CRM (-), LN (+) önce cerrahi mi, neoadjuvan tedavi mi ?

Dr. Emre Balık
Koç Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı

Soru

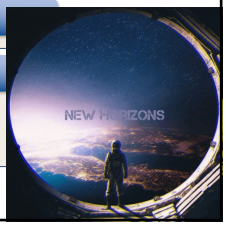
CRM - LN +

NEOADJUVAN TEDAVI ?

CERRAHI TEDAVI ?

Rektum Kanseri Standart Tedavi Yöntemi

- 2000- ERUS ve BT
- 2010 sonrasında MR
- cT1-2 Cerrahi
- cT3-T4- cTxN+ Trimodalite
  - Neoadjuvan tedavi
  - Cerrahi
  - Adjuvan tedavi



Rektum Kanseri

- Lokal nüks sorunu
  - %15-25
- Neoadjuvan tedavi
  - %5-10
- Ancak DFS – OSS üzerine etki ?
  - Evre 2-3 : %30-40 uzak metastaz
  - Başarısızlık?

Sorun

- Neoadjuvan tedavi sonrası bekleme
- KT tedavisinin gecikmesi
  - 20 hafta
  - mikrometastaz
  - Sadece 5 FU

Sorun

- T evresi MR %90 üzeri
- CRM MR. %90 üzeri
- Lenf nodu %55 -69
  - N < 2mm + %18-22*

Cevap

Neoadjuvan tedavi

NCCN : EVRE II- III

ESMO: T3 N1

Cevap

- Tümör lokalizasyonu
- Evreleme ?
- T3 a-b- c- d
- Lenf nodu
  - Boyut
  - Sayı
  - Lokalizasyon
- CRM
- EMVI

Hastaya Yansıyan

- Hastanın beklentisi
- Yaşam kalitesi
- Sfinkter koruma

Magnetic Resonance Imaging–Detected Tumor Response for Locally Advanced Rectal Cancer Predicts Survival Outcomes: MERCURY Experience

Uday B. Patel, Fiona Taylor, Lennart Blomqvist, Christopher George, Hywel Evans, Paris Tekkis, Philip Quirke, David Sebag-Montefiore, Brendan Moran, Richard Heald, Ashley Guthrie, Nicola Bees, Ian Swift, Kjell Pennert, and Gina Brown

A B S T R A C T

Purpose
To assess magnetic resonance imaging (MRI) and pathologic staging after neoadjuvant therapy for rectal cancer in a prospectively enrolled, multicenter study.

Methods
In a prospective cohort study, 111 patients who had rectal cancer treated by neoadjuvant therapy were assessed for response by MRI and pathology staging by T, N and circumferential resection margin (CRM) status. Tumor regression grade (TRG) was also assessed by MRI. Overall survival (OS) was estimated by using the Kaplan-Meier product-limit method, and Cox proportional hazards models were used to determine associations between staging of good and poor responders on MRI or pathology and survival outcomes after controlling for patient characteristics.

Results
On multivariate analysis, the MRI-assessed TRG (mrTRG) hazard ratios (HRs) were independently significant for survival (HR, 4.40; 95% CI, 1.65 to 11.7) and disease-free survival (DFS; HR, 3.28; 95% CI, 1.22 to 8.80). Five-year survival for poor mrTRG was 27% versus 72% ($P = .001$), and DFS for poor mrTRG was 31% versus 64% ($P = .007$). Preoperative MRI-predicted CRM independently predicted local recurrence (LR; HR, 4.25; 95% CI, 1.45 to 12.51). Five-year survival for poor post-treatment pathologic T stage (ypT) was 39% versus 76% ($P = .001$); DFS for the same was 38% versus 84% ($P = .001$); and LR for the same was 27% versus 6% ($P = .018$). The 5-year survival for involved pCRM was 30% versus 59% ($P = .001$); DFS, 28 versus 62% ($P = .02$); and LR, 56% versus 10% ($P = .001$). Pathology node status did not predict outcomes.

Conclusion
MRI assessment of TRG and CRM are imaging markers that predict survival outcomes for good and poor responders and provide an opportunity for the multidisciplinary team to offer additional treatment options before planning definitive surgery. Postoperative histopathology assessment of ypT and CRM but not post-treatment N status were important postsurgical predictors of outcome.

J Clin Oncol 29:3753-3760. © 2011 by American Society of Clinical Oncology

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Analysis of Data

Tumors were categorized into good and poor responders to enable binary comparison by multivariate analysis. On the basis of known histopathologic outcomes according to ypT stage, good ypT or ymrT stage was defined as stages T0, T1, T2, and T3a; poor was defined as ypT or ymrT stages T3b, T3c, T3d, or T4. Stages T3a and T2 tumors have similar outcomes and therefore are classified as good.[16,17]

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Preoperative Magnetic Resonance Imaging Assessment of Circumferential Resection Margin Predicts Disease-Free Survival and Local Recurrence: 5-Year Follow-Up Results of the MERCURY Study

Fiona G.M. Taylor, Philip Quirke, Richard J. Heald, Brendan J. Moran, Lennart Blomqvist, Ian R. Swift, David Sebag-Montefiore, Paris Tekkis, and Gina Brown

Results

Surviving patients were followed for a median of 62 months. The 5-year OS was 62.2% in patients with MRI-clear CRM compared with 42.2% in patients with MRI-involved CRM with a hazard ratio (HR) of 1.97 (95% CI, 1.27 to 3.04; $P < .01$). The 5-year DFS was 67.2% (95% CI, 61.4% to 73%) for MRI-clear CRM compared with 47.3% (95% CI, 33.7% to 60.9%) for MRI-involved CRM with an HR of 1.65 (95% CI, 1.01 to 2.69; $P < .05$). Local recurrence HR for MRI-involved CRM was 3.50 (95% CI, 1.53 to 8.00; $P < .05$). MRI-involved CRM was the only preoperative staging parameter that remained significant for OS, DFS, and LR on multivariate analysis.

Conclusion

High-resolution MRI preoperative assessment of CRM status is superior to AJCC TNM–based criteria for assessing risk of LR, DFS, and OS. Furthermore, MRI CRM involvement is significantly associated with distant metastatic disease; therefore, colorectal cancer teams could intensify treatment and follow-up accordingly to improve survival outcomes.

J Clin Oncol 32:34-43. © 2013 by American Society of Clinical Oncology

Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone

A Prospective, Multicenter, European Study

Fiona G.M Taylor, MBBS, FMRCS, Philip Quirke, PhD, BM, FRCPath†, Richard J Heald, MB, Bch, FRCS‡, Brendan Moran, MB, Bchir, FRCSI‡, Lennart Blomqvist, MD, PhD§, Ian Swift, MS, FRCS, FICS*, David J Sebag-Montefiore, FRCP, FRCR¶, Paris Tekkis, BMBS, MD, FRCS**, and Gina Brown, MBBS, MD, FRCR†† for the MERCURY study group*

MRI feature	Good prognosis	Poor prognosis
CRM	>1mm clear	<1mm involved
Low rectal <5cm T stage	intersphincteric plane clear of tumor T1/T2, T3a<1mm, T3b, 1-5mm extramural spread	intersphincteric plane involved by tumor T3c>5mm extramural spread, T4
EMVI	negative	positive
N stage	any	any

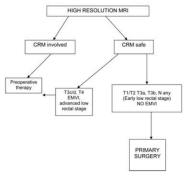

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TABLE 1. Demographics of 122 Patients (actual numbers in brackets)

Demographic Variable	Frequency (%)
Male	71 (58.2)
Female	51 (41.8)
Operation	
Anterior resection	102 (83.6)
Abdominoperineal excision	13 (10.7)
Hartmanns	6 (4.9)
Other	1 (0.8)
Height of tumor	
Low rectal (<5 cm)	20 (16.4)
Mid rectal (5–10 cm)	62 (50.8)
Upper rectal (10–15 cm)	40 (32.8)
MRI TN stage	
Stage I	T2N0 57 (46.7) 57
Stage II	T3a N0 24 (19.7)
	T3b N0 19 (15.6) 43
Stage III	T2 N1 7 (5.7) 1 = $CRM_{\geq 1 mm}$ on path
	T3a N1 6 (4.9) 1 = $CRM_{\geq 1 mm}$ on path
	T3b N1 7 (5.7) 2 = $CRM_{\geq 1 mm}$ on path
	T3b N2 2 (1.6) 22

MRI indicates magnetic resonance imaging; CRM, cross-enactive material; TN, tumor and node.

TABLE 2. Final Pathology for the Study Patients (n = 122)

	Frequency (%)	Path TN Stage Total
Variable		
Path CRM	Clear	118 (96.7)
	Involved	4 (3.3)
Stage I or less		Actual no. of local recurrence
pT0N0	7 (5.7)	0
pT1N0	8 (6.6)	0
pT2N0	34 (27.9)	49 1
Stage II		
pT3aN0	28 (16.4)	0
pT3bN0	7 (5.7)	0
pT4N0	2 (1.6)	29 1
Stage III		
pT1N1	1 (0.8)	0
pT2N1	9 (7.4)	0
pT2N2	1 (0.8)	0
pT3aN1	8 (6.6)	1
pT3bN1	9 (7.4)	0 (2 = $CRM_{\geq 1}$)
pT3bN2	7 (5.7)	1 (1 = $CRM_{\geq 1}$)
pT4aN0	3 (2.5)	0
pT4bN1	4 (3.3)	0 (1 = $CRM_{\geq 1}$)
pT4N1	2 (1.6)	44 0
	Total	122

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TABLE 3. Outcomes for MRI-predicted Good Prognosis Patients and Effect of Univariate and Multivariate Analysis Local Recurrence, 5-year Overall Survival and Disease-free Survival

MERCURY—MRI-predicted Good Prognosis Patients	Local Recurrence	5-Year Overall Survival	5-Year Disease-free Survival
Total patients (n = 122)	3.3%	68.2% (95% CI, 60.3%–7.0%)	84.7% (95% CI, 76.0%–90.4%)
T3a/b N0, N1, and N2 (n = 58)	1.7%	67.9% (95% CI, 53.9%–78.5%)	81% (95% CI, 66.1%–89.8%)
T1,2, or, 3b, N positive disease (n = 22)	0%	81% (95% CI, 48.7%–78.2%)	95% (95% CI, 69.5%–99.3%)

Univariate analysis

Preoperative Factor	Local Recurrence		Overall Survival		Disease-free Survival	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Height of tumor (low)	1.546 (0.161–14.863)	0.706	0.646 (0.253–1.651)	0.362	1.938 (0.682–5.505)	0.214
Type of operation (APE)	0.050 (0.000–7361.65)	0.622	1.499 (0.97–2.317)	0.068	1.384 (0.432–4.436)	0.584
Age (>65), y	0.783 (0.107–5.392)	0.760	2.854 (1.352–5.986)	0.004	1.009 (0.394–2.585)	0.985
Sex (male)	0.244 (0.025–2.345)	0.222	1.230 (0.649–2.334)	0.526	0.932 (0.368–2.365)	0.883

Multivariate analysis

Preoperative Factor	Local recurrence		Overall Survival		Disease-free Survival	
	Hazard Ratio	*P*	Hazard Ratio	*P*	Hazard Ratio	*P*
Height of tumor (low)	2.580 (0.268–24.829)	0.412	0.457 (0.171–1.220)	0.118	1.917 (0.598–6.152)	0.274
Type of operation (APE)	No events	n/a	2.128 (1.049–4.317)	0.036	1.031 (0.270–3.936)	0.964
Age (>65), y	0.821 (0.114–5.899)	0.845	2.967 (1.407–6.255)	0.004	0.968 (0.375–2.501)	0.947
Sex (male)	0.244 (0.025–2.374)	0.224	1.120 (0.585–2.146)	0.733	0.955 (0.376–2.428)	0.923

APE indicates abdominoperineal excision

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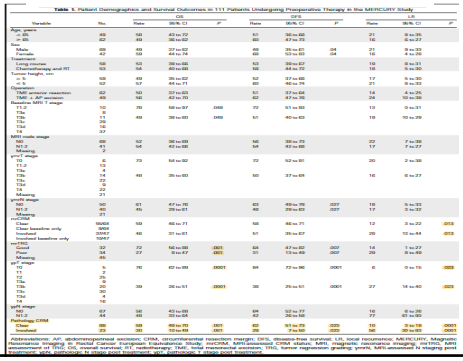

ESMO

Annals of Oncology 28 (Supplement 4): iv22–iv40, 2017
doi:10.1093/annonc/mdx224

CLINICAL PRACTICE GUIDELINES

Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

R. Glynne-Jones[1], L. Wyrwicz[2], E. Tiret[3,4], G. Brown[5], C. Rödel[6], A. Cervantes[7] & D. Arnold[8], on behalf of the ESMO Guidelines Committee*

Table 6. Recommended choice of treatment options within TNM risk category of primary rectal cancer without distant metastases

Risk group	TN substage	Possible therapeutic options	Further considerations
Very early	cT1 sm1 N0 (on ERUS and MRI)	Local excision (TEM) If pT1 and no adverse features, TEM is sufficient If adverse histopathology (lm ≥ 2, G3, V1, L1), requires radical resection (TME) as standard	Alternatively, in the case of adverse features on pathology, TEM plus salvage (or adjuvant) CRT in perioperative high-risk patients (but unproven benefit—with high risk of local recurrence for pT2)
Early (Good)	cT1–cT2; cT3a/b if middle or high, N0 (or also cN1 if high), MRF clear, no EMVI	Surgery (TME) alone is standard. If unexpected poor prognostic signs on histopathology (CRM+, extramodal/N2), consider postoperative CRT/CT (see postoperative recommendations in Table 7)	For fragile, high-risk patients or those rejecting radical surgery (CRT with evaluation, local excision or if achieving cCR, 'watch-and-wait', organ preservation)
Intermediate	cT3a/b very low, levators clear, MRF clear or cT3a/b in mid- or high rectum, cN1–2 (not extramodal), no EMVI	Surgery (TME) alone is a standard only if good-quality mesorectal resection assured (and local recurrence ≤0.5% or, if not, preoperative SCPRT (5 × 5 Gy) or CRT followed by TME	If CRT is given and cCR is achieved, 'watch-and-wait' in high-risk patients for surgery may be considered
Bad	cT3c/d or very low localisation levators threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extramodal), EMVI+, limited cT4aN0	Preoperative SCPRT (5 × 5cGy) or CRT followed by TME, depending on need for regression	If CRT and cCR achieved, 'watch-and-wait' in high-risk patients may be considered
Advanced (Ugly)	cT3 with any MRF involved, any cT4a/b, lateral node+-	Preoperative CRT followed by surgery (TME and more extended surgery if needed due to tumour overgrowth), or preoperative SCPRT (5 × 5 Gy) plus FOLFOX and delay to surgery	Alternatively, 5 × 5 Gy alone with a delay to surgery in fragile/elderly or in patients with severe comorbidity who cannot tolerate CRT

ESMO
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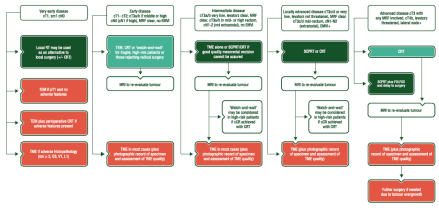


Neoadjuvant Radiotherapy Versus Surgery Alone for Stage II/III Mid-low Rectal Cancer With or Without High-risk Factors

A Prospective Multicenter Stratified Randomized Trial

Xiangbing Deng, MD, Ping Liu, MD,† Dan Jiang, MD,‡ Mingtian Wei, MD,* Xin Wang, MD,§ Xuyang Yang, MD,* Yuanchuan Zhang, MD,¶ Bing Wu, MD,|| Yanjun Liu, MD,¶ Meng Qiu, MD,§ Hua Zhuang, MD,** Zongguang Zhou, MD,* Yunfeng Li, MD,†✉ Feng Xu, MD,§✉ and Ziqiang Wang, MD*✉*

TABLE 1. Criteria for Inclusion, Exclusion, and Low and High-Risk in This Study

Inclusion criteria
1. Histologically verified adenocarcinoma of rectum
2. The lower border of the tumor within 10 cm of the anal verge
3. Age between 18 to 80
4. ECOG (Eastern Cooperative Oncology Group, ECOG) ≤2
5. Preoperative TRUS or high definition MRI with abdomino-pelvic CT diagnosis as T3 and T4a or N+(short axis diameter over 8 mm)
6. No evidence of metastasis with chest and abdminopelvic CT

Exclusion criteria
1. With simultaneous multiple colorectal cancers or other cancer;
2. T4b tumor (invasion on uterus, vagina, bladder, seminal vesicle, prostate, bone, pelvic nerve plexus) during operation (tumor with levator or external anal sphincter invasion which can undergo R0 resection with a standard extralevator APR were not excluded)
3. A history of malignant tumor within 5 years (except the skin cancer);
4. Locally recurrent rectal cancer
5. Pregnant or lactating women
6. Has contraindication for the preoperative adjuvant radiotherapy or operation
7. History of chemotherapy or radiation before this trial
8. Any evidences of distal metastasis before surgery

Low-risk criteria
1. T3 tumor with extramural invasion of mesorectum ≤5 mm on the posterior or lateral aspect of rectum, but without threatening the CRM
2. T4a tumor above the reflection without >5 mm mesorectal invasion
3. An anteriorly located T3 tumor involved the full thickness of bowel wall, but without obvious features of invading extramural fat tissue (such as high density of the mesorectum on CT or as indicated by TRUS)
3. No lymph node >8 mm

High-risk criteria
1. T3 tumor with extramural invasion of mesorectum >5 mm on the posterior or lateral aspect of rectum.
2. An anteriorly located T3 tumor with obvious features of invading extramural fat tissue (such as high density of the mesorectum on CT or as indicated by TRUS)
3. Lymph nodes >8 mm
4. T3 tumor with a full circular growth on digital or endoscopic examination

Düşük vs Yüksek Risk

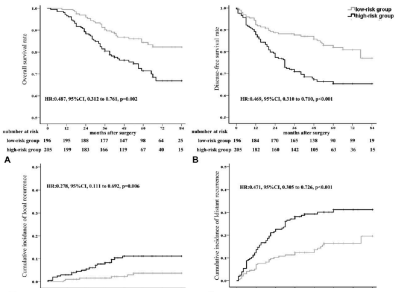


FIGURE 1. Survival differences between the low-risk and high-risk cohort with a median of 54-month follow-up. A, Overall survival rate [hazard ratio (HR): 0.487, 95% confidence interval (CI) 0.312–0.761, $P = 0.002$]; B, Disease-free survival rate (HR: 0.469, 95% CI 0.310–0.710, $P < 0.001$); C, Cumulative incidence of local recurrence (HR: 0.278, 95% CI 0.111–0.692, $P = 0.006$); D, Cumulative incidence of distant recurrence (HR: 0.471, 95% CI 0.305–0.726, $P < 0.001$).

Düşük risk – non-RT vs RT

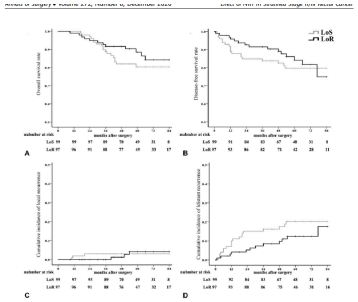


FIGURE 2. No survival difference between radiated (LoR) and non-radiated (LoS) group in low-risk patients. A, Overall survival rate [hazard ratio (HR): 1.486, 95% confidence interval (CI) 0.716–3.087, $P = 0.287$]; B, Disease-free survival rate (HR: 1.292, 95% CI 0.656–2.543, $P = 0.459$); C, Cumulative incidence of local recurrence (HR: 1.018, 95% CI 0.205–5.046, $P = 0.983$); D, Cumulative incidence of distant metastasis rate (HR: 1.675, 95% CI 0.812–3.455, $P = 0.163$).

Yüksek Risk non RT vsRT

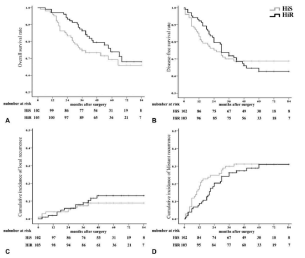
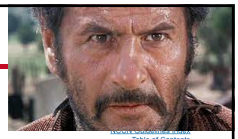
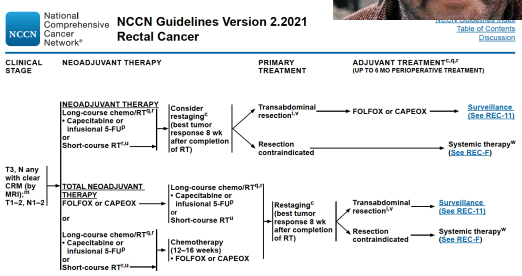


FIGURE 3. Survival difference between radiated (HiR) and non-radiated (HiS) group in high-risk- patients. A, Overall survival rate (hazard ratio [HR]: 0.731, 95% confidence interval (CI) 0.430 to 1.243, $P = 0.247$); B, Disease-free survival rate (HR: 0.957, 95% CI 0.592–1.547, $P = 0.858$); C, Cumulative incidence of local recurrence (HR: 0.726, 95%CI, 0.297–1.776, $P = 0.483$); D, Cumulative incidence of distant recurrence (HR: 1.150, 95% CI 0.696–1.900, $P = 0.586$).

NCCN





NCCN

- Kısa
- Uzun
- TNT
- Kemoterapi gecikmesi : 21 haftayı bulabilmekte

TNT

- 5 ay önce KT
- Hasta performansı
- İndüksiyon
- Konsolidasyon
- Kısa RT – Uzun dönem RT

TNT- Memorial Sloan Kettering Cancer

- 32 hasta
- Tm 5-12 cm
- Folfox + Bevasizumap
- RT –
- %25 patolojik tam yanıt
- %0 Lokal nüks
- %72 N +

BACCHUS: A randomised non-comparative phase II study of neoadjuvant chemotherapy (NACT) in patients with locally advanced rectal cancer (LARC)

- Bacchus Trial
  - Folfox plus Bevacizumap
  - Folfoxiri plus bevacizumap
    - cT3
    - Crm 1 mm
    - N +
- Patolojik tam yanıt cevabı düşük
- T ve N de belirgin gerileme

Prospect Çalışması

- Prospect trial
- Rt vs KT – Selektif RT
  - Faz II
  - Hasta alımı 2019
- Sonuçlar bekleniyor

FOWARC

Sonuçlar
- 495 hasta
- Sonlanım: 3 yıllık DFS

pCR :
- %27.5 Folfox + RT
- % 14 RT
- %6.6 KT

Komplikasyon
- 1 ve 2 grup %18- %20 KT %8

3 yıllık DFS
- %73, 78, 74

Lokal nüks
- % 8 , 7 ve 7.3

pCR ve Tümör regresyonu KRT ve KT arasında fark yok

Folfox + RT pCR ve tümör regresyonunda üstün ancak DSF

İndüksiyon vs Konsolidasyon

The Timing of Rectal Cancer Response Chemoradiation Consortium
- Uzun dönem Rt vs :Uzun dönem RT + 2 ,4,6siklüs FOLFOX
  - pCR %18-25-30-38
  - DSF %50 -81

KONCLUDE
- Rt + 8Folfox vs adjuvan Folfox
- pCR ve DFS %15

İndüksiyon vs Konsalidasyon

The Rectal Cancer Consortium – ABD
- 8 kür CAPOX, FOLFOX indüksiyon vs konsolidasyon
- pcR ve DFS
- Uzun döneme sonuç bekleniyor

Alman Rektal Kanser Çalışma
- 3 kür Folfox – İndüksiyon – Konsolidasyon
- pCR % 17-25
- Uzun dönem sonuç bekleniyor

Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial

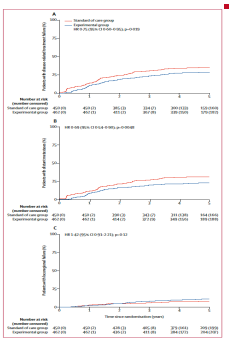
Uzun RT CAPOX + Cerrahi

Kısa RT + 6 kür CAPOX

pCR %28 – 14

3 yıllık DFS % 23.7 - %30.4

3 Lokal nüks %8



	Experimental group	Standard of care group	p value
All eligible patients			
Surgery with curative intent within 6 months after the end of preoperative treatment			
Yes	426/462 (92%)	400/450 (89%)	0·086*
No	36/462 (8%)	50/450 (11%)	–
Disease-related treatment failure, first occurring	128 (23·7%)†	152 (30·4%)†	0·019†
Locoregional failure			
Local progression, unresectable tumour	1/128 (1%)	1/152 (1%)	–
R2 resection	0	0	–
Local recurrence	22/128 (17%)	13/152 (10%)	–
Locoregional failure and distant metastasis‡			
Local progression, unresectable tumour	4/128 (3%)	2/152 (1%)	–
R2 resection	1/128 (1%)	0	–
Local recurrence	7/128 (5%)	4/152 (3%)	–
Distant metastasis	86/128 (67%)	123/152 (81%)	–
New primary colorectal tumour	3/128 (2%)	5/152 (3%)	–
Treatment-related death	4/128 (3%)	4/152 (3%)	–
Patients with a resection within 6 months after the end of preoperative treatment			

Tümör lokalizasyonu

- Proksimal ve orta
  - – Sfinkter koruyucu cerrahi
- Distal
  - – Sfinkter koruyamama

N + --- NOM

Organ Preservation Among Patients With Clinically Node-Positive Rectal Cancer: Is It Really More Dangerous?

Angelita Habr-Gama, M.D., Ph.D.[1,2] • Guilherme Pagin São Julião, M.D.[1] • Bruna Borba Vailati, M.D.[1] • Laura M. Fernandez, M.D.[1] • Cinthia D. Ortega, M.D.[3] Nuno Figueiredo, M.D., Ph.D.[4] • Joaquim Gama-Rodrigues, M.D., Ph.D.[1,2] Rodrigo Oliva Perez, M.D., Ph.D.[1,2,5]

RESULTS: A total of 117 patients with node-positive and 218 with node-negative cancer at baseline were reviewed. Overall, 62 (53.0%; node positive) and 135 (61.9%; node negative) achieved a complete clinical response and were managed nonoperatively ($p = 0.13$). Patients with baseline node-positive cancer had similar rates of pathologic nodal metastases at the time of recurrence. Five-year surgery-free (39.7% vs 46.8%; $p = 0.2$) and distant metastases–free survival (77.5% vs 80.5%; $p = 0.49$) were similar between baseline node-positive and node-negative patients.

CEVAP

CRM - LN +

NEOADJUVAN TEDAVI ?

CERRAHI TEDAVI ?

Sonuç

- Tümör lokalizasyonu
- T evresi T3a-b
- N sayı, boyut, lokalizasyon
- Neoadjuvan protokolleri
- Hasta ve cerrah
- Cerrah eğitimi

27- 29 Ekim 2022

16-20 Mayıs 2023