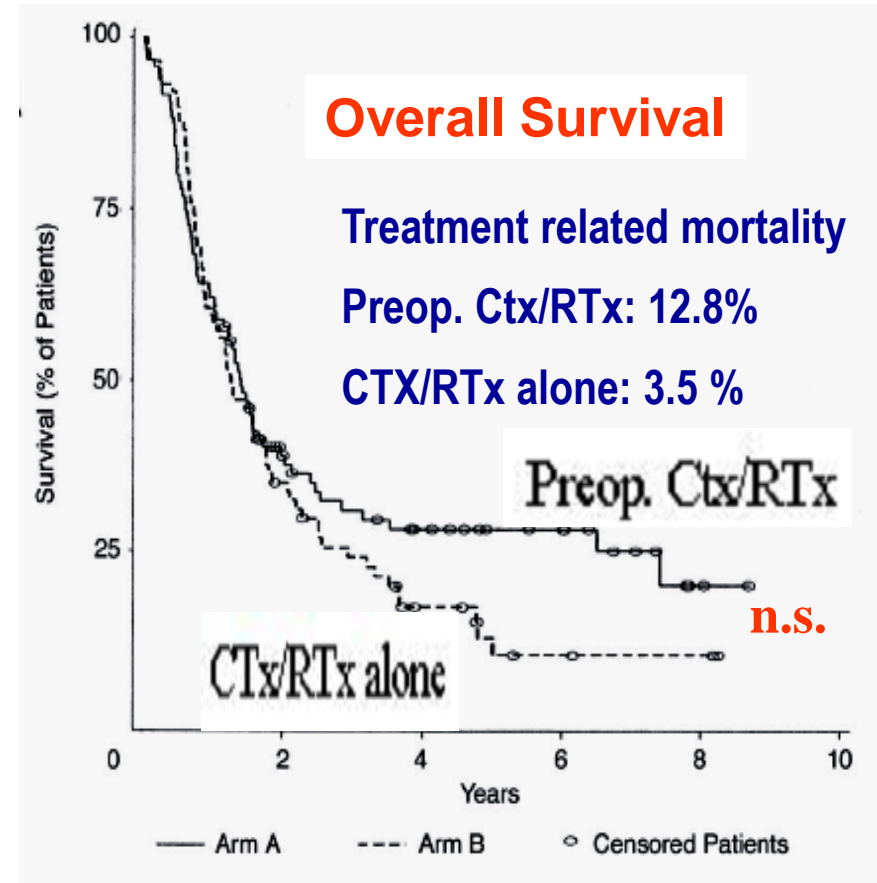
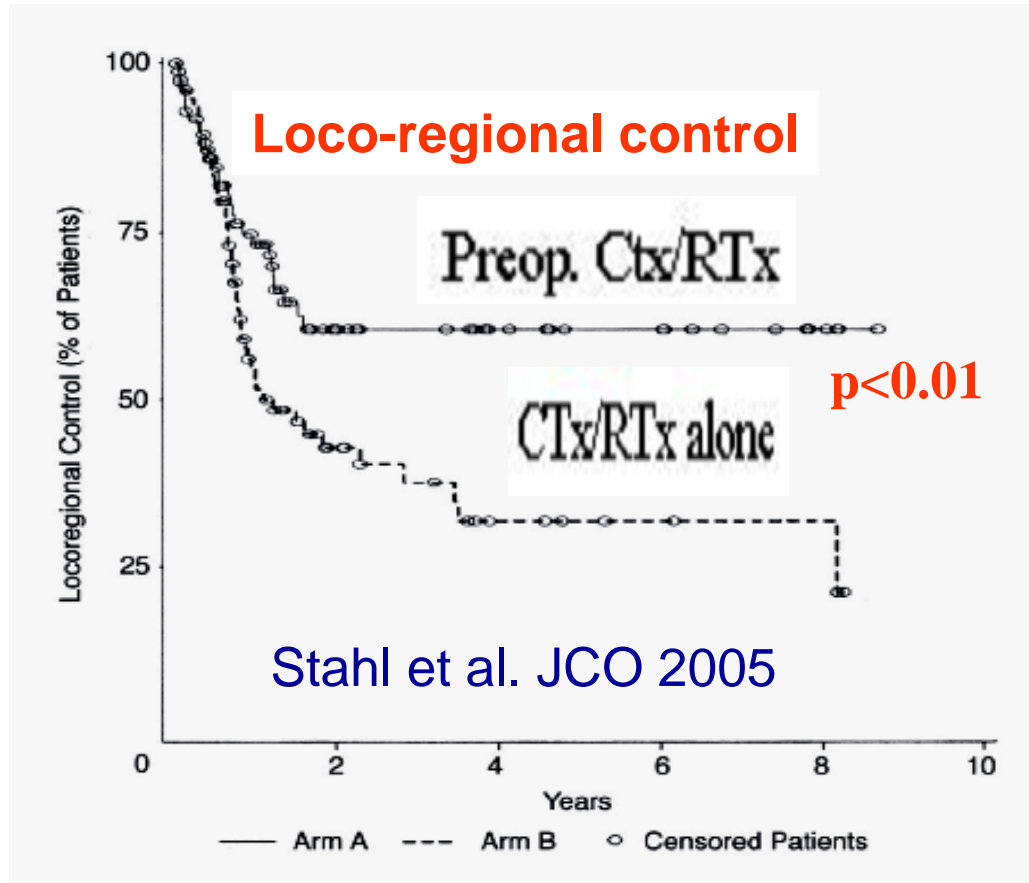
Ösophagus-Ca: Random. Studien zum Stellenwert der Chirurgie

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Ösophagus-Ca: Random. Studien zum Stellenwert der Chirurgie

Plattenepithel-Ca.: CHX+RT+OP vs. RT+CHX

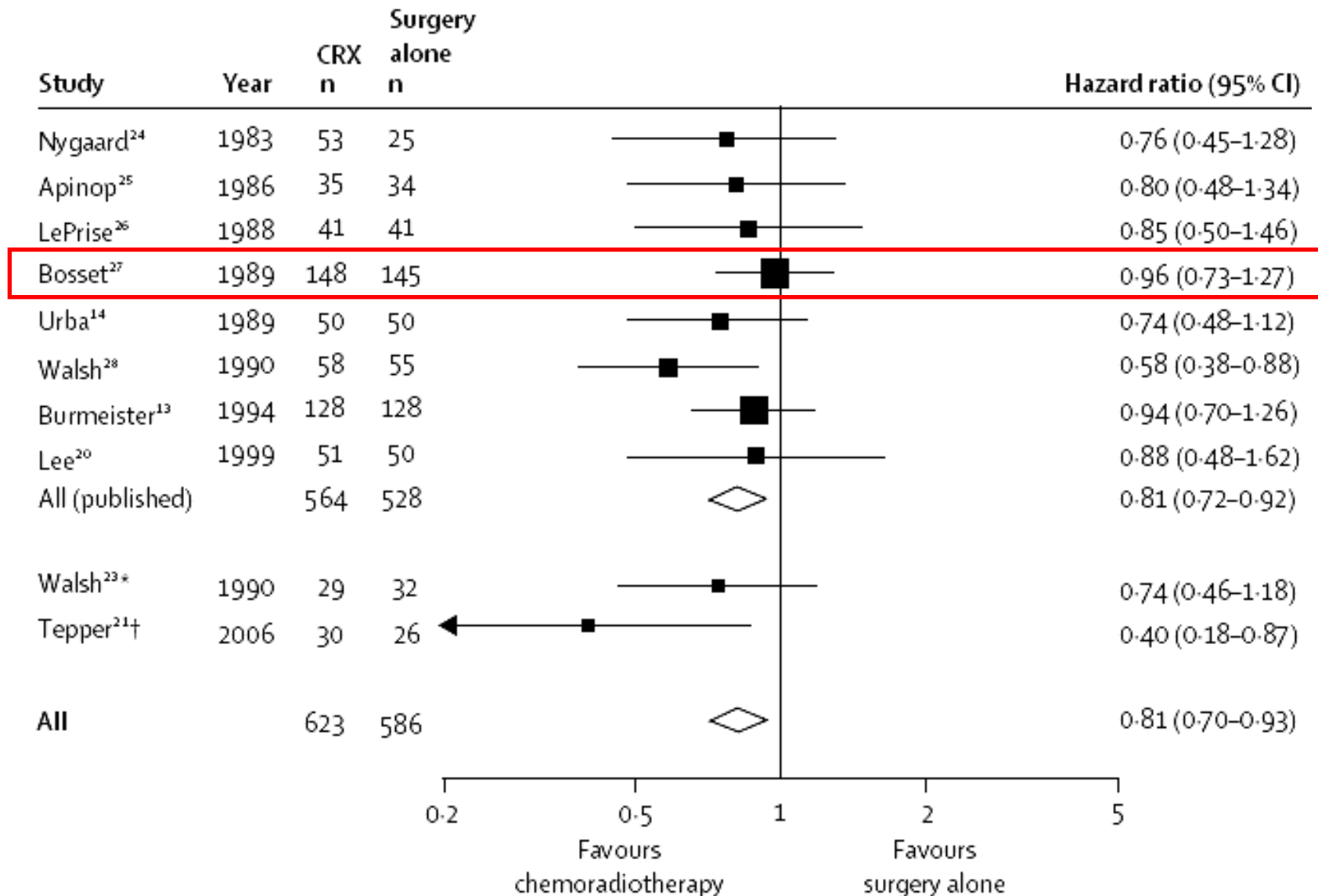


Bei CR/PR nach CHX: 3J. Überleben A vs. B: 58% vs. 55%

Bei NC/PD nach CHX: 3J. Überleben A vs. B: 17,9% vs. 9,4% (n.s.) (R0: 32%)

Chirurgie verbessert das Überleben nur bei „Nichtansprechern“ auf CHX sofern eine R0-Resektion gelingt

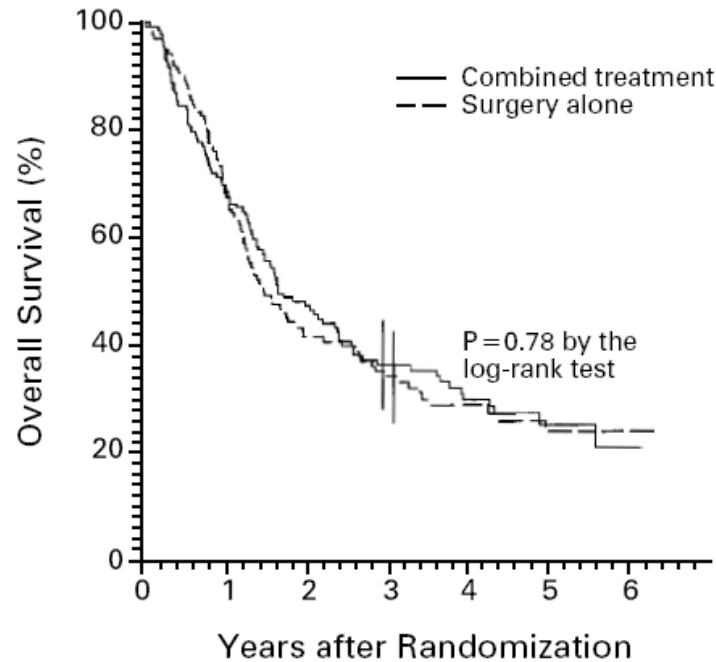
Esophageal-Ca. (SCC+Adeno-Ca.): pre-OP RT+CHX



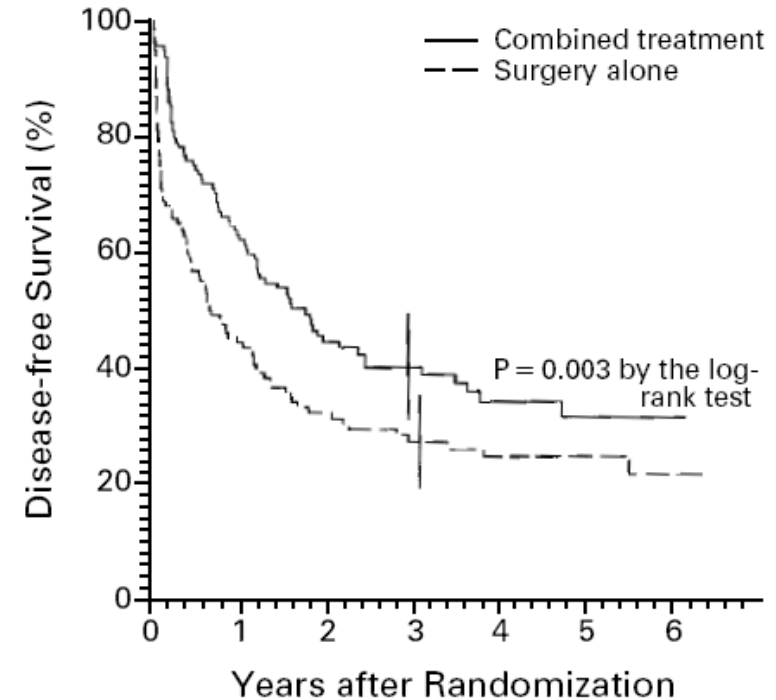
Esophageal-Ca. (SCC): pre-OP RT+CHX

10x 3.7 Gy to 37 Gy one week split
+80 mg/m² + 50 mg/m² cisplatin

	SURGERY ALONE (N=145)	COMBINED TREATMENT (N=148)
	no. (%)	
Postoperative complications:	5 (5.0)	17 (16.7)

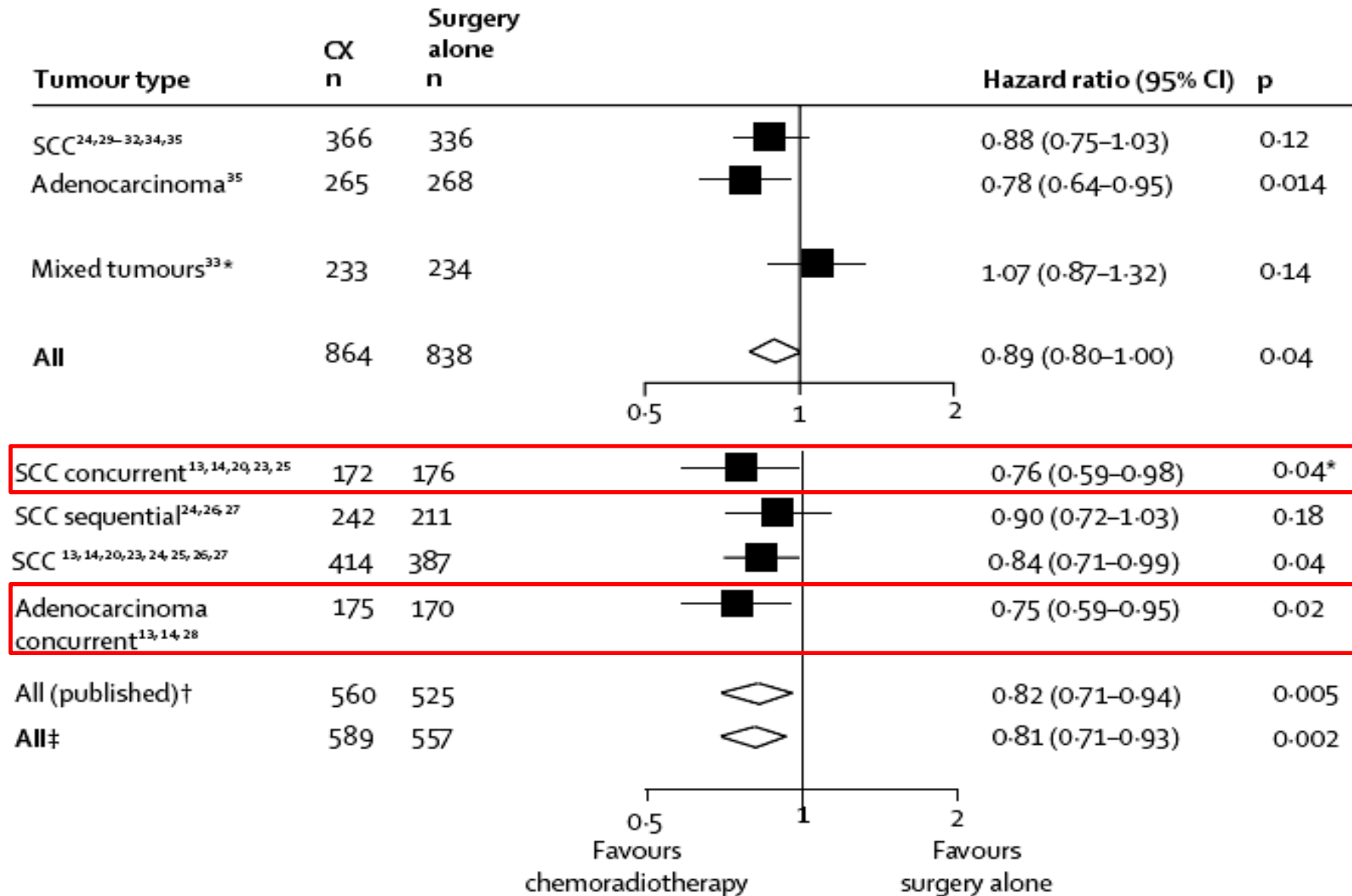


Combined treatment						
Patients at risk	143	96	59	38	26	10
No. of deaths	0	45	75	87	93	96
Surgery alone						
Patients at risk	139	92	48	35	24	12
No. of deaths	0	46	79	87	92	95



Combined treatment						
Patients at risk	143	75	45	30	18	5
No. of treatment failures	0	51	71	76	79	80
Surgery alone						
Patients at risk	139	57	33	24	19	10
No. of treatment failures	0	76	91	95	97	97

Esophageal-Ca. (SCC+Adeno-Ca.): pre-OP RT+CHX



CROSS

Dutch Phase III

van der Gaast et al. ASCO 2010

Histology	Surgery	CRT + Surgery
AC	139 (74%)	129 (74%)
SCC	44 (23%)	40 (23%)
Other	5 (3%)	6 (3%)

Esophageal
Cancer

(T2-3N0-1M0)

Tumor location	Surgery	CRT + Surgery
proximal	4	3
mid	18	27
distal	145	122
GEJ	21	23

188pts

175pts

Paclitaxel 50mg/m²
Carbo AUC 2
weekly x 5
+ 41.4 Gy/23fx

S
U
R
G
E
R
Y

R0: 65%
Death: 3.7%

R0: 92%
Death: 3.8%

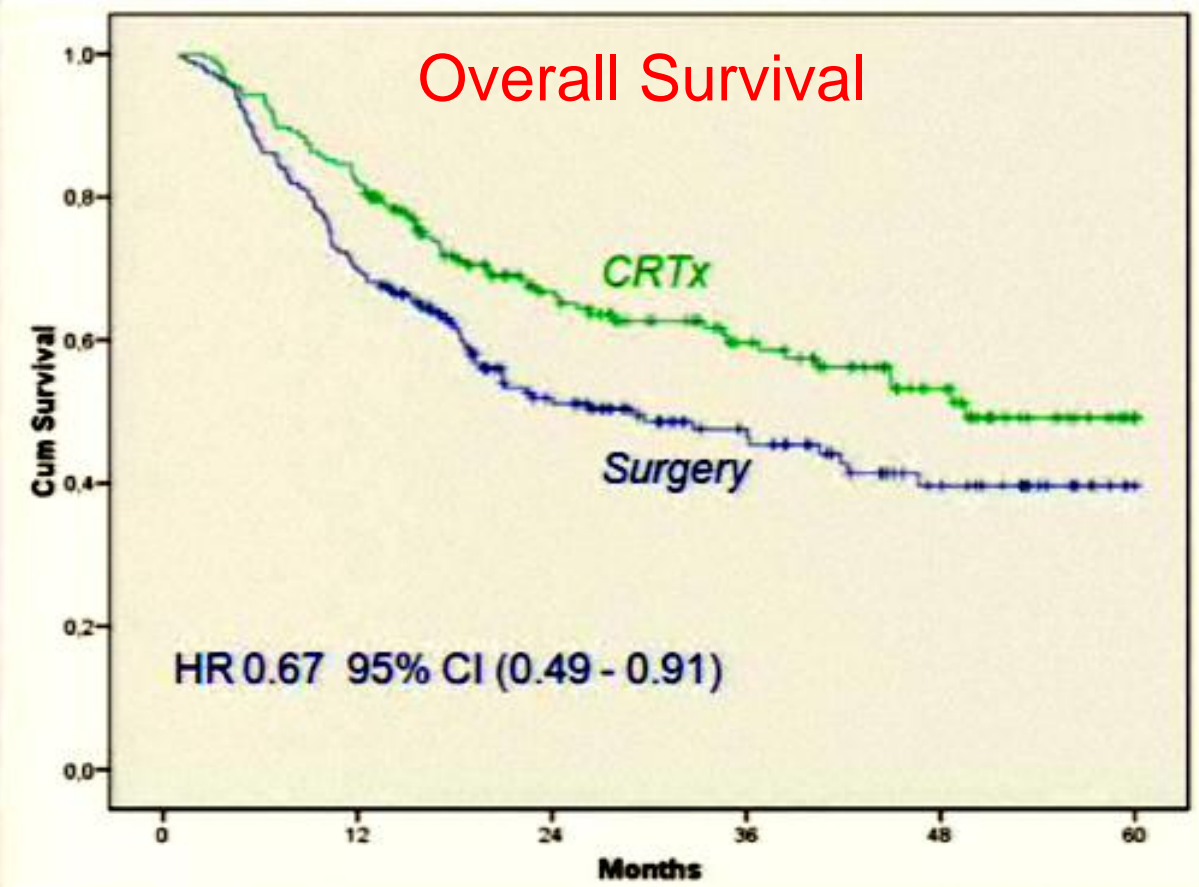
- Chemoradiotherapy regimen:
 - Paclitaxel 50mg/m² + Carboplatin AUC=2 on days 1, 8, 15, 22 and 29
 - Concurrent radiotherapy of 41.4 Gy in 23 fractions of 1.8 Gy
- Surgery within 6 weeks after completion of chemoradiotherapy (THE/TTE)

CROSS (locally advanced): Surgery vs. RT-CHX + Surgery

(T2-3N0-1M0)

Tumor location	Surgery	CRT+Surgery
proximal	4	3
mid	18	27
distal	145	122
GEJ	21	23

Histology	Surgery	CRT+ Surgery
AC	139 (74%)	129 (74%)
SCC	44 (23%)	40 (23%)
Other	5 (3%)	6 (3%)



No's at risk	0	12	24	36	48	60
Surgery alone	188	131	71	44	22	1
CRT+ surgery	175	144	85	55	30	2

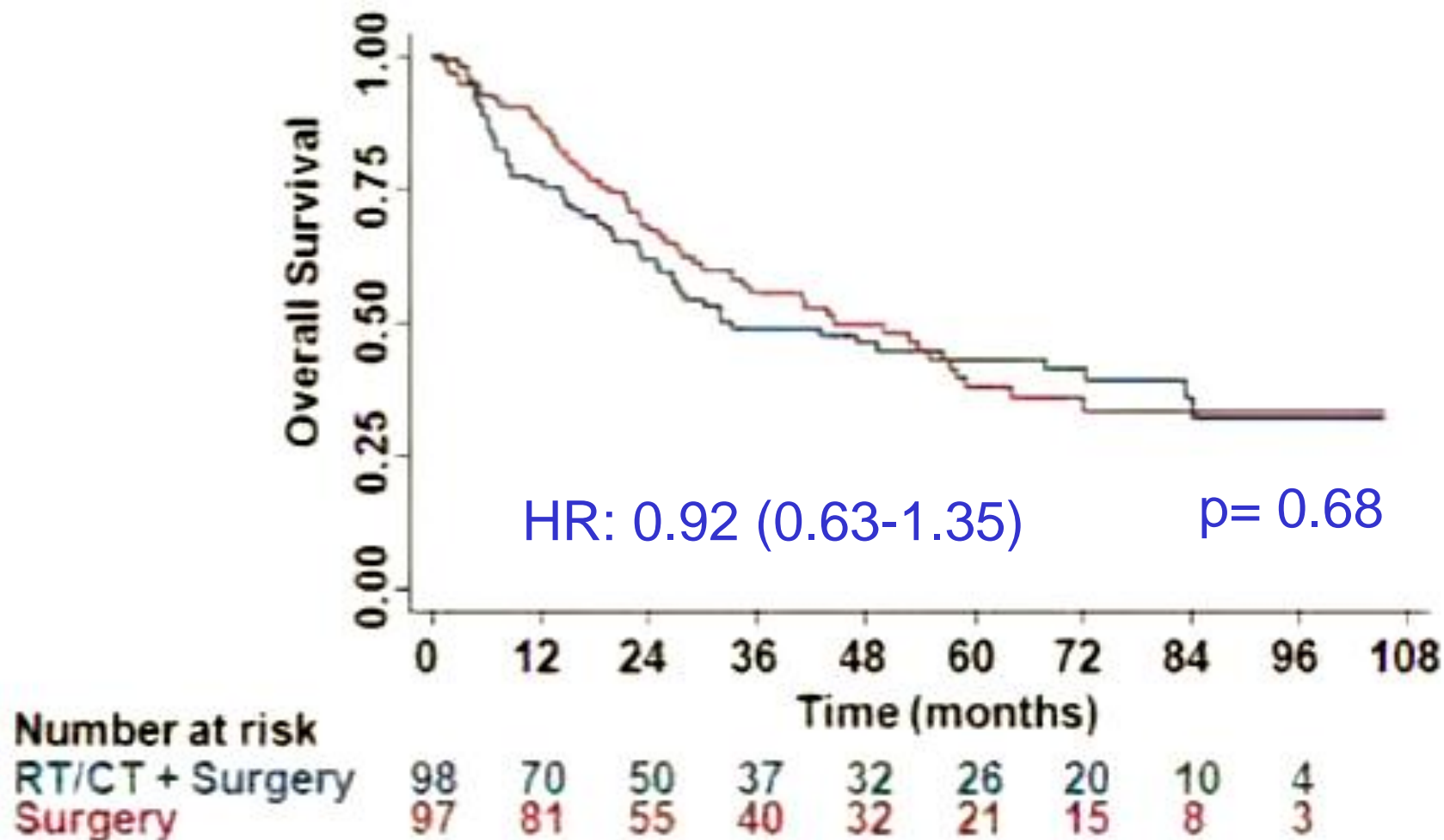
FFCD 9901 (early stages): Surgery vs. RT-CHX + Surgery



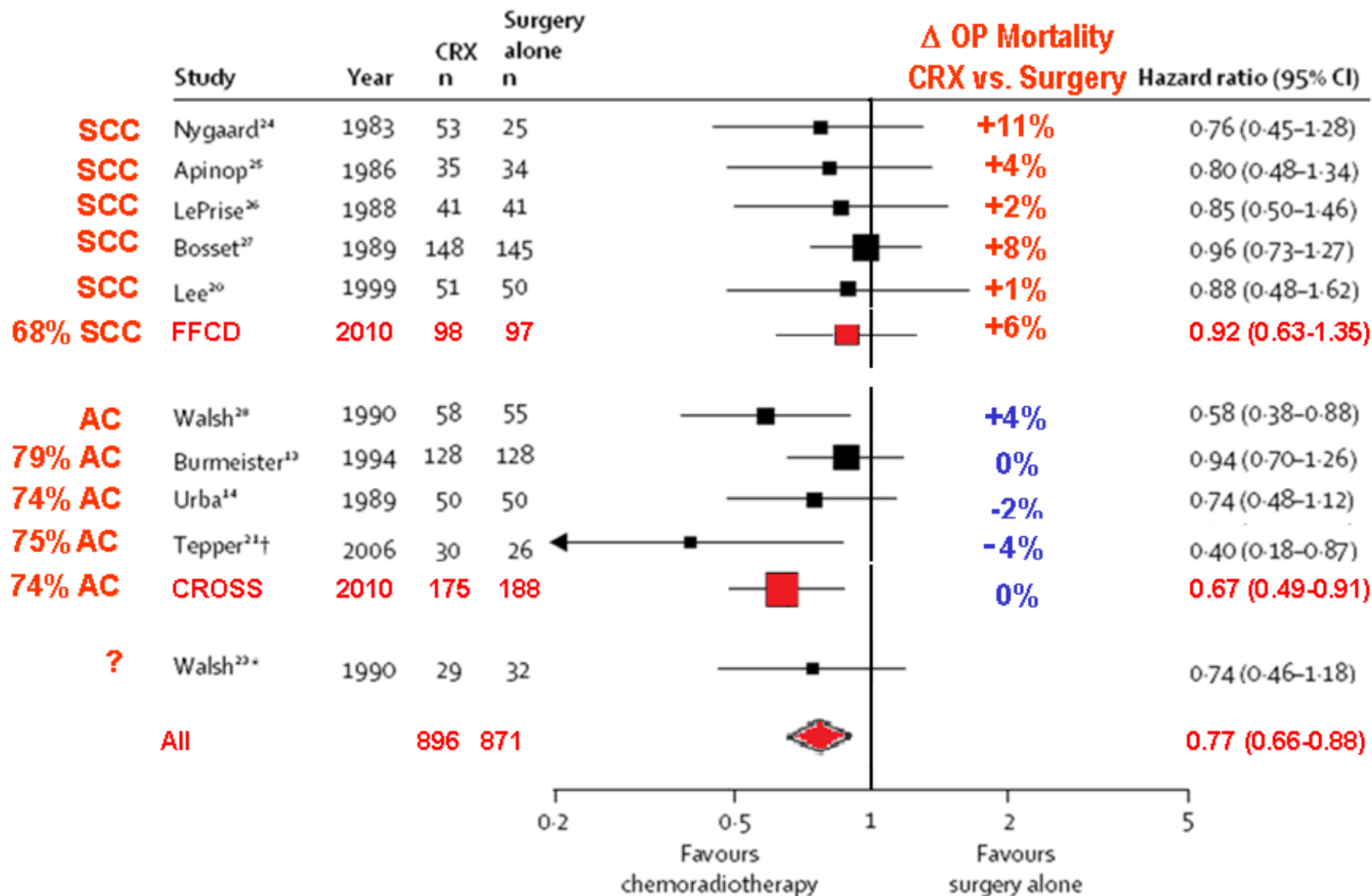
Histology	CRT +S group N = 98	S group N = 97
SCC	67 (68.4%)	70 (72.2%)
ADC	30 (30.6%)	27 (27.8%)
UICC clinical stage		
stage I	17 (17.3%)	18 (18.6%)
stage IIA	49 (50.0%)	49 (50.5%)
stage IIB	32 (32.7%)	30 (30.9%)
Tumoral location		
Above carena	8 (8.2%)	10 (10.3%)
Below carena	90 (91.8%)	87 (89.7%)

FFCD 9901 (early stages): Surgery vs. RT-CHX + Surgery

Overall Survival

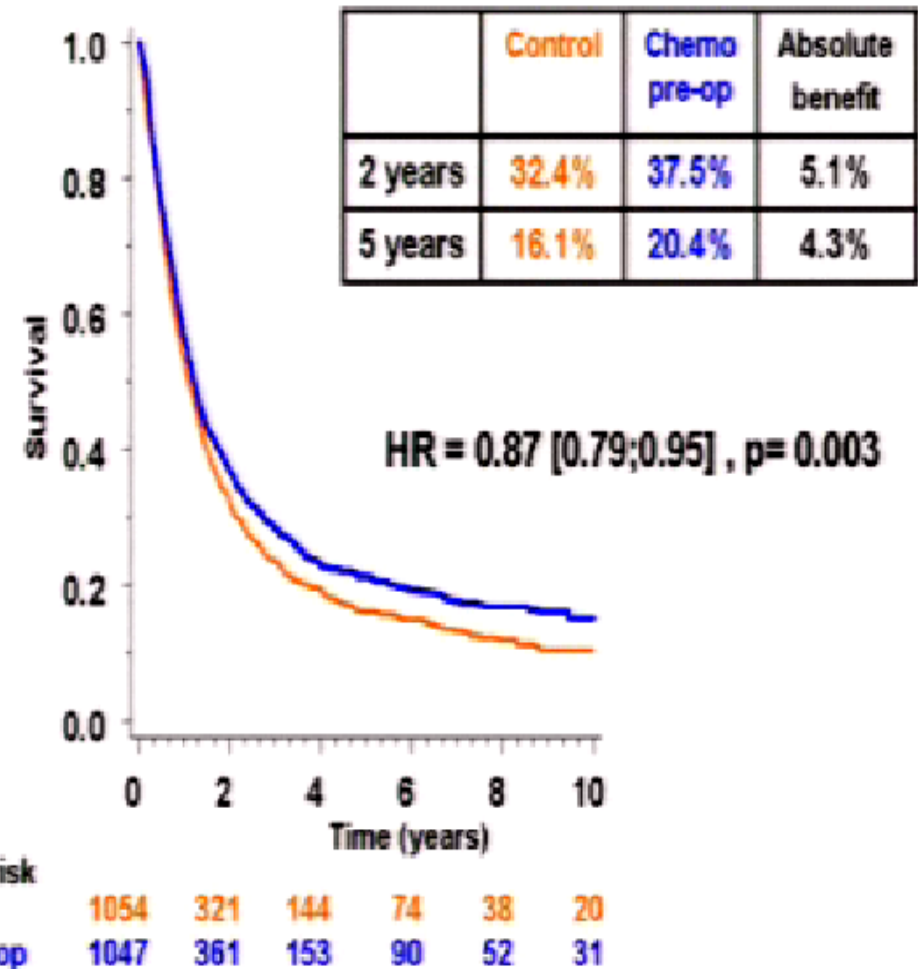
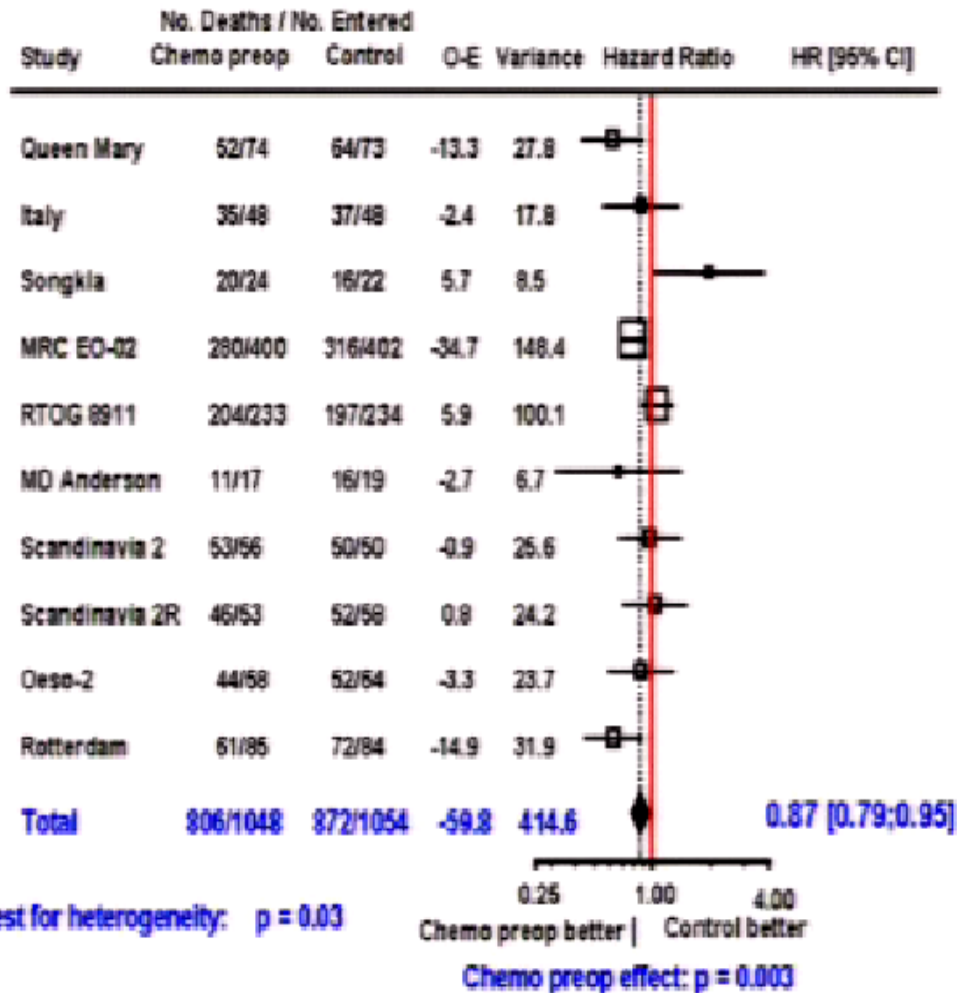


Esophageal-Ca. (SCC+Adeno-Ca.): OP vs. pre-OP-RT+CHX + OP



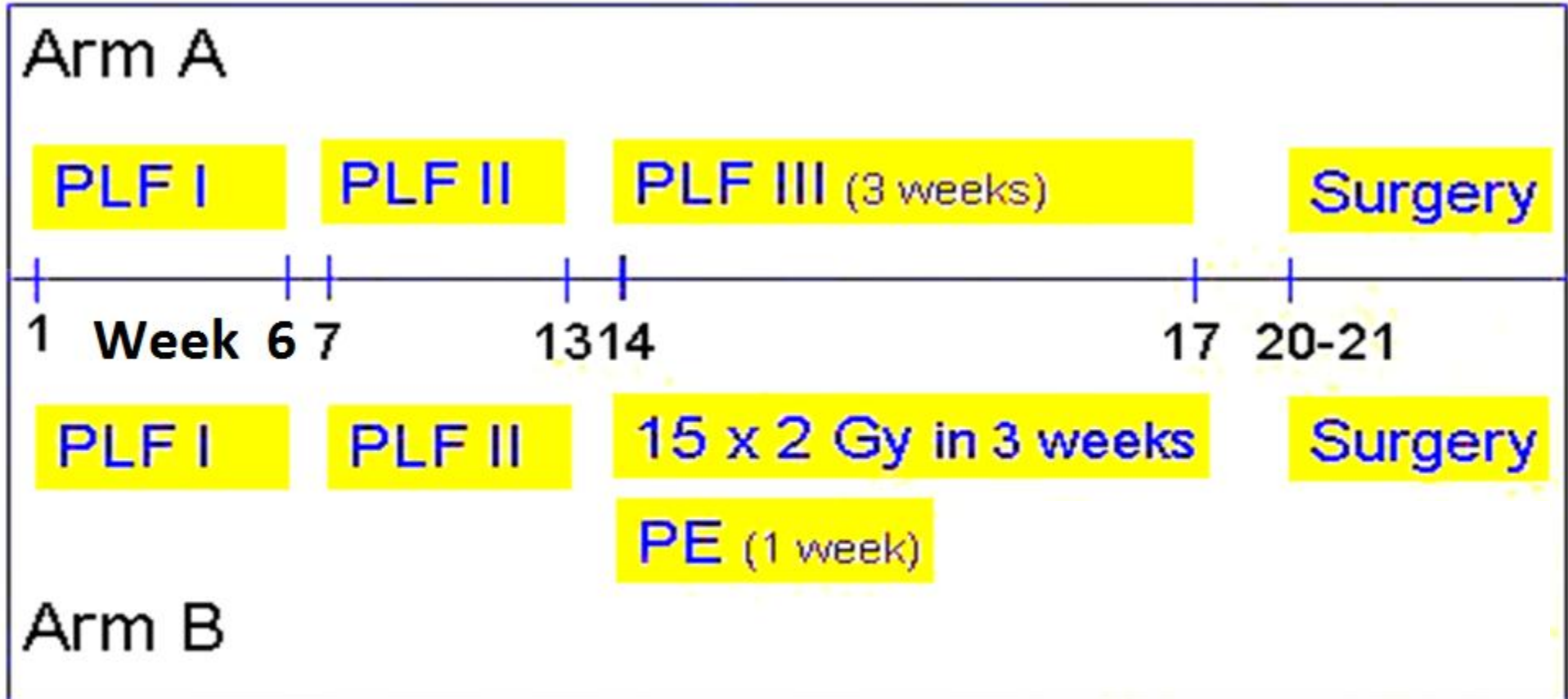
Ergänzte Meta-Analyse: modifiziert nach GebSKI et al. Lancet Oncol 2007

Esophageal-Ca. (SCC+Adeno-Ca.): OP vs. pre/peri-OP CHX + OP



Gastroesophageal- Junction-Adeno-Ca.

POET



PLF: Cisplatin 50mg/m², 1h, d 1,15,29. Leukovorin/5-FU 500mg/m² 2h / 2g/m² 24h, d 1,8,15,22,29,36

PE: Cisplatin 50 mg/m², 1h, d 2+8. Etoposide 80 mg/m², 1h, d 3-5

Gastroesophageal- Junction-Adeno-Ca.

POET

Pathohistologic Results

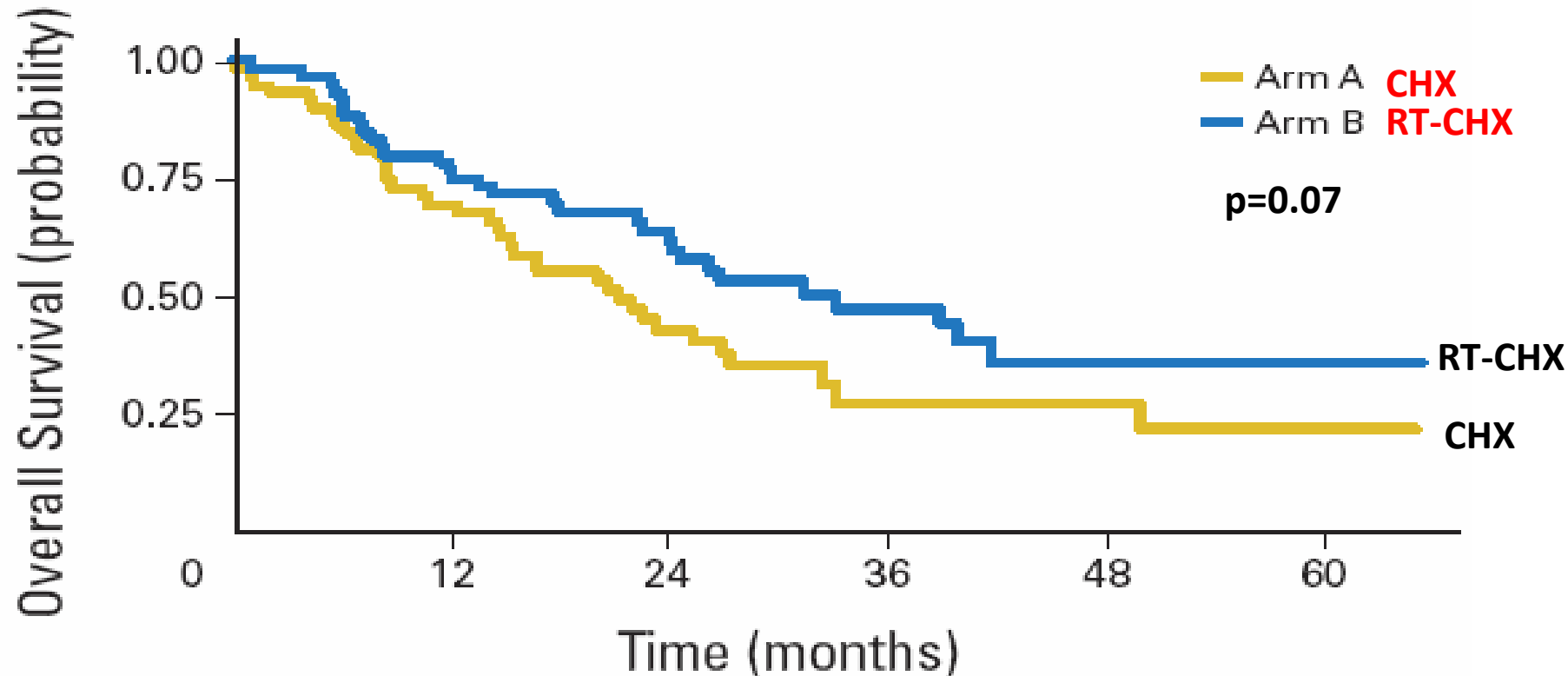
Treatment	CHX Arm A		RT-CHX Arm B		P
	No.	%	No.	%	
Patients with resection	49	100.0	45	100.0	
pT0 N0 M0	1	2.0	7	15.6	.03*
pT1-4 N0 M0	17	34.7	22	48.9	
pT0-4 N0 M0†	18	36.7	29	64.4	.01*
pT0-4 N0 M0	18	36.7	29	64.4	.01*
pTall N+ M0	27	55.1	14	31.1	
pTall N+ M1	4	8.2	2	4.5	

*Fisher's exact test.

†Bold text indicates data summarized from patients with pT0 N0 M0 and pT1-4 N0 M0.

Gastroesophageal- Junction-Adeno-Ca.

POET



No. of patients at risk

A:	59	41	19	6	5	2
B:	60	45	30	15	7	1

Gastroesophageal- Junction-Adeno-Ca.

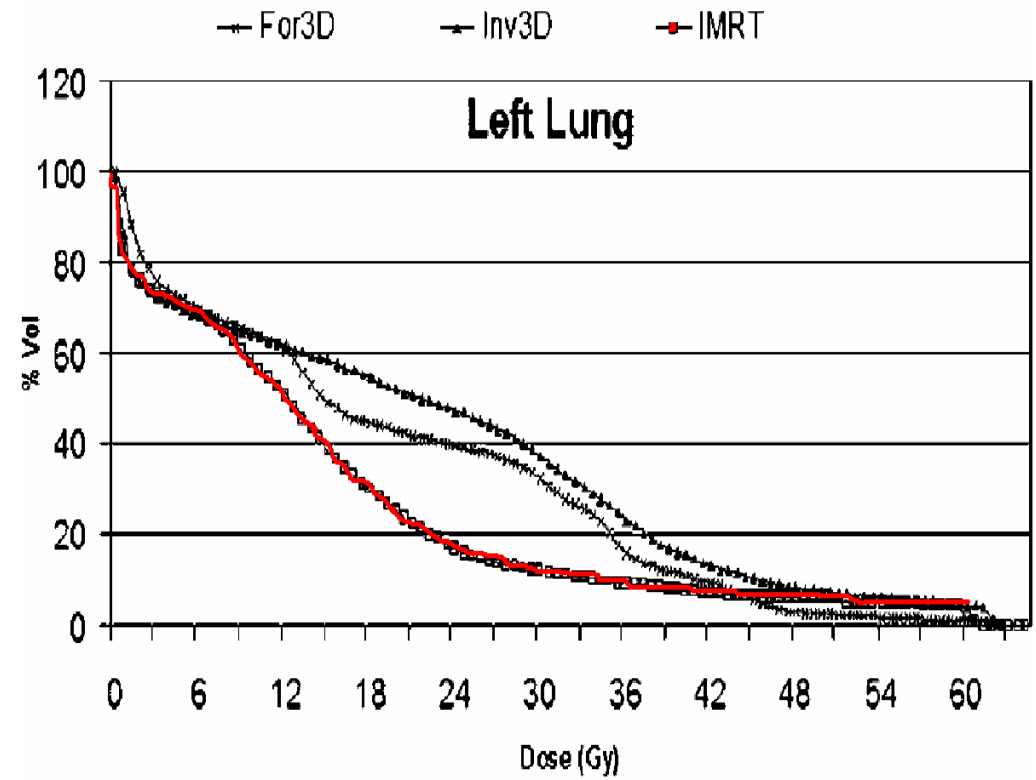
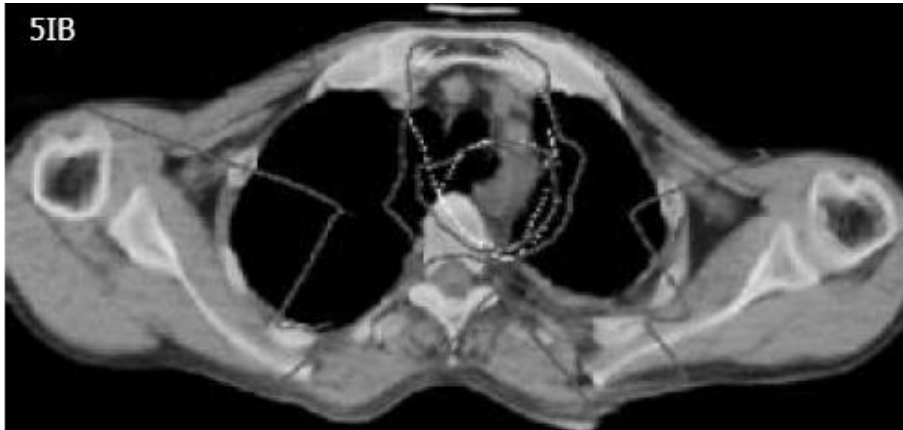
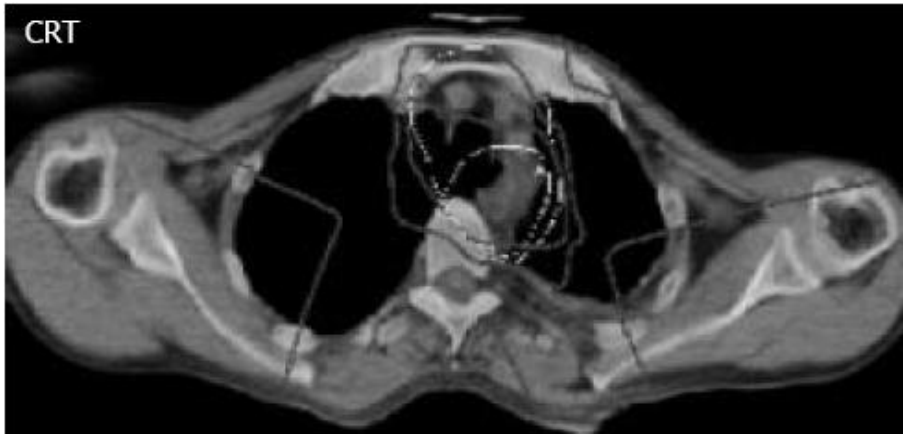
Perioperative mortality

	RT+/-CHX +surgery	surgery +/- CHX	p
Zhang (RT)	1 (0.6%)	5 (2.5%)	n.s.
Walsh (RT-CHX)	5 (8.6 %)	2 (3,6%)	n.s.
Tepper (RT-CHX)	0 (0 %)	1 (3,8%)	n.s.
van der Gaast (RT-CHX)*	7 (3.9%)	7 (3.8%)	n.s.
Stahl (RT-CHX)	5 (10.2%)	2 (3.8%)**	n.s.
Total	18/484 (3,7%)	17/527 (3,2%)	n.s.

*= 23% SCC

**= neoadjuvant CHX

3D vs. IMRT



Wu et al. 2004

Ösophagus-Karzinom:

Adenokarzinom versus Plattenepithelkarzinom

- Kein Unterschied im Ansprechen auf RT-CHX
- Nach präoperativer RT-CHX ist die post-OP Mortalität nur beim SCC signifikant erhöht
- Eine präoperative RT-CHX ist bei lokal fortgeschrittenen Tumoren indiziert
- Cave bei Patienten mit schlechter Lungenfunktion / hoher Komorbidität