

Özefagus SCC, Neo adjuvan & definitif KRT? Tam yanıt var, ameliyat şart mı?



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Ege Üniversitesi Tıp fakültesi
Genel Cerrahi

6. Ulusal cerrahi Onkoloji Kongresi 24-27 Şubat 2022

Lokal ileri Özefagus kanserinde tedavi

CROSS

- Neoadjuvan radyokemoterapi
- 41.4 Gy+Karboplatin+Paklitaksel
- Ivor-Lewis veya McKeown özefajektomi

FLOT

- Perioperatif kemoterapi (5-FU, Oksaliptin ve Docetaxel)
- Ivor-Lewis veya McKeown özefajektomi

Patolojik tam yanıt

Skuamöz hücreli
karsinom %49

Adenokanser
%16-35

Al-Batran SE. *Lancet Oncol*. 2016
van Hagen P. *N Engl J Med*. 2012

Patolojik tam yanıt

Primer tümör bölgesinde veya rezeke edilen bölgesel lenf düğümlerinde
histolojik tümör hücrelerinin saptanamamasıdır.

Diseases of the Esophagus, 2017

Patolojik tam yanıt

Study	Study Design (N, Control)	Country/Recruitment Time	FCR Rate after CRT (Surgery Group)	On-Demand Surgery Rate During Surveillance
Park 2019 [12] (NSOPK2502)	Phase III RCT (3)	South Korea (2012-2016)	49%	33%
Indroney 2007 [13] (NCT00130202)	Phase III RCT (NA)	France (1995-2000)	NA	NA
Stahl 2007 [14]	Phase III RCT (11)	Germany (1994-2002)	33%	4%

A Scoping Review, *Cancers*, 2021

Tam yanıt sonrası tedavi

Cerrahi

Takip + Gerektiğinde cerrahi

Diseases of the Esophagus, 2017

Özefajektomi

Morbidite %36-80

Mortalite %4-11

Yaşam kalitesi ↓

Nimptsch U, BMJ, 2017
Talolli E, Semin Thorac Cardiovasc Surg, 2017
van der Sluis PC, Ann Surg, 2019

Tam yanıt sonrası tedavi

Cerrahi

Takip + Gerektiğinde cerrahi

Diseases of the Esophagus, 2017

Tam yanıtı belirleme

Neo-adjuvan tedaviden 4-6 hafta sonra

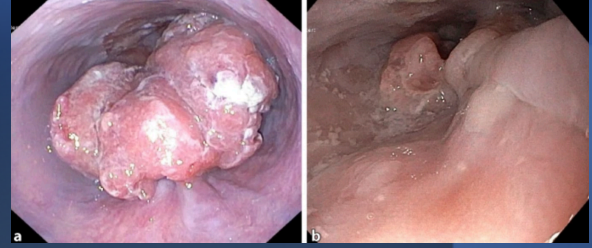
BT

PET/BT

Endoskopi-Biopsi

Yukarıdakiler negatifse

Sano trial, 2018, BMC cancer



Tam yanıtı belirleme

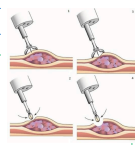
6-8 hafta sonra ikinci genişletilmiş tarama yapılmalı

Endoskopi-EUS

- Tümör kalınlığı
- Derin Biopsi (bite-on-bite)
- Şüpheli lenf nodundan aspirasyon biopsisi
- Yanlış negatif < %10

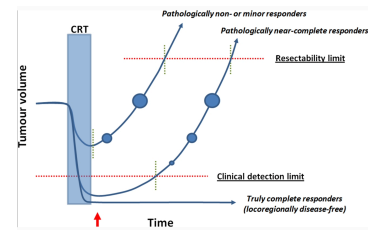
PET-CT

- %9 uzak metastaz saptanır



Sano trial, 2018, BMC cancer

Takip



Diseases of the Esophagus, 2017

Neoadjuvan sonrası takip

3 ay ilk 2 yıl

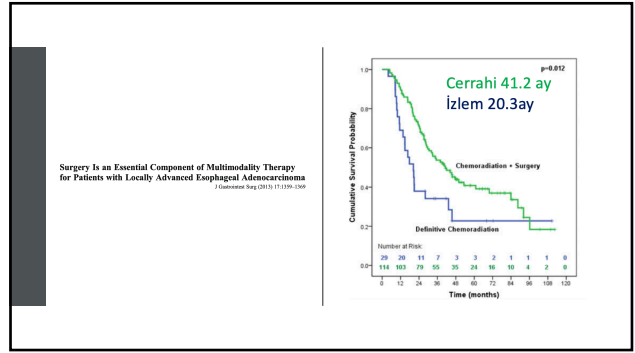
6 ay sonraki 5 yıl

BT ve endoskopik biopsi, EUS her 6 ay

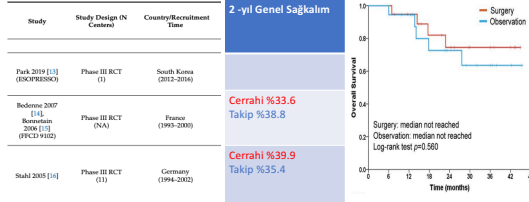
A Scoping Review, Cancers, 2021

Study	Study Design (N Centers)	Country/Recruitment Time	Description of Patients (TNM Stage)	Study Arms	Chemotherapy	Radiotherapy (Total Dose)	Intervention after RT	Results (Overall HR)
Park 2019 [13] (EORTC18084)	Phase III RCT (1)	South Korea (2012-2016)	Patients aged 20-75 with histologically confirmed, resectable locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	Capecitabine + Etoposide Capecitabine + Etoposide	54.18 Gy/27 fractions 54.18 Gy/27 fractions	None/None	None/None
Bedenne 2007 [14] (Borismatin 2006) (FFCD 9302)	Phase III RCT (2)	France (1993-2000)	Patients with histologically confirmed or pathologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	5-FU + Etoposide 5-FU + Etoposide	NA 54.18 Gy/27 fractions	None/None	None/None
Stahl 2005 [14]	Phase III RCT (1)	Germany (1994-2002)	Patients aged 20 years with histologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	5-FU + Etoposide 5-FU + Etoposide	54.18 Gy/27 fractions 54.18 Gy/27 fractions	None/None	None/None
Nguyen 2006 [15]	MAO (1)	Spain (2004-2005)	Patients with histologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	Capecitabine + Etoposide Capecitabine + Etoposide	54.18 Gy/27 fractions 54.18 Gy/27 fractions	None/None	None/None
Nomura 2010 (JCOA0902)	Phase III RCT (2)	The Netherlands (2007-2007)	Patients aged 20 years with histologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	Capecitabine + Etoposide Capecitabine + Etoposide	54.18 Gy/27 fractions 54.18 Gy/27 fractions	None/None	None/None
de Wit 2012 (EORTC18084)	Phase III RCT (1)	China (2007-2010)	Patients aged 20-75 with histologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	Capecitabine + Etoposide Capecitabine + Etoposide	54.18 Gy/27 fractions 54.18 Gy/27 fractions	None/None	None/None
Bedenne 2007 [14] (Borismatin 2006) (FFCD 9302)	Phase III RCT (2)	France (1993-2000)	Patients with histologically confirmed or pathologically confirmed locally advanced (cT3-4, N1-2, M0) esophageal adenocarcinoma	Chemotherapy + Surgery Chemotherapy + Radiotherapy + Surgery	5-FU + Etoposide 5-FU + Etoposide	NA 54.18 Gy/27 fractions	None/None	None/None
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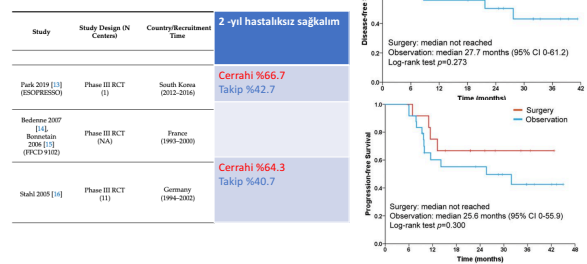
A Scoping Review, Cancers, 2021



Genel sağkalım-RKÇ



Hastalısız sağkalım-RKÇ



Lokal nüks

- Rekürrens ortalama 5.9 ay
 - Cerrahi %31.6
 - İzlem % 44.4
 - Tamamina yakını rezektabl
- Uzak organ metastazı benzer

	Entire population (n=82)	Surgery (n=19)	Observation (n=63)	p-Value
Alive	52 (63.4%)	15 (78.9%)	37 (58.7%)	0.736
Without recurrence or disease progression	41 (50.0%)	12 (63.2%)	29 (46.0%)	
With recurrence	11 (13.4%)	3 (15.8%)	8 (12.6%)	
Death	30 (36.6%)	4 (21.1%)	26 (41.3%)	0.762
Cancer-related	19 (23.2%)	3 (15.8%)	16 (25.4%)	
Surgery-related	6 (7.3%)	1 (5.3%)	5 (7.8%)	
Other cause	2 (2.4%)	0 (0%)	2 (3.2%)	
Unknown	3 (3.7%)	0 (0%)	3 (4.8%)	
First failure pattern				0.056
Locoregional relapse	13 (15.9%)	3 (15.8%)	10 (15.9%)	
Distant metastasis	4 (4.9%)	0 (0%)	4 (6.3%)	
Locoregional relapse + distant metastasis	3 (3.7%)	3 (15.8%)	0 (0%)	

Anticancer Res, 2019, ESOPRESSO Trial

Active Surveillance Versus Immediate Surgery in Clinically Complete Responders After Neoadjuvant Chemoradiotherapy for Esophageal Cancer: A Multicenter Propensity Matched Study

Annals of Surgery
December 2021

- 3-yıl genel sağkalm
 - İzlem %77
 - Cerrahi %55
- 3-yıl hastaliksız sağkalm
 - İzlem %60
 - Cerrahi %54
- Uzak metastaz %28
- Radikal rezeksiyon %100
- Postop komplikasyon
 - İzlem %43
 - Cerrahi %45

Sonuç

- İzlem
 - RO düşük
 - Daha ileri evrede saptandı

	Entire population (n=82)	Surgery (n=19)	Observation (n=63)	p-Value
Surgery*				
Yes	51 (62.2%)	19 (100%)	32 (50.8%)	
No	31 (37.8%)	0 (0%)	31 (49.2%)	
Extent of surgery**				0.071
R0	41 (50.0%)	12 (63.2%)	29 (46.0%)	
R1	4 (4.9%)	1 (5.3%)	3 (4.8%)	
R2	3 (3.7%)	0 (0%)	3 (4.8%)	
Open & Close†	1 (1.2%)	0 (0%)	1 (1.6%)	
Type of surgery**				1.000
Ivor-Lewis operation	29 (35.4%)	9 (47.4%)	20 (31.7%)	
Mekdivan operation	20 (24.4%)	5 (26.3%)	15 (23.8%)	
Others	2 (2.4%)	1 (5.3%)	1 (1.6%)	
Postoperative hospital stay (days)**	15 (18.3%)	16 (84.2%)	15 (23.8%)	0.084
Postoperative death within 30 days after surgery**	1 (1.2%)	0 (0%)	1 (1.6%)	
Postoperative complications**				0.129
Wound and pain†	19 (23.2%)	3 (15.8%)	16 (25.4%)	
Pneumonia	10 (12.2%)	2 (10.5%)	8 (12.6%)	
Cardiac arrhythmia	4 (4.9%)	1 (5.3%)	3 (4.8%)	
Wound infection	3 (3.7%)	0 (0%)	3 (4.8%)	
Chest infection	2 (2.4%)	0 (0%)	2 (3.2%)	
Anastomosis site leakage	3 (3.7%)	0 (0%)	3 (4.8%)	
Malnutrition	3 (3.7%)	0 (0%)	3 (4.8%)	
Bronchial fistula	1 (1.2%)	0 (0%)	1 (1.6%)	

Anticancer Res, 2019, ESOPRESSO Trial

Sonuç

- Cerrahi
 - daha düşük T ve TNM,
 - daha yüksek patolojik yanıt elde edilmiştir.

	Entire population (n=82)	Surgery (n=19)	Observation (n=63)	p-Value
Pathologic T stage***				0.008
T0	17 (20.7%)	9 (47.4%)	8 (12.7%)	
T1	2 (2.4%)	1 (5.3%)	1 (1.6%)	
T2	6 (7.3%)	1 (5.3%)	5 (7.8%)	
T3	31 (37.8%)	2 (10.5%)	29 (46.0%)	
T4	2 (2.4%)	0 (0%)	2 (3.2%)	
T5	4 (4.9%)	0 (0%)	4 (6.3%)	
Pathologic N stage***				0.148
N0	27 (32.9%)	9 (47.4%)	18 (28.6%)	
N1	15 (18.3%)	6 (31.6%)	9 (14.3%)	
N2	7 (8.5%)	0 (0%)	7 (11.1%)	
N3	1 (1.2%)	0 (0%)	1 (1.6%)	
Pathologic TNM stage***				0.002
0	15 (18.3%)	9 (47.4%)	6 (9.5%)	
Ia	2 (2.4%)	1 (5.3%)	1 (1.6%)	
Ib	3 (3.7%)	0 (0%)	3 (4.8%)	
IIa	4 (4.9%)	0 (0%)	4 (6.3%)	
IIb	10 (12.2%)	1 (5.3%)	9 (14.3%)	
IIIa	4 (4.9%)	0 (0%)	4 (6.3%)	
IIIb	3 (3.7%)	0 (0%)	3 (4.8%)	
IV	2 (2.4%)	0 (0%)	2 (3.2%)	
Other (T0N1M0)	2 (2.4%)	0 (0%)	2 (3.2%)	
Other (T0N1M1)	2 (2.4%)	0 (0%)	2 (3.2%)	
Other (T0N1M2)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M3)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M4)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M5)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M6)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M7)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M8)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M9)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M10)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M11)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M12)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M13)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M14)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M15)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M16)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M17)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M18)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M19)	1 (1.2%)	0 (0%)	1 (1.6%)	
Other (T0N1M20)	1 (1.2%)	0 (0%)	1 (1.6%)	

Anticancer Res, 2019, ESOPRESSO Trial

Komplikasyon

- Cerrahi
 - Daha az lokal rekürrens
 - Daha az disfaji
 - Daha az disfajiye müdahale edilir.

	End Point	Surgery (n=19)	Chemoradiation (n=63)	Observation (n=63)	p
Intention-to-treat analysis					0.016
Cumulative hospital stay, days		68	62	60	
SD		5	4	4	
Hospital stay > 5 days per month of survival, %		61	76	76	<.008
Therapeutic grade 3 or higher dysphagia, %		12	1	1	<.0001
No. of patients		3	0	0	
Relative intervention for dysphagia		9.3	0.6	0.6	<.0002
No. of patients		31	60	60	
SD		24.0	46.2	46.2	
Chelation		24	18	18	
%		76.9	30.0	30.0	
Stent		7	42	42	
%		22.6	66.7	66.7	
Dysphagia < c grade 3 at last follow-up before death		38/60	36/79	36/79	0.4
No. of patients		63.3	45.6	45.6	
%		63.3	45.6	45.6	

P<0.001

JOURNAL OF CLINICAL ONCOLOGY, JCO 9102, 2007

Hastaya sorulim

Original article

Patients' preferences for treatment after neoadjuvant chemoradiotherapy for oesophageal cancer

B. J. Noordman¹, B. W. de Bekker-Grob^{2,3}, P. E. L. O. Coenen⁴, E. van der Ham⁵, S. M. Lagendijk⁶, J. Shapiro⁷, B. P. L. Wijnhoven¹ and J. J. B. van Lanschot¹ (1) Radboud University Medical Center, (2) University of Groningen, (3) University of Twente, (4) University of Groningen, (5) University of Groningen, (6) University of Groningen, (7) University of Groningen

Hastalar ameliyat olmamak için 5 yıllık genel sağkalmın %16 sından feragat edebileceğini belirtmişlerdir

	1. Active surveillance A	2. Active surveillance B	3. Immediate surgery
Mean time to quality of life (QoL) decline after treatment (n=100 patients)	76	66	60
Long-term quality of life (n=100 patients)	76	66	79
Risk that surgery is necessary	3	2	1
Physical burden of surveillance (n=100 patients)	3	2	1
Chance of being alive in 10 years	100	100	100

Hastama ne söylemeliyim?

Neoadjuvan sonrası tam yanıtta cerrahinin izleme üstünlüğü yok

Genel sağkalım, hastaksız sağkalım, cerrahi uygulanan kolda daha uzun; ancak anlamlı değil

Lokal nüks izlem kolunda daha fazla, anlamlı değil

Yukarıdaki sonuçları elde etmek için neoadjuvan tedavi, tam yanıtın değerlendirilmesi ve gözlem hastalarında yakın takip önemlidir

Devam eden çalışmalar var; sonuçları önemli

- SAKO (Hollanda)-2025
- CELASC (Çin)
- ESOTRATE (Fransa)

