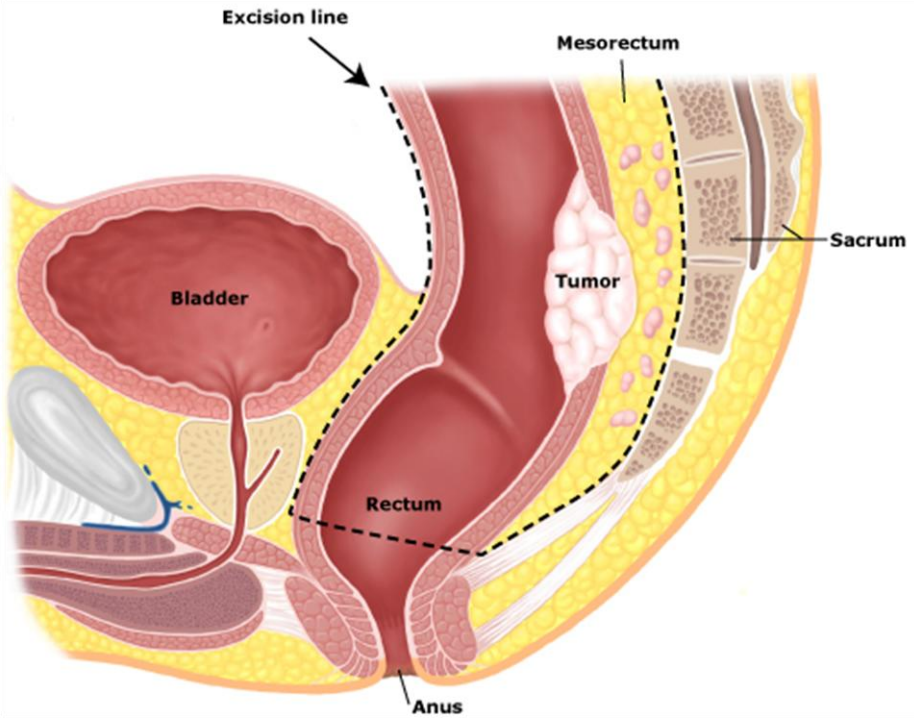
REKTUM KANSERİNDE ADJUVAN NEOADJUVAN TEDAVİ YAKLAŞIMLARI

Prof Dr Gökhan Demir

İstanbul Bilim Üniversitesi

Tıbbi Onkoloji Bilim Dalı

Rektum Kanserinde Cerrahi



- Total mezorektal eksizyon sonrası T3-4 ve N + hastalıkta lokal nüks oranı %25-50
- “Dutch” çalışmasında TME sonrası N+ hastalarda nüks oranı %15
- Distal rektum tümörlerin de nüks oranı daha fazla

Rektum Kanserinde Kemoradyoterapi

Çalışma	Tedavi	Lokal nüks (%)	Hastalıksız SK (%)	Genel SK (%)
GITSG 7175	Kontrol RT KT RT+KT	24 20 27 11 (0.08)	46 52 54 70 (0.009)	43 - - 59 (0.005)
Mayo/NCCTG 79-47-51	RT RT+KT	25 14 (0.04)	38 58 (0.002)	48 63 (0.025) (7 Yıl)
NSABP R-O1	Kontrol RT KT	25 16 (0.06) 21	30 34 37 (0.006)	42 41 52 (0.05)
Norveç	Kontrol RT+KT	30 12 (0.01)	53 63 (0.01)	50 64 (0.05)

Phase III Trial of Fluorouracil-Based Chemotherapy Regimens Plus Radiotherapy in Postoperative Adjuvant Rectal Cancer: GI INT 0144

Stephen R. Smalley, Jacqueline K. Benedetti, Stephen K. Williamson, John M. Robertson, Norman C. Estes, Tracy Maher, Barbara Fisher, Tyvin A. Rich, James A. Martenson, John W. Kugler, Al B. Benson III, Daniel G. Haller, Robert J. Mayer, James N. Atkins, Christine Cripps, John Pedersen, Phillip O. Periman, Michael S. Tanaka Jr, Cynthia G. Leichman, and John S. Macdonald

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ORIGINAL REPORT

Faz III randomize

T3-4N0M0

T1-4N1-2, M0

Opere rektum kanserli 1917 hasta 3 kola randomize

Medyan takip 5.7 yıl

Tedavi Kollari

- 5-FU 500 mg/m2,İV,D1-D5,28 günde bir 2 kür 5040 cGy RT ile aynı anda ve RT süresince 5-FU 225 mg/m2/gün,sürekli İV infüzyon RT bittikten sonra yine 5-FU 500 mg/m2,İV,D1-D5, 28 günde 2 kür daha

- 5-FU 300mg/m2 D1-42, iki hafta ara ardından RT ile aynı anda ve RT süresince 5-FU 225 mg/m2/gün,sürekli İV infüzyon ardından 5-FU 300mg/m2 /gün D1-56

- 5-FU 425mg/m2 ve LV 20mg/m2 D1-5 28 günde bir iki kez, RT ile birlikte D57-60 ve D85-88 arası, 5-FU 400 mg/m2 ve LV 20mg/m2, ardından 5-FU 380mg/m2 ve LV 20mg/m2 28 günde bir iki kez daha

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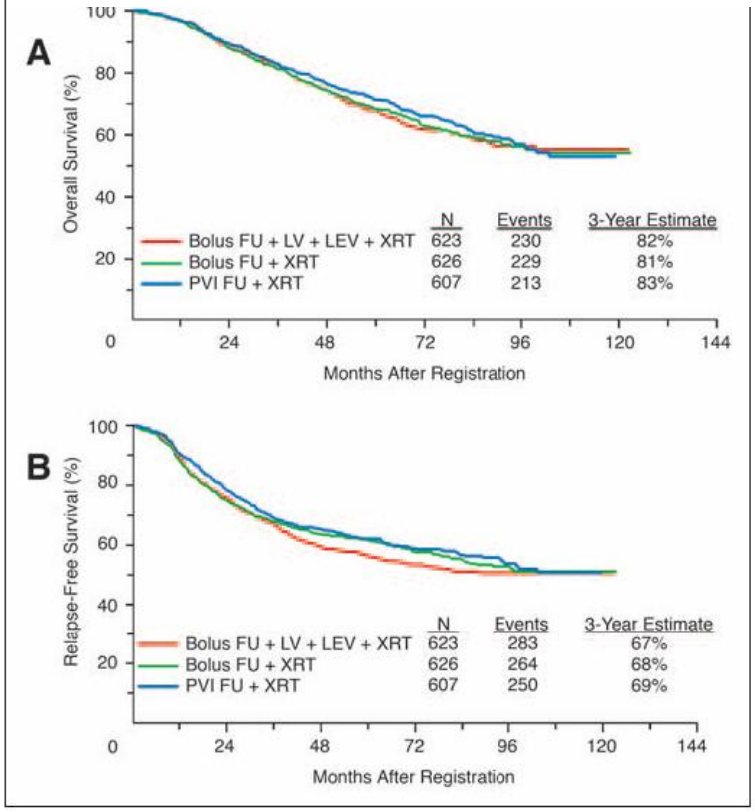


Table 2. Toxicity by Treatment Arm

Toxicity	Bolus FU (%)	PVI FU (%)	Bolus FU + LV + LEV (%)
GI grade 3-4	41	42	44
Hematologic grade 3-4	55	4	49
Infection grade 3-4	10	6	9
Catheter grade 3-4	2	3	< 0.5
Lethal	0.8	0.8	1
Patients who completed protocol regimen	79	70	78

NOTE. No. of patients assessable for toxicity by treatment arm: 618 in arm 1, 590 in arm 2, and 614 in arm 3.

Abbreviations: FU, fluorouracil; PVI, protracted venous infusion; LV, leucovorin; LEV, levamisole.

Neo-adjuvan Tedavi Sorular

1. Tokisite azalır mı ?
2. Tedaviye uyum artar mı ?
3. Evre indirgemesi “downstaging” yapabilir mi?
4. Sfinkter koruyucu cerrahi oranını arttırabilir mi?
5. Genel sağkalıma ve hastalıksız sağkalıma etkisi var mı?

Randomize Neoadjuvan Çalışmalar

Table 1. pCR, LRC, rate of metastases, and OS rate from the chemoradiation arms of recently published randomized trials

Trial	*n* of patients	pCR	5-Yr LRC	Metastases	5-Yr OS
CAA/ARO/AIO-94, Sauer et al. (2004) [2]	394	8%	6%	36%	4-yr, 74%
Polish trial, Bujko et al. (2004) [3]	157	16%	4-yr, 15.6%	34.6%	4-yr, 66%
FFCD 9203, Gerard et al. (2006) [4]	375	11.4%	8%	36%	66%
EORTC 22921, Bosset et al. (2005, 2006) [5, 20]	505	13.4%	8.7%	34%	65%

Abbreviations: EORTC, European Organization for Research and Treatment of Cancer; FFCD, Fédération de Francophone de Cancérologie Digestive; LRC, locoregional control; OS, overall survival; pCR, pathological complete response rate.

FFCD 9203 Çalışması

- 1993-2003 arasında distal ve orta rektuma lokalize rezektable T3-4 tümörü olan 762 hasta
- Randomizasyon preoperatif RT versus KRT
  - RT: 45 Gy (25 fraksiyonda 1.8 Gy , 5 haftada)
  - KRT: Bolus 5-FU 350 mg/m²/d +LV RT sırasında birinci ve beşinci haftada
- Cerrahi : 3-10 hafta sonra; **TME zorunlu**
- Adjuvan kemoterapi (iki kolda da): Bolus 5-FU/LV dört haftada bir dört kez
- Evreleme: TRUS rutin uygulanmış

FFCD 9203 Çalışması :

- 1º Sonlanım :
  - **Sağkalım farkı yok** (5-yıl) → 67.9% RT v. 67.4% KRT (p=0.684)
- 2º Sonlanım:
  - **Hastalıksız sağkalım farkı yok** (5-yıl) → 55.5% RT v. 59.4% KRT
  - **Lokal nükste fark var** (5-yıl) → 16.5% RT v. 8.1% KRT (p=0.004)

FFCD 9203 Çalışması

Table 3. Surgical Procedures and Pathologic Staging

Group	RT No. of Patients	RT %	CT-RT No. of Patients	CT-RT %	P
Eligible patients	367		375		
Surgery					
Yes	360	98.1	359	95.7	.16
No	4	1.1	11	3.0	
Missing data	3	0.8	5	1.3	
Patients undergoing surgery	360		359		
Surgery performed					
Abdominoperineal resection	150	41.7	152	42.3	.837
Anterior resection	185	54.4	188	52.4	
Other surgery	22	6.1	17	4.7	
Missing data	3	0.8	2	0.6	
Stoma					
No	64	17.8	69	19.2	.785
Temporary	134	37.2	131	36.5	
Permanent	160	44.4	156	43.5	
Other	1	0.3	0		
Missing data	1	0.3	3	0.8	
Gross complete resection					
Yes (R0-R1)	336	93.3	338	94.2	.791
No (R2)	20	5.6	15	4.2	
No resection	3	0.8	5	1.4	
Missing data	1	0.3	1	0.3	
Sterilization					
Complete sterilized specimen	13	3.6	41	11.4	.000
Few residual cells	37	10.3	67	18.7	
Evolutive residual cells	304	84.4	241	67.1	
Missing data	6	1.7	10	2.8	
ypN0	234	65.0	239	66.6	.847
ypN1-2	122	34.0	117	32.6	
Missing data	4	1.1	3	0.8	
Patients with gross complete resection	336		338		
ypT0	13	3.9	41	12.1	.000
ypT1	27	8.0	14	4.1	
ypT2	84	25.0	98	29.0	
ypT3	207	61.6	182	53.8	
Missing data	5	1.5	3	0.9	
CRM*					
Negative	188	56.0	185	54.7	.132
Positive	23	6.8	21	6.2	
Not assessable	83	24.7	69	20.4	
Missing data	42	12.5	63	18.6	

Abbreviations: RT, radiotherapy; CR-RT, chemotherapy and radiotherapy; CRM, circumferential rectal margin.
*Considered as positive if the microscopic tumor extension reached the margin.

Abdominoperineal rezeksiyon oranları farklı değil (41.7% & 42.3%, p=0.837)

Patolojik tam yanıt oranı farklı 11.4% KRT and 3.6% RT, p<0.0001

Toksisteler farklı RT (2.9%) versus KRT (14.9%), p<0.0001

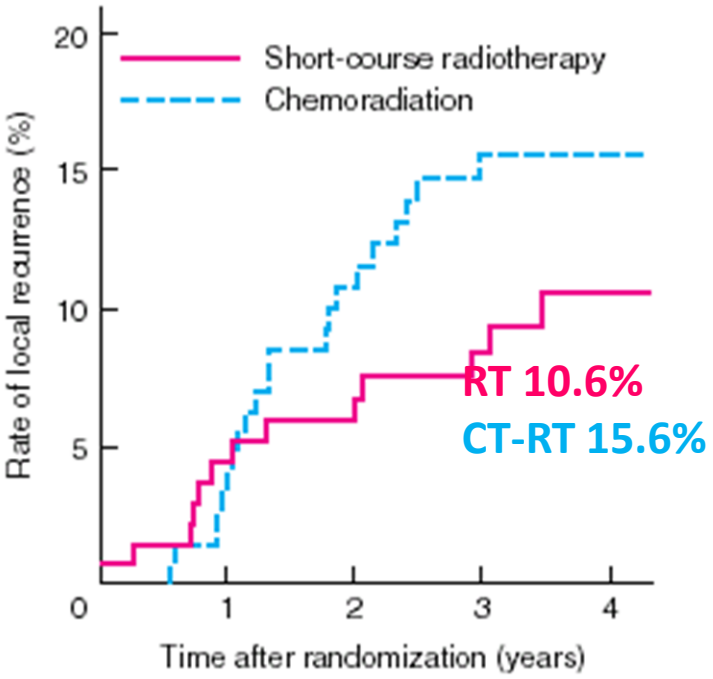
Polonya Çalışması

- 1999-2002 arasında rezektable T3-4 rektum kanserli 316 hasta randomize edilmiş
- Radyoterapi versus Kemoradyoterapi
  - RT → Preoperatif RT (kısa) with 5 Gy/gün x 5 gün
  - CRT → 50.4 Gy (1.8 Gy günde 5.5 haftada) + bolus 5-FU 325 mg/m²/gün + LV D1-5 RT ilk ve beşinci haftası
- Cerrahi : RT grubunda 7 gün içerisinde
- Kemoradyoterap grubunda 4-6 hafta içinde
- **TME zorounlu**
- Adjuvan kemoterapi Tercihe bağlı; bolus 5-FU/LV x 4 aylık (KRT grubunda) veya x 6 ay(RT grubunda)

Polonya Çalışması : 1º & 2º Sonlanım (4-yıllık)

- **pCR KRT de daha yüksek** – 16.1% KRT v. 0.7% RT (p<0.001)
- **Sfinkter koruyucu fark yok** - RT 61.2% v. KRT 58% (p=0.57)
- **Lokal nüks farkı yok** - RT 10.6% v. KRT 15.6% (p=0.210)
- **Uzak metastaz farkı yok** - RT 31.4% v. KRT 34.6% (p=0.540)

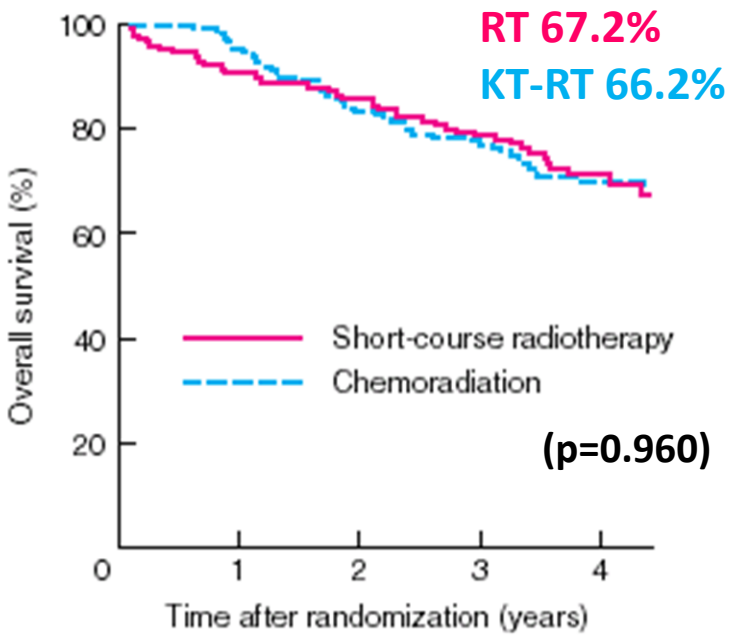
Lokal Nüks



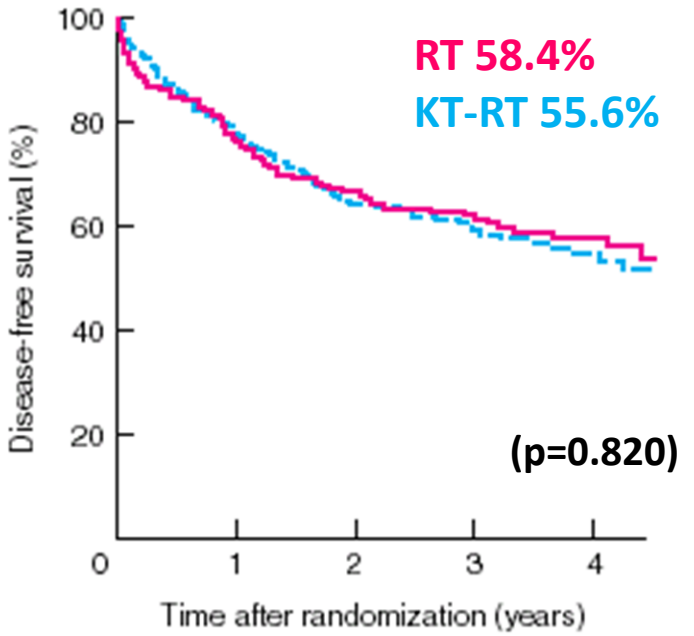
(p=0.210)

Polonya Çalışması : 1º & 2º Sonlanım (4-yıllık)

Genel Sağkalım



Hastalıksız Sağkalım



EORTC 22921 Çalışması

- 1993-2003 rezektable T3-4 rektum kanserli 1,011 hasta randomize edilmiş
- Dört kol 2X2 faktöryel dizayn
  - Kol 1 – preop RT (standart)
  - Kol 2 – preop KRT
  - Kol 3 – preop RT and postop KT
  - Kol 4 – preop KRT and postop KT
- Kemoterapi →
  - Bolus 5-FU 350 mg/m²/gün IV & LV x D1-5 RT birinci ve beşinci haftası
  - Kol 3 ve 4 dört siklus daha postop KT
- Radiotherapy → 45 Gy (25 farksiyonda 1.8 Gy) 5 hafta
- Cerrahi → 3 -10 hafta sonra; TME zorunlu
- Evreleme : **TRUS** zorunlu değil (% 64.8 yapılmış)

EORTC 22921

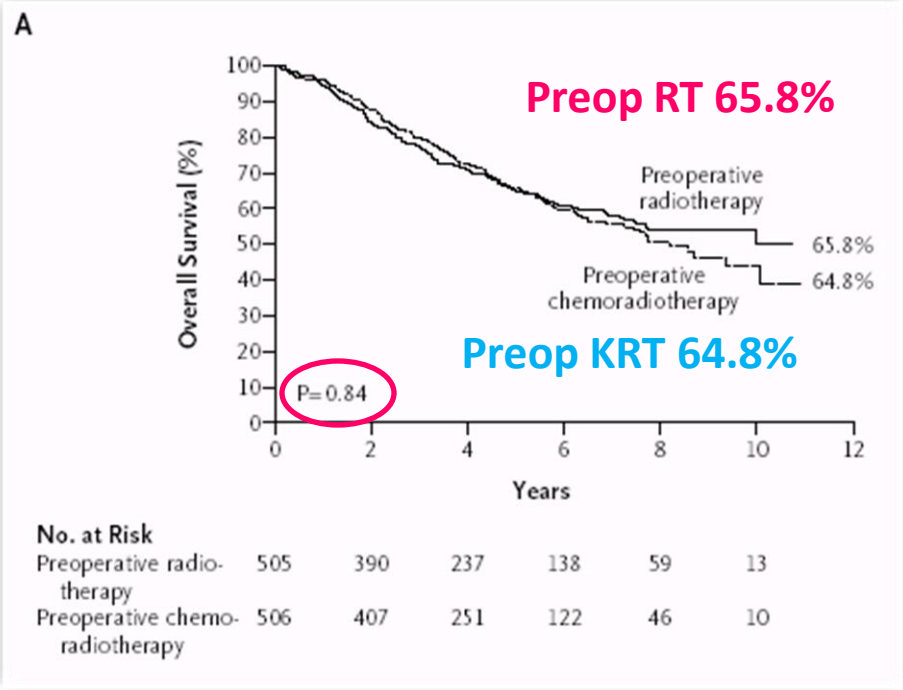
Table 3. Pathologic Characteristics

Characteristic	RT Group (n = 476)		RT-CT Group (n = 473)		P
	No. of Patients	%	No. of Patients	%	
Tumor size, mm					
Median	30.0		25.0		< .0001
90% range	10.0-70.0		8.0-110.0		
Tumor stage					
0	25	5.3	65	13.7	< .001
1	36	7.6	49	10.4	
2	141	29.6	156	33.0	
3	233	48.9	175	37.0	
4	25	5.3	18	3.8	
Missing	16	3.4	10	2.1	
Nodes					
Total examined, No.					
Mean	9		7		.046
Range	0.0-45.0		0.0-39		
N0	288	60.5	340	71.9	
N1	108	22.7	84	17.8	
N2	57	12.0	34	7.2	< .001
Missing	23	4.8	15	3.2	
Positive in all patients, No.					
Mean	1.52		0.86		< .0001
SD	0.16		0.10		
Metastases status at surgery					
M0	442	92.9	436	92.2	
M1	20	4.2	22	4.7	
Missing	14	2.9	15	3.2	

Abbreviations: CT, chemotherapy; RT, radiotherapy; SD, standard deviation.

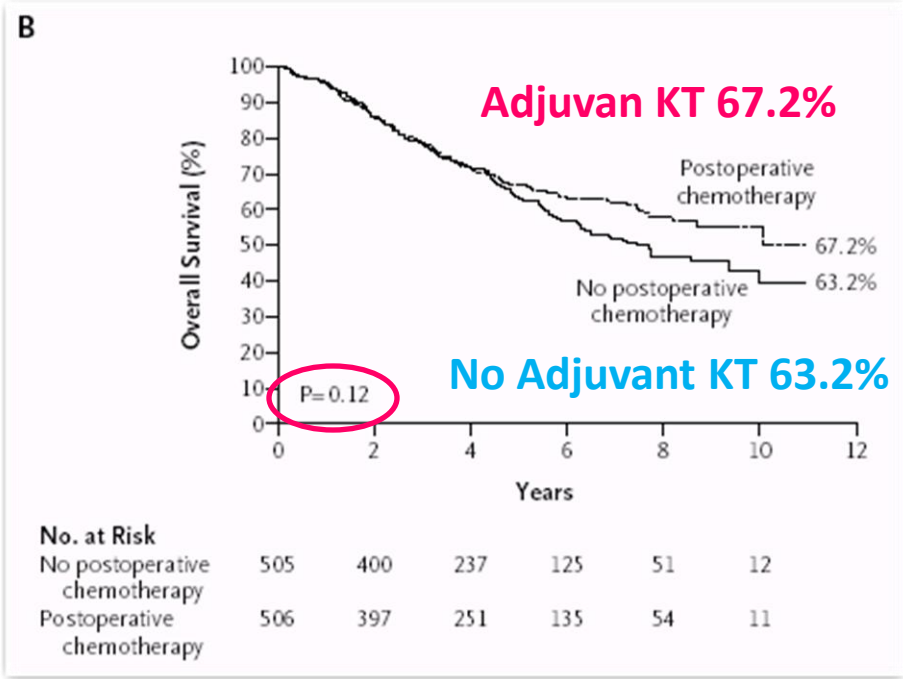
EORTC 22921: Genel Sağkalım(5-yıl)

Preoperatif RT vs KRT



Genel Sağkalım Farkı Yok

Postoperative KT vs Postoperative KT



Adjuvan KT alan ve almayan grupta fark yok

EORTC 22921: Hastalıksız Sağkalım (5-yıllık)

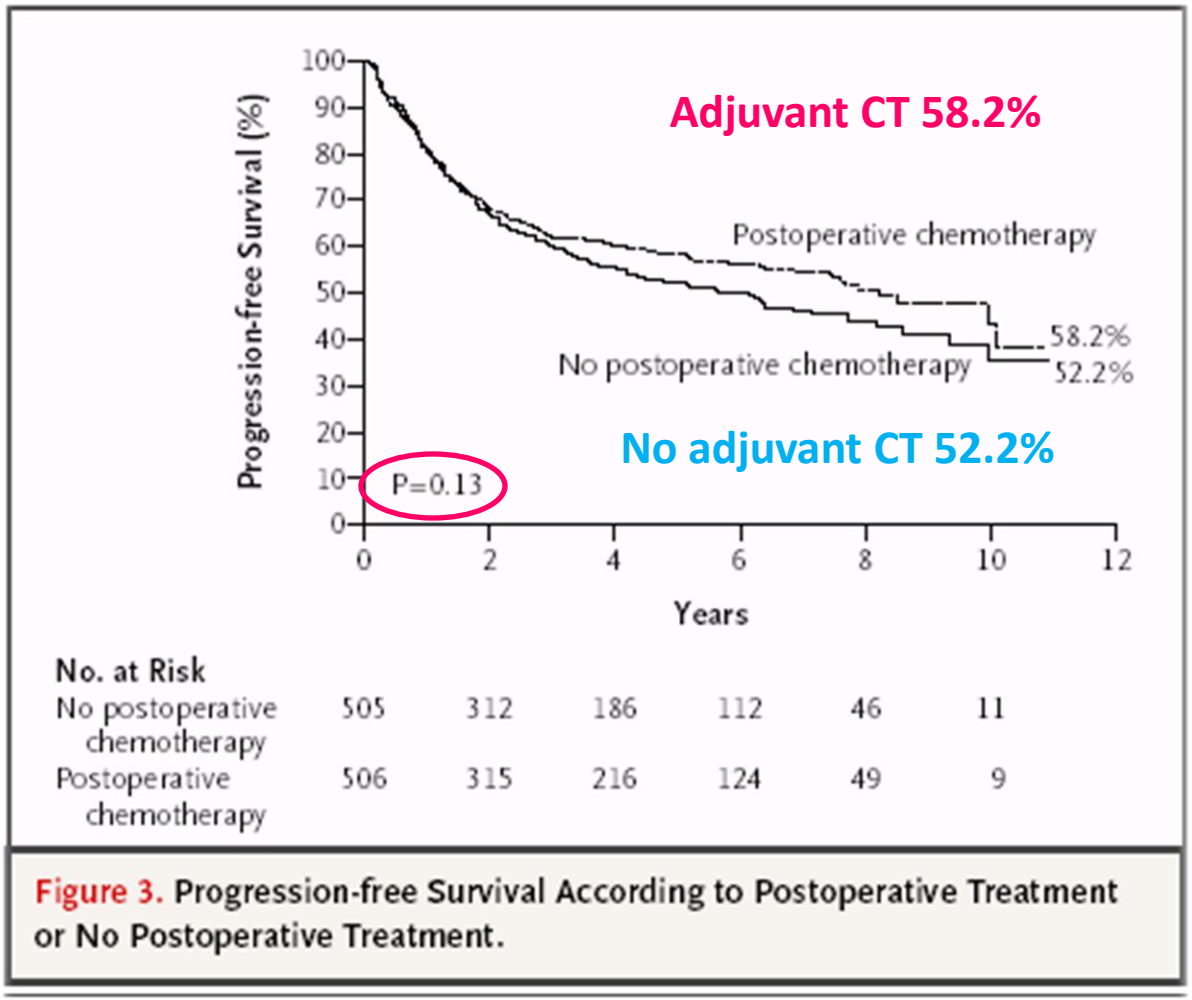
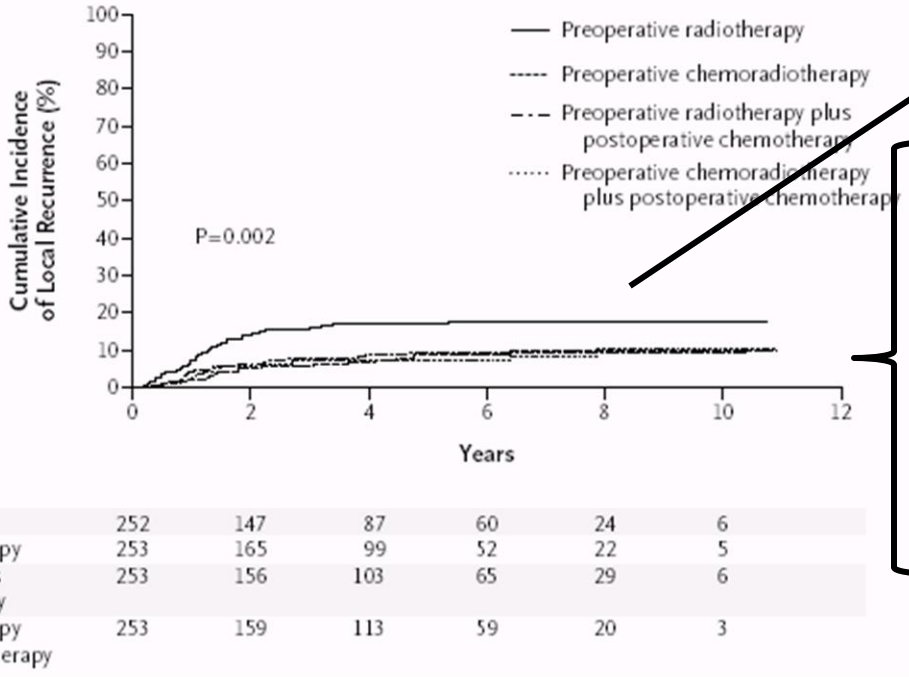


Figure 3. Progression-free Survival According to Postoperative Treatment or No Postoperative Treatment.

- **Adjuvan KT alan almayan fark yok (p=0.50)**
- **Preop RT ve pre op KRT fark yok (p=0.13)**

EORTC 22921:
Kemoterapi Grubunda Lokal Nüks daha az



No. at Risk

Preoperative radiotherapy	252	147	87	60	24	6
Preoperative chemoradiotherapy	253	165	99	52	22	5
Preoperative radiotherapy plus postoperative chemotherapy	253	156	103	65	29	6
Preoperative chemoradiotherapy plus postoperative chemotherapy	253	159	113	59	20	3

Figure 4. Cumulative Incidence of Local Recurrence as a First Event.

The cumulative incidence of local recurrence as a first event at 5 years was 17.1% in the preoperative-radiotherapy group, 8.7% in the preoperative-chemoradiotherapy group, 9.6% in the group receiving preoperative radiotherapy and postoperative chemotherapy, and 7.6% in the group receiving preoperative chemoradiotherapy and postoperative chemotherapy.

RT 17.1%

KRT 8.7%

RT + Postop KT 9.6%

KRT + Postop KT 7.6%

EORTC 22921 - SONUÇ

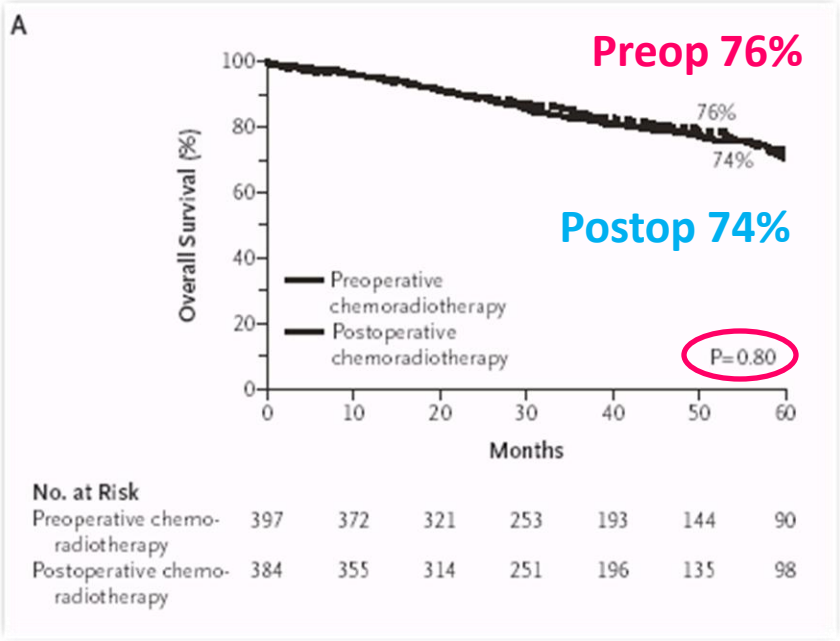
- Sfinkter koruyucu cerrahi oranlarında fark yok → 50.5% RT and 52.8% KRT
- Uzak metastaz kümülatif sıklığı cerrahi sonrası KT alan ve almayan gruplarda farklı değil (p=0.14, 0.62)
- Adjuvan KT hastalıksız ve genel sağkalımda fark yaratmıyor

Alman CAA/ARO/AIO-94 Çalışması

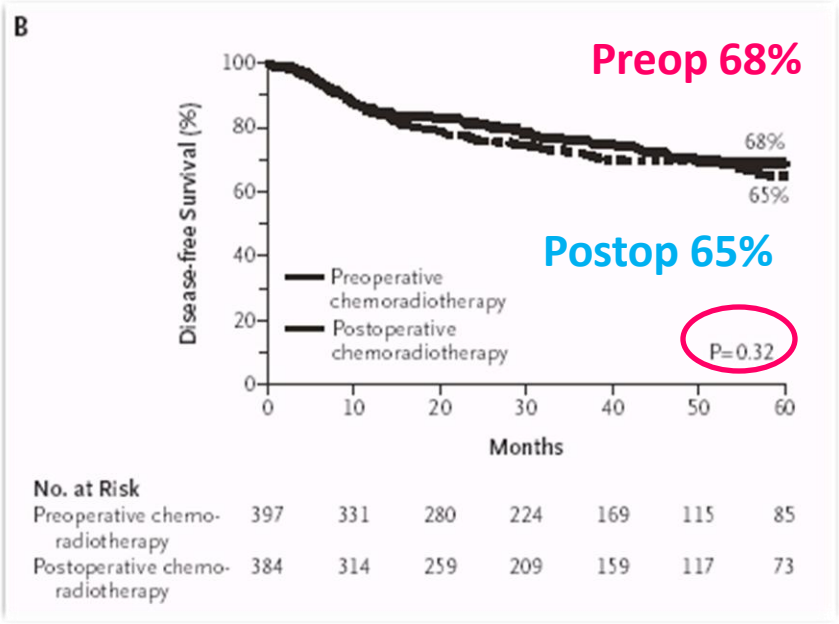
- 1995-2002 arası rezektable T3/T4 veya N+ tümörü 823 rektum kanserli hasta (anal verjden 16 cm) randomize edilmiş
- Preoperatif versus postopertif kemoradyoterapi
- Evreleme: TRUS
- Preoperatif KRT:
  - 50.4 Gy 28 fraksiyonda 1.8 Gy/gün
  - 5-FU 1000 mg/m²/d CIVI 120 saat birinci ve beşinci hafta
  - Cerrahi tedavi bitiminden 6 hafta sonra TME
  - Adjuvant KT (postop 1 ay sonra)→ bolus 5-FU 500 mg/m², 5 gün dört haftada bir 4 kez
- Postoperative KRT:
  - Preoperatif grup gibi sadece tümör yatağına boost yok (5.4 Gy)

Alman Çalışması : 1º and 2º Sonlanım Noktaları

Genel Sağkalım (5-yıl)



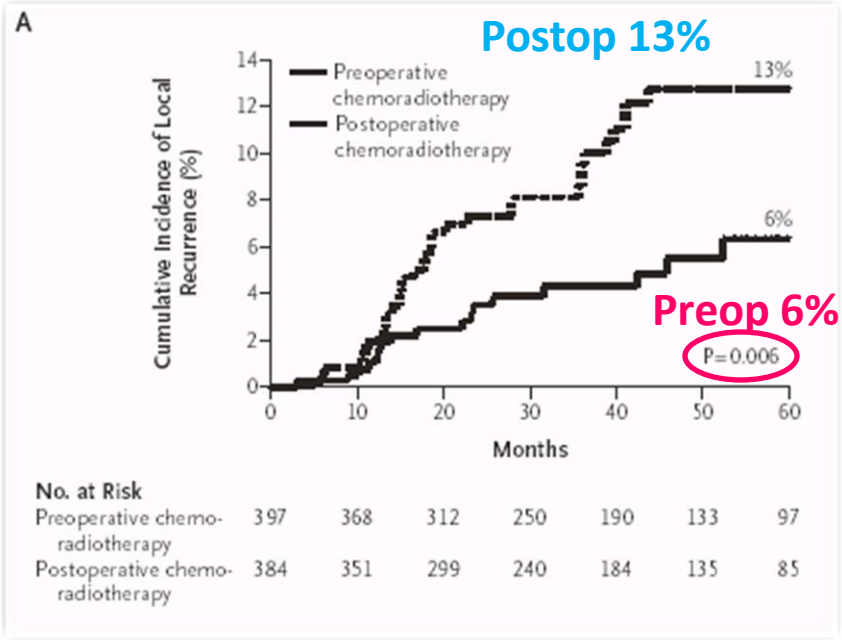
Hastalıksız Sağkalım (5-yıl)



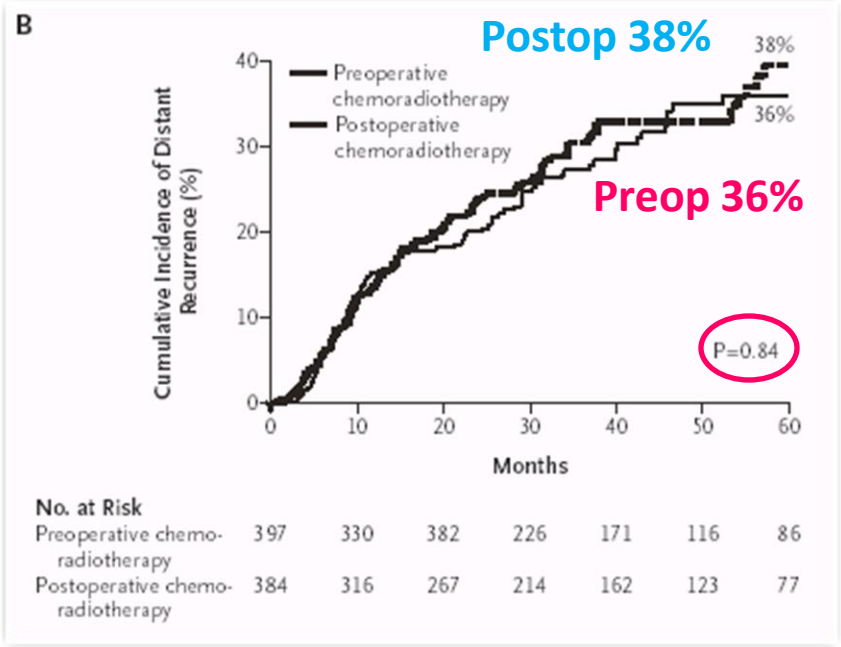
Preop postop tedaviler arasında fark yok

Alman Çalışması : 2º Sonlanım

Cumulative Incidence of Local Recurrence (5-year)



Cumulative Incidence of Distant Recurrence (5-year)



Preopertif grupta kümülatif lokal nüks daha düşük

Alman Çalışması : Diğer 2^{o} Sonlanım

- ↑ pCR preopertif grupta daha fazla (8% v. 0%, p<0.001)
- Grad 3 veya 4 akut toksisite (27% versus 40%, p=0.001)
- Uzun süreli toksiste (14% versus 24%, p=0.01)

Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer
Sauer R et al NEJM, 2005

Table 4. Rates of Sphincter-Sparing Surgery in 194 Patients Determined by the Surgeon before Randomization to Require Abdominoperineal Resection, According to Actual Treatment Given.

Variable	Preoperative Chemoradiotherapy (N=415)	Postoperative Chemoradiotherapy (N=384)	P Value
Abdominoperineal resection deemed necessary — no. (%)	116 (28)	78 (20)	
Sphincter-preserving surgery performed — no./total no. (%)	45/116 (39)	15/78 (19)	0.004

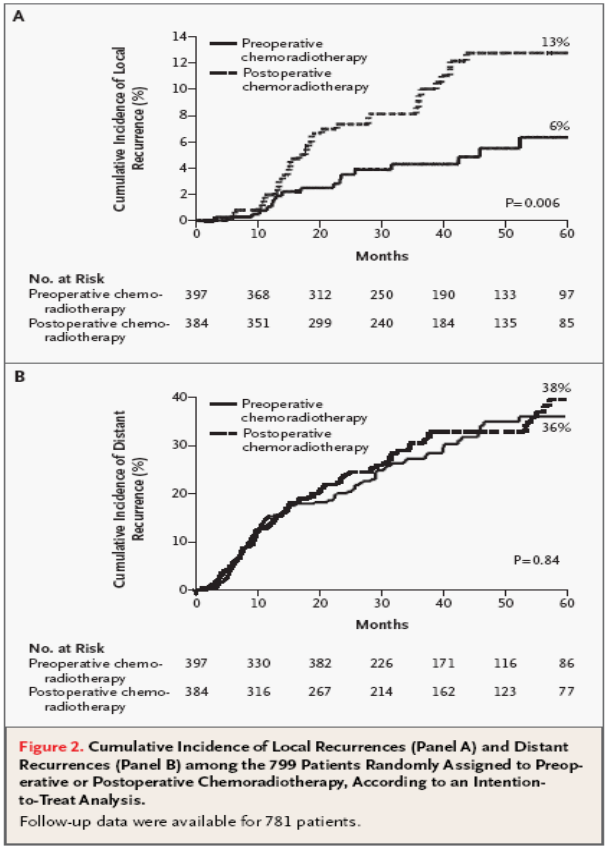


Figure 2. Cumulative Incidence of Local Recurrences (Panel A) and Distant Recurrences (Panel B) among the 799 Patients Randomly Assigned to Preoperative or Postoperative Chemoradiotherapy, According to an Intention-to-Treat Analysis.
Follow-up data were available for 781 patients.

T3, T4, N+
5040 cGy (180cGy/g)
5-FU 1000mg/m2
120 st, sp, 1. ve 5. Hafta

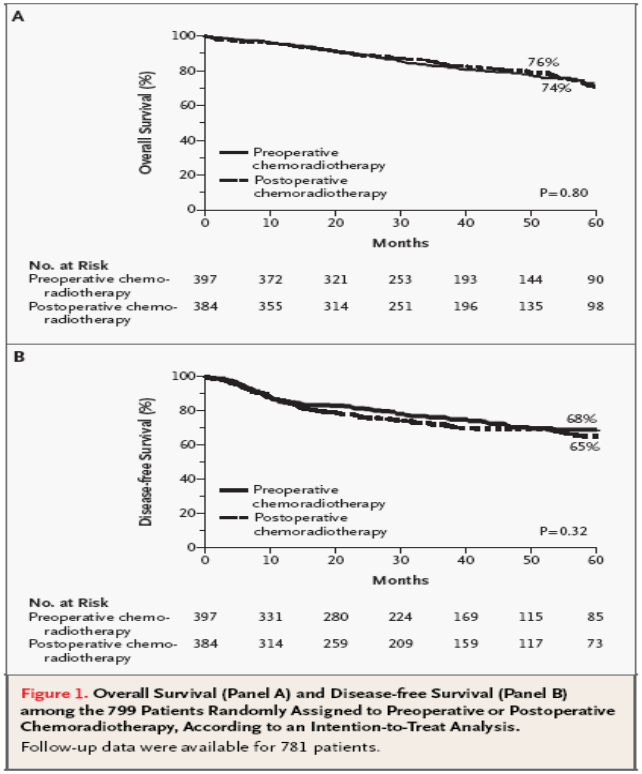


Figure 1. Overall Survival (Panel A) and Disease-free Survival (Panel B) among the 799 Patients Randomly Assigned to Preoperative or Postoperative Chemoradiotherapy, According to an Intention-to-Treat Analysis.
Follow-up data were available for 781 patients.

Table 5. Grade 3 or 4 Toxic Effects of Chemoradiotherapy, According to Actual Treatment Given.*

Type of Toxic Effect	Preoperative Chemoradiotherapy (N=399)	Postoperative Chemoradiotherapy (N=237)	P Value
	% of patients		
Acute			
Diarrhea	12	18	0.04
Hematologic effects	6	8	0.27
Dermatologic effects	11	15	0.09
Any grade 3 or 4 toxic effect	27	40	0.001
Long-term			
Gastrointestinal effects†	9	15	0.07
Strictures at anastomotic site	4	12	0.003
Bladder problems	2	4	0.21
Any grade 3 or 4 toxic effect	14	24	0.01

Randomize Çalışmalar Özet - I

1. Neoadjuvan KRT ile Evre İndirgenmesi (pCR) ?
   - FFCD 9203 Çalışması: **EVET**(11.4% CRT v. 3.6% RT; p<0.0001)
   - Polonya Çalışması : **EVET** (16.1% CRT v. 0.7% RT; p<0.001)
   - EORTC 22921 Çalışması : **EVET** (13.7% CRT v. 5.3%; p<0.001)
   - Alman Çalışması : **EVET** (8% Preop CRT v. 0% Postop CRT)
2. Neoadjuvan Tedavi Sfinkter Koruyucu Cerrahi Şansını arttırır mı ?
   - FFCD 9203 Çalışması: **HAYIR**
   - Polonya Çalışması: **HAYIR**
   - EORTC 22921 Çalışması: **HAYIR**
   - Alman Çalışması: **HAYIR** (Preop vs Postop KRT)

Randomize Çalışmalar Özet - II

3. Neoadjuvan kemoradyoterapi sağkalımı (OS, DFS) arttırır mı ?
   - FFCD 9203 Çalışmasıl: **Hayır** - 67.4% / 59.4% (5-yıl)
   - Polonya Çalışması: **Hayır**- 66.2% / 55.6% (4-yıl)
   - EORTC 22921 Çalışması: **Hayır** - 64.8% / 56.1% (5-yıl)
   - Alman Çalışması : **Hayır** - 76% / 68% (5-yıl)
4. Neoadjuvan kemoradyoterapi lokal / sistemik nüksü azaltır mı ?
   - FFCD 9203 Çalışması: **EVET** (8.1% KRT v. 16.5% RT) // **HAYIR** (36%)
   - POlonya Çalışması : **HAYIR** (15.6% CRT v. 10.6% RT) // **HAYIR** (34.6%)
   - EORTC 22921 Çalışması : **EVET** (13.7% CRT v. 5.3%) // **HAYIR** (34.4%)
   - Alman Çalışması : **EVET** (6% Preop CRT v. 13% Postop CRT) // **HAYIR** (36% Pre)

Randomize Çalışmalar Özet -III

5. Neoadjuvan Kemoradyoterapi ile toksiste artıyormu ?
   - FFCD 9203 Çalışması: **EVET** (14.9% KRT v. 2.9%; p<0.0001)
   - Polonya Çalışması: **EVET** (18.2% KRT v. 3.2% RT; p<0.001)
   - EORTC 22921 Çalışması: **EVET** (KRT>RT)
   - Alman Çalışması: **HAYIR** (27% Preop v. 40% Postop; p=0.001)
6. Hasta Uyumluluğu Nasıl?
   - FFCD 9203 Çalışması: 93% Neoadj KT & 78.1% Adjuvan KT
   - Polish Trial: ?
   - EORTC 22921 Çalışması: 82% Neoadj & Adjuvan KT 42.9%
   - German Çalışması : 92% Preop KT & 53% Postop KT

Yeni Ajanlar

Neoadjuvant Chemoradiotherapy plus Oxaliplatin in Locally Advanced Rectal Cancer

Trial	Patient population	N	Regimens*	Primary endpoint
ACCORD 12/0405	T3-4 N0-2 M0 DRE accessible	598	RT+ CapOx 50 vs. RT + Cap 45	ypCR
STAR-01	T3-4 and/or N+ M0 ≤ 12 cm of anal verge	747	RT + 5-FU + Oxal vs. RT + 5-FU	OS

*RT + CapOx 50: 50 Gy/5wk + capecitabine 800mg/m^2 bid 5 of 7 days qw + oxaliplatin 50 mg/m^2 qw for 5 weeks
RT + Cap 45: 45 Gy/5wk + capecitabine 800mg/m^2 bid 5 of 7 days qw for 5 weeks

RT + 5-FU + Oxal: 50.4 Gy + 5-fluorouracil 225 mg/m^2/d + oxaliplatin 60 mg/m^2 qw for 6 weeks
RT + 5-FU: 50.4 Gy + 5-fluorouracil 225 mg/m^2/d for 6 weeks

Gerard et al. *J Clin Oncol* 2009; 27(suppl):797s (LBA 4007)
Aschele et al. *J Clin Oncol* 2009; 27(suppl):804s (CRA4008)

Neoadjuvant Chemoradiotherapy plus Oxaliplatin in Locally Advanced Rectal Cancer

	ACCORD 12/0405		STAR-01	
	CRT + Oxal (n = 276)	CRT (n = 282)	CRT + Oxal (n = 368)	CRT (n = 379)
pCR	19%	14%	16%	16%
	P = .11		*P* = .94	
CRM* R1	7%	12%	NR	NR
	P = .21			
N1/2	NR	NR	27%	25%
M1	3%**	4%**	0.5%	3%
			P = .014	
	(n = 291)	**(n = 293)**	**(n = 353)**	**(n = 379)**
Toxicity (G3/4)	**25%**	**11%**	**24%**	**8%**
	***P* < .0001**		***P* < .0001**	

*CRM – circumferential resection margin

** abdominal cavity

Gerard et al. *J Clin Oncol* 2009; 27(suppl):797s (LBA 4007)
Aschele et al. *J Clin Oncol* 2009; 27(suppl):804s (CRA4008)

Yeni Neoadjuvan Yaklaşımlar

- **Cetuximab İçeren Rejimler**
  - Cape/ox/cetux/50Gy → TME → FOLFOX4 + Cetux
- **Bevacizumab içeren rejimler**
  - Preop Cape + Bevacizumab + RT
  - Preop FOLFOX + Bevacizumab radyoterapi verilmeden
  - Cape/ox/bevacizumab → Cerrahi → FOLFOX/bevacizumab
- **Kısa Süreli RT + KT versus Konvansiyonel Kemoradyoterapi**
  - Kısa Süreli RT + FOLFOX4 x 3 versus Konvansiyonel RT + bolus 5-FU + ox
- **Irinotecan versus Oxaliplatin**
  - Cape + irino + RT vs. Cape + oxali + RT

Neoadjuvan KRT sonrası adjuvan?
Neoaduvan KRT öncesi induksiyon ?

Patients With Curative Resection of cT3-4 Rectal Cancer After Preoperative Radiotherapy or Radiochemotherapy: Does Anybody Benefit From Adjuvant Fluorouracil-Based Chemotherapy? A Trial of the European Organisation for Research and Treatment of Cancer Radiation Oncology Group

Laurence Collette, Jean-Francois Bosset, Marcel den Dulk, France Nguyen, Laurent Mineur, Philippe Maingon, Ljiljana Radosevic-Jelic, Marianne Piérart, and Gilles Calais

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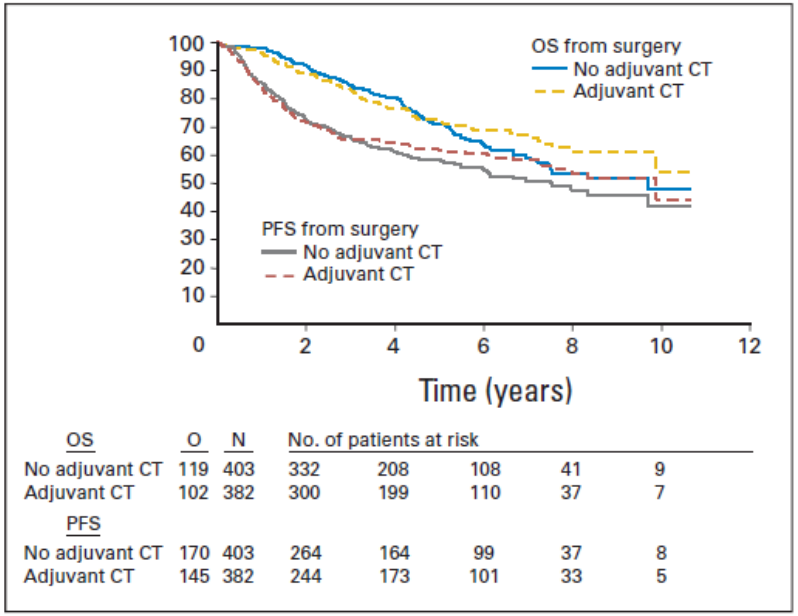
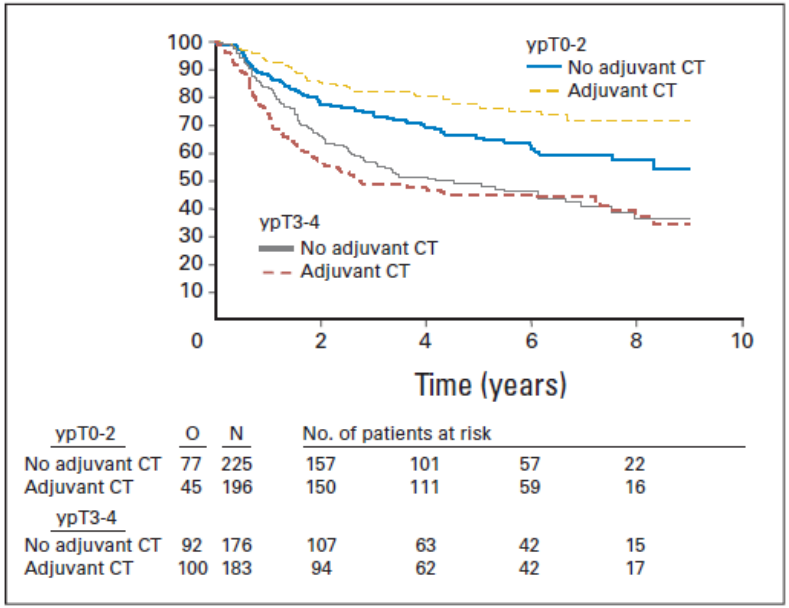
ORIGINAL REPORT



	O	N	No. of patients at risk				
OS							
No adjuvant CT	119	403	332	208	108	41	9
Adjuvant CT	102	382	300	199	110	37	7
PFS							
No adjuvant CT	170	403	264	164	99	37	8
Adjuvant CT	145	382	244	173	101	33	5



	O	N	No. of patients at risk				
ypT0-2							
No adjuvant CT	77	225	157	101	57	22	
Adjuvant CT	45	196	150	111	59	16	
ypT3-4							
No adjuvant CT	92	176	107	63	42	15	
Adjuvant CT	100	183	94	62	42	17	

Phase II, Randomized Study of Concomitant Chemoradiotherapy Followed by Surgery and Adjuvant Capecitabine Plus Oxaliplatin (CAPOX) Compared With Induction CAPOX Followed by Concomitant Chemoradiotherapy and Surgery in Magnetic Resonance Imaging–Defined, Locally Advanced Rectal Cancer: Grupo Cáncer de Recto 3 Study

Carlos Fernández-Martos, Carles Pericay, Jorge Aparicio, Antonieta Salud, MariaJose Safont, Bertomeu Massuti, Ruth Vera, Pilar Escudero, Joan Maurel, Eugenio Marcuello, Jose Luis Mengual, Eugenio Saigi, Rafael Estevan, Moises Mira, Sonia Polo, Ana Hernandez, Manuel Gallen, Fernando Arias, Javier Serra, and Vicente Alonso

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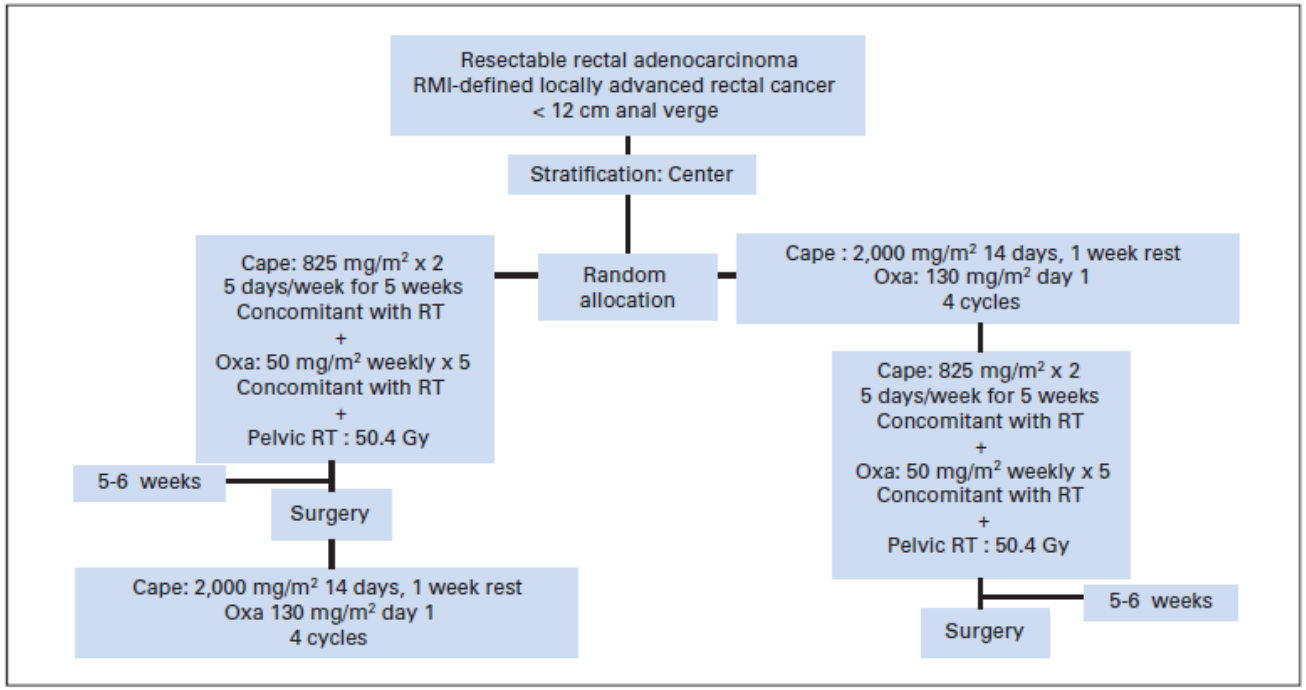

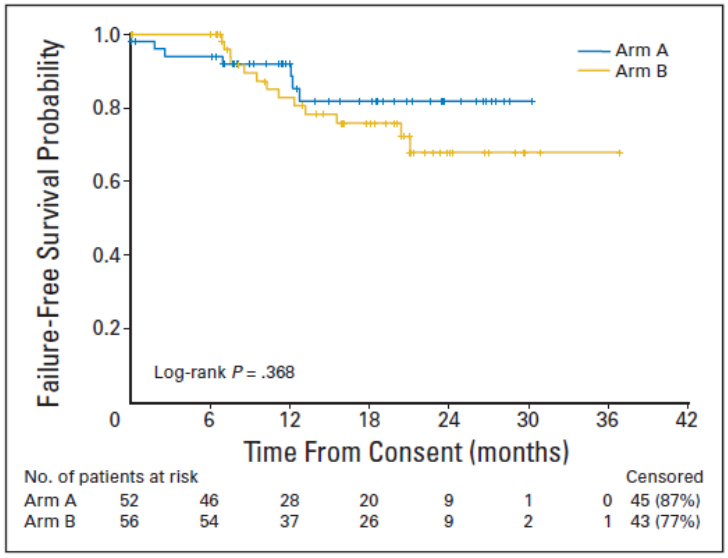

Table 3. End Points for the Total Patient Group

End Point	Arm A: Post-operative Adjuvant CT (n = 52) No.	%	Arm B: Induction CT (n = 56) No.	%	P*
pCR	7	13	8	14	.94
95% CI, %	5.6 to 25.8		6.4 to 26.2		
Downstaging	30	58	24	43	.13
95% CI, %	43.2 to 71.3		29.7 to 56.8		
R0 resection rates	45	87	48	86	.40
TRG†					
4: complete regression	7	15	8	15	.88
3: > 50% of tumor mass	22	48	20	37	
2: ≥ 25%-50% of tumor mass	11	24	13	24	
1: < 25% of tumor mass	2	4	3	6	
0: no regression	1	2	3	6	
Not otherwise specified	3	7	7	13	

Abbreviations: CT, chemotherapy; pCR, pathologic complete response; TRG, tumor regression grade.
*Fisher's exact test.
†The denominators were the patients who actually underwent resection.