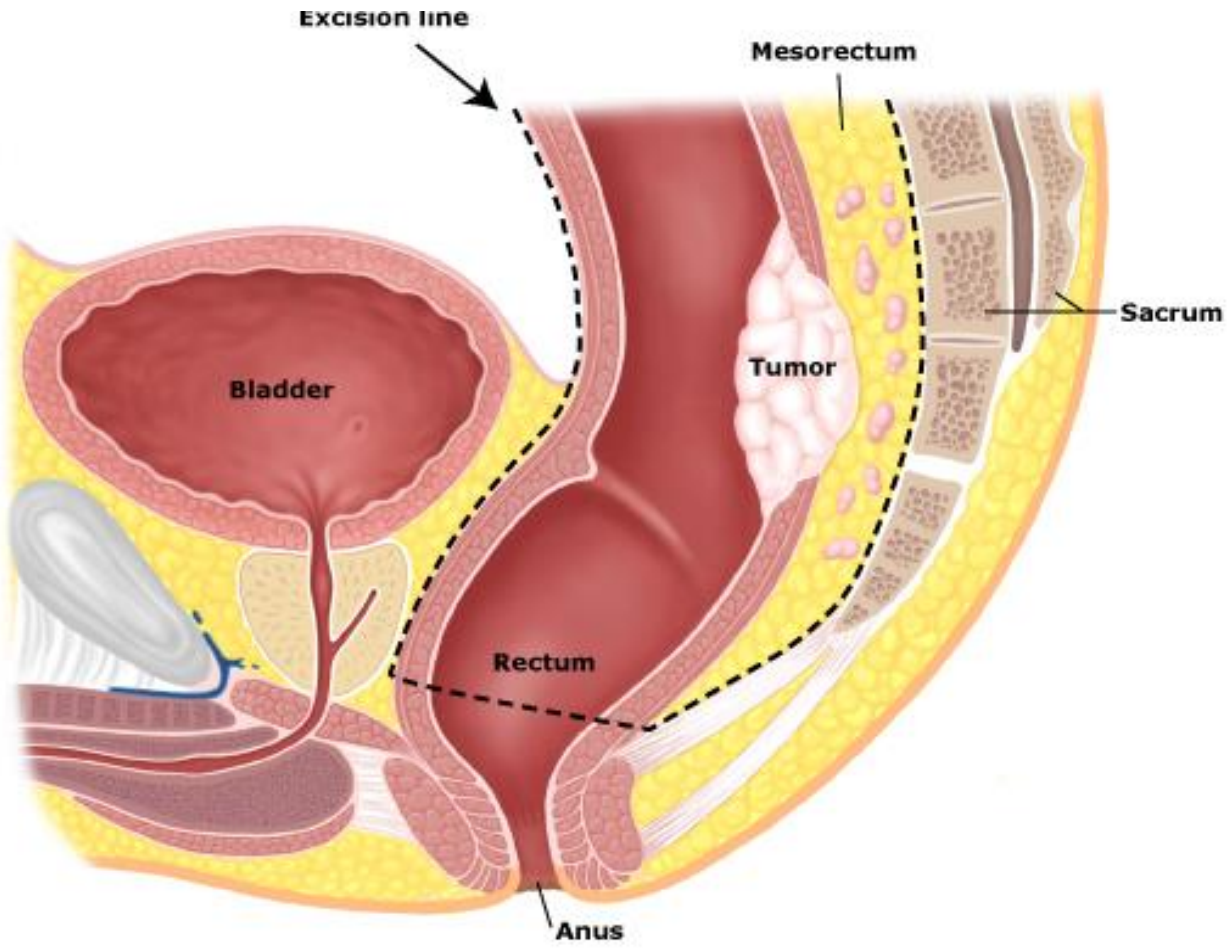
Gastrointestinal Kanserlerde Yeni Onkolojik Tedaviler

Prof.Dr.Sezer Sağlam
Gayrettepe Florence Nigthingale
Medikal Onkoloji Uzmanı

XIV. İstanbul Dahiliye Klinikleri Buluşması
2.Kasım.2024

Rektum Kanserindeki Yenilikler



- Lokal nüks %10'nun altına çekildi.
- İleostomi,kolostomi açılması %70'lerden %6'ya kadar düştü.
- Sağkalım uzadı.
- Ameliyat öncesi tedaviler bugün standarttır.Ameliyat sonrası tedavi kalktı.

The NEW ENGLAND JOURNAL of MEDICINE

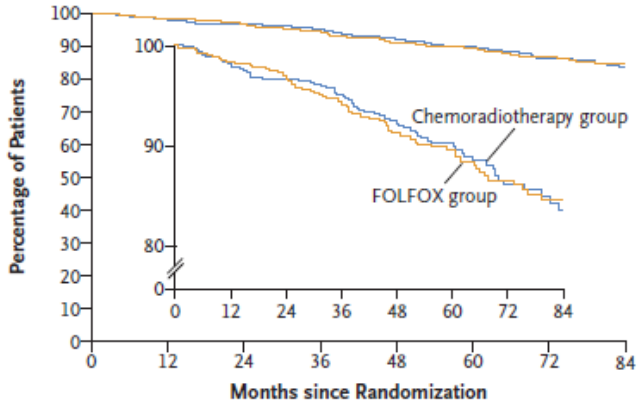
ORIGINAL ARTICLE

Preoperative Treatment of Locally Advanced Rectal Cancer

Deborah Schrag, M.D., M.P.H., Qian Shi, Ph.D., Martin R. Weiser, M.D.,

This article was published on June 4, 2023, at NEJM.org.

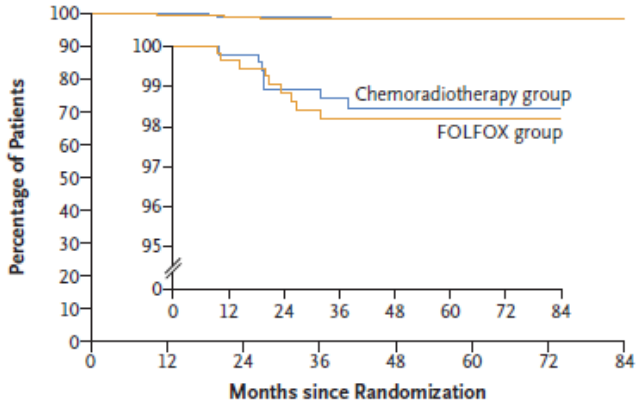
C Overall Survival



No. at Risk								
FOLFOX group	585	565	551	531	429	287	212	120
Chemoradiotherapy group	543	527	513	486	380	273	182	107

Group	No. of Events/ Total No.	Hazard Ratio (95% CI)	5-Year Estimate *percent*
FOLFOX group	74/585	1.04 (0.74–1.44)	89.5 (87.0–92.2)
Chemoradiotherapy group	67/543	Reference	90.2 (87.6–92.9)

D Freedom from Local Recurrence



No. at Risk								
FOLFOX group	585	542	483	438	339	195	95	39
Chemoradiotherapy group	543	499	455	389	289	175	78	36

Group	No. of Events/ Total No.	Hazard Ratio (95% CI)	5-Year Estimate *percent*
FOLFOX group	9/585	1.18 (0.44–3.16)	98.2 (97.1–99.4)
Chemoradiotherapy group	7/543	Reference	98.4 (97.3–99.6)

original repo

Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy

Julio Garcia-Aguilar, MD, PhD[1]; Sujata Patil, PhD[2]; Marc J. Gollub, MD[3]; Jin K. Kim, MD[1]; Jonathan B. Yuval, MD[1];

RESULTS Median follow-up was 3 years. Three-year DFS was 76% (95% CI, 69 to 84) for the INCT-CRT group and 76% (95% CI, 69 to 83) for the CRT-CNCT group, in line with the 3-year DFS rate (75%) observed historically. Three-year TME-free survival was 41% (95% CI, 33 to 50) in the INCT-CRT group and 53% (95% CI, 45 to 62) in the CRT-CNCT group. No differences were found between groups in local recurrence-free survival, distant metastasis-free survival, or overall survival. Patients who underwent TME after restaging and patients who underwent TME after regrowth had similar DFS rates.

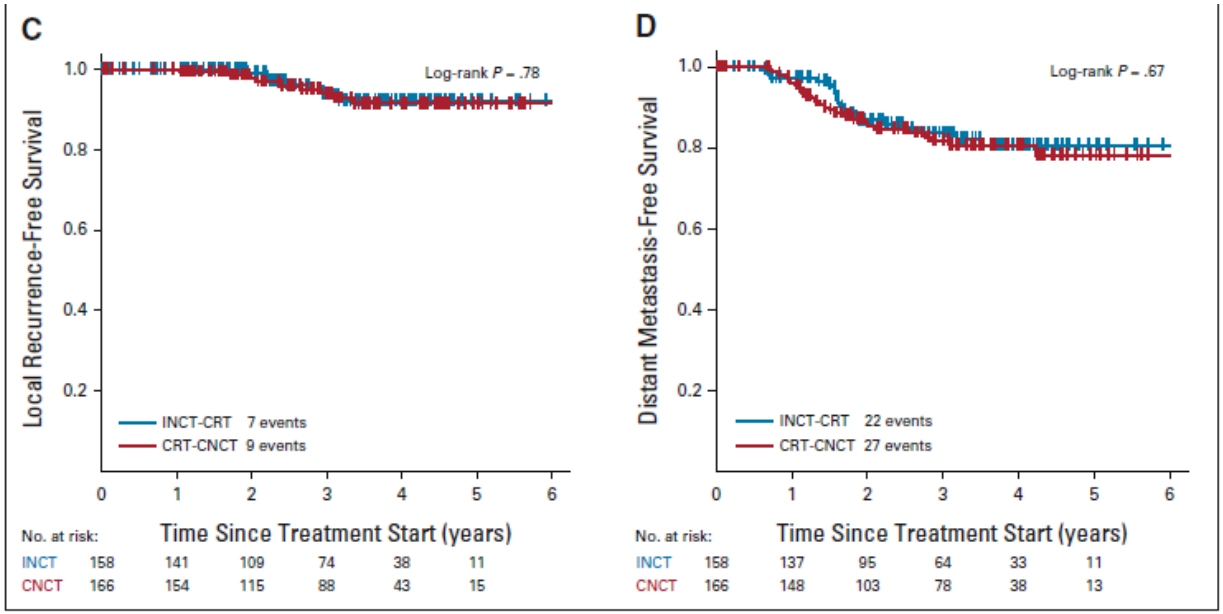
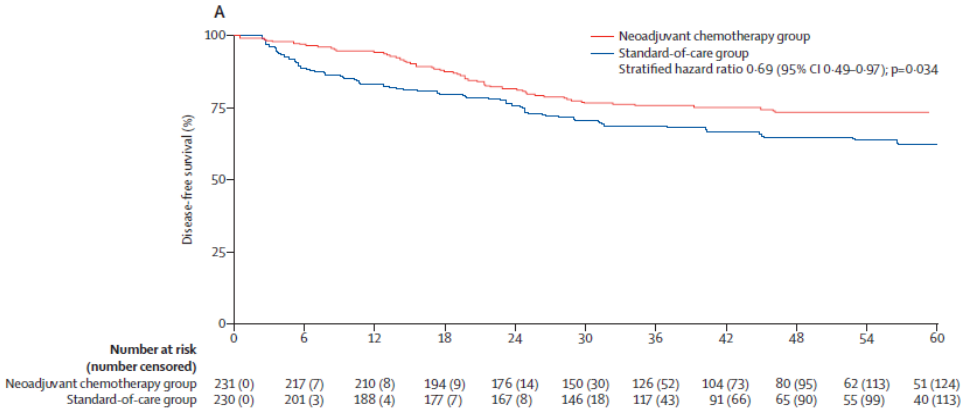


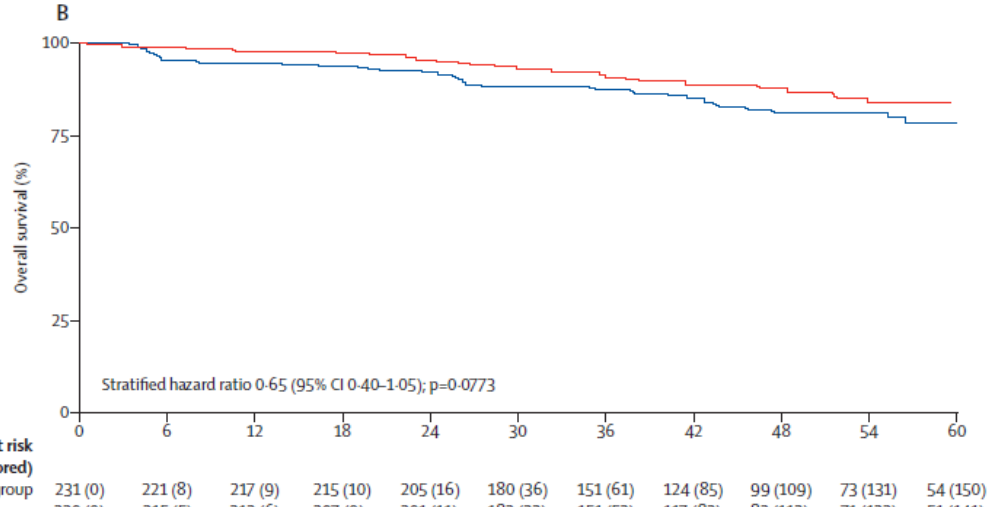
FIG 2. Kaplan-Meier estimates of (A) DFS, (B) overall survival, (C) local recurrence-free survival, and (D) distant metastasis-free survival in the intention-to-treat population by study group. CRT-CNCT, chemoradiotherapy followed by consolidation chemotherapy; DFS, disease-free survival; INCT-CRT, induction chemotherapy followed by chemoradiotherapy.

Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial

Thierry Conroy, Jean-François Bosset, Pierre-Luc Etienne, Emmanuel Rio, Éric François, Nathalie Mesgouez-Nebout, Véronique Vendrely,



Lancet Oncol 2021; 22: 702–15

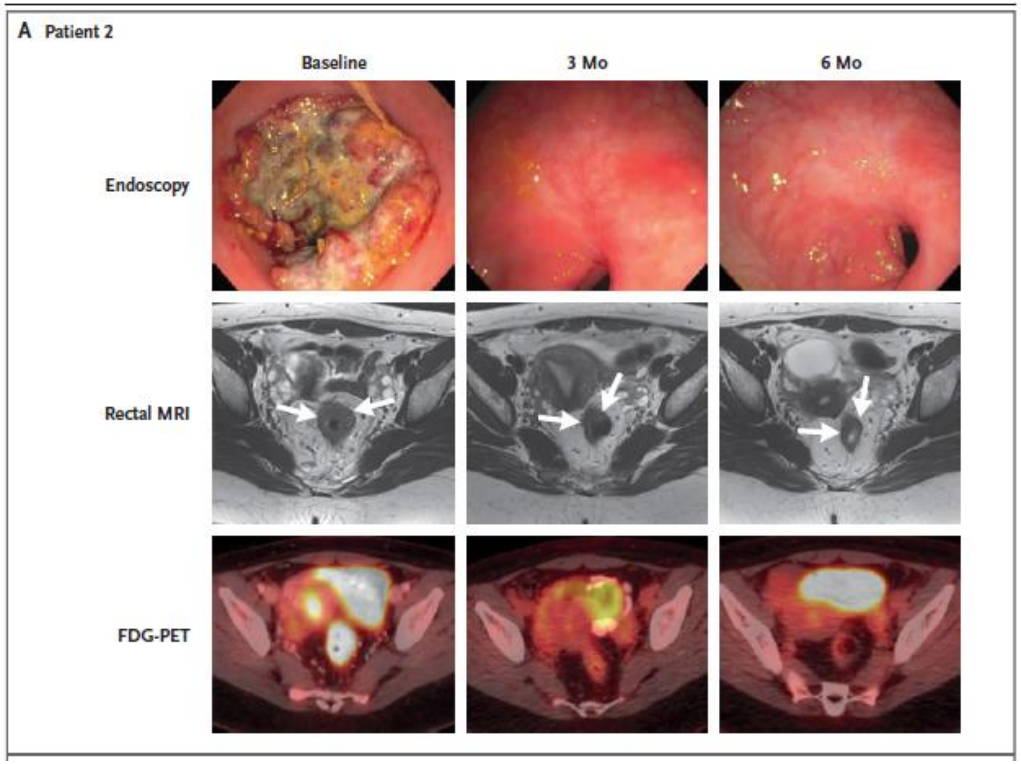


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 23, 2022 VOL. 386 NO. 25

PD-1 Blockade in Mismatch Repair–Deficient, Locally Advanced Rectal Cancer

A. Cercek, M. Lumish, J. Sinopoli, J. Weiss, J. Shia, M. Lamendola-Essel, I.H. El Dika, N. Segal, M. Shcherba,



Pankreas Kanserinde Yenilikler

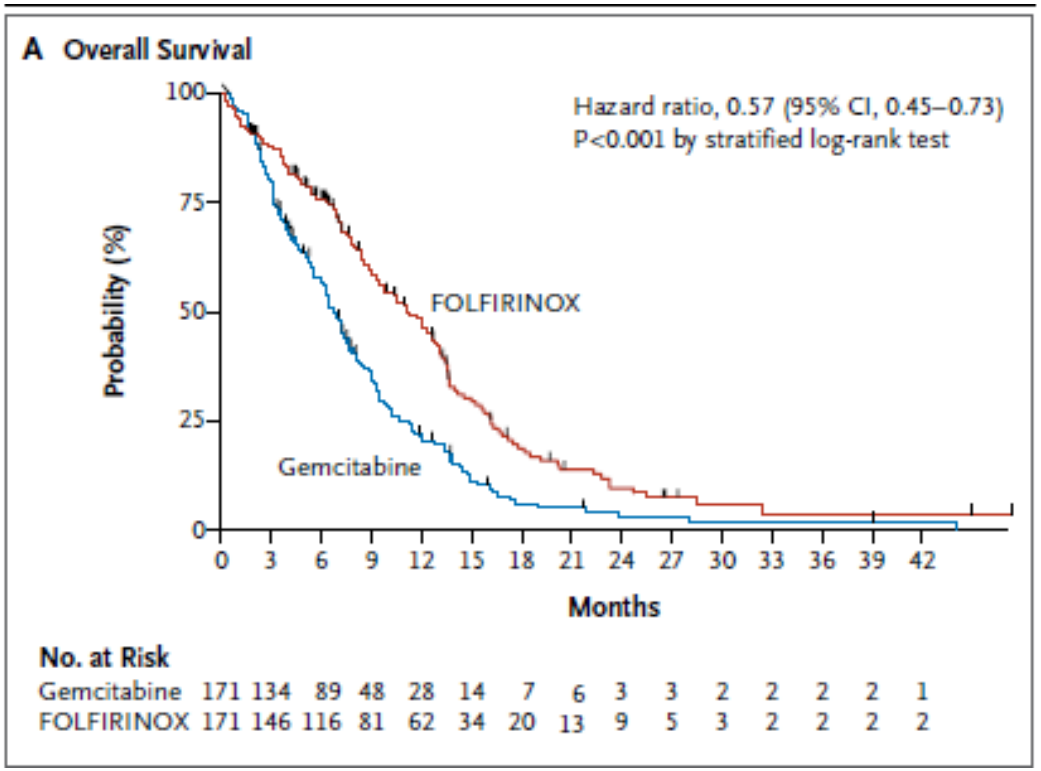
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer

N Engl J Med 2011;364:1817-25.

Thierry Conroy, M.D., Françoise Desseigne, M.D., Marc Ychou, M.D., Ph.D.,



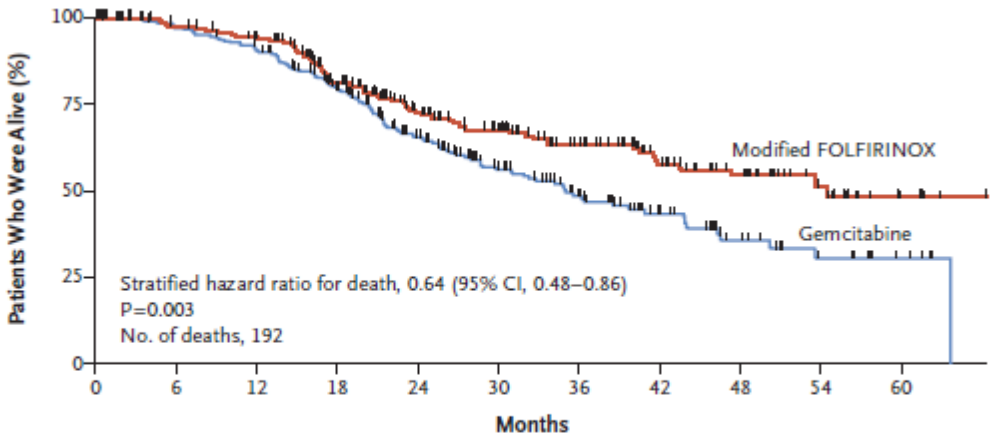
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 20, 2018 VOL. 379 NO. 25

FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer

T. Conroy, P. Hammel, M. Hebbar, M. Ben Abdelghani, A.C. Wei, J.-L. Raoul, L. Choné, E. Francois, P. Artru,

B Overall Survival



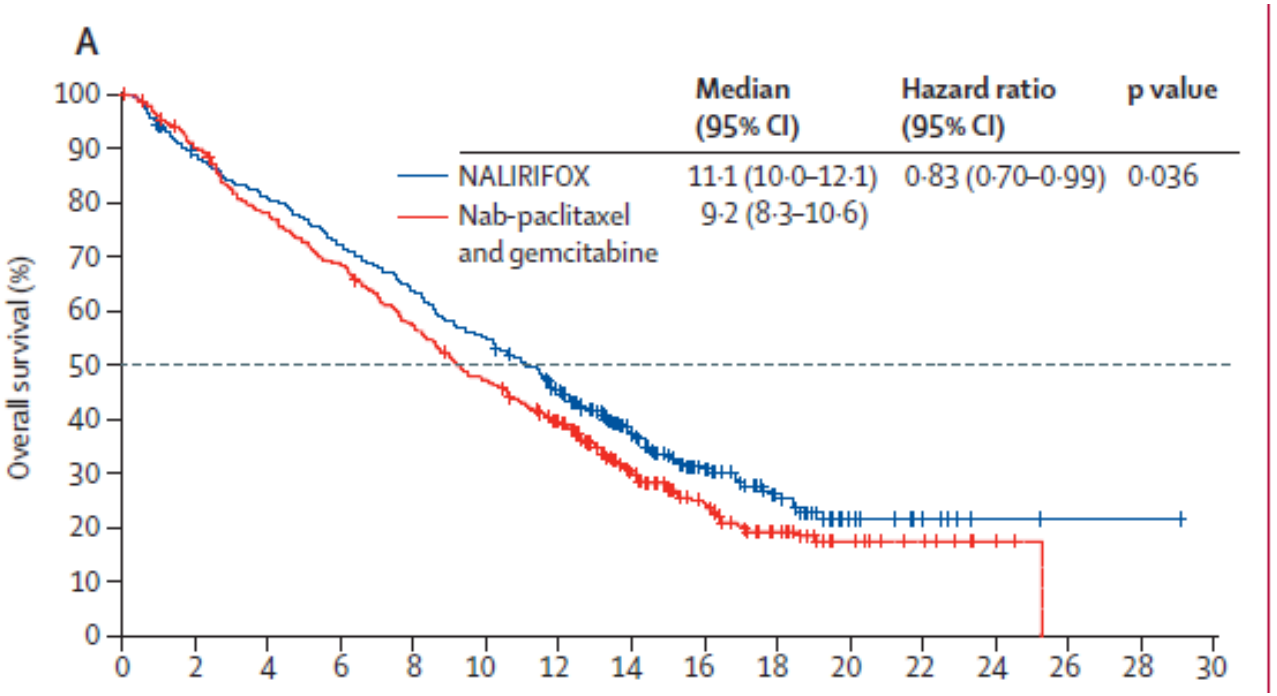
No. at Risk

Modified FOLFIRINOX	247	223	210	165	119	91	68	46	32	16	4
Gemcitabine	246	233	215	171	120	81	55	33	18	9	4

NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial

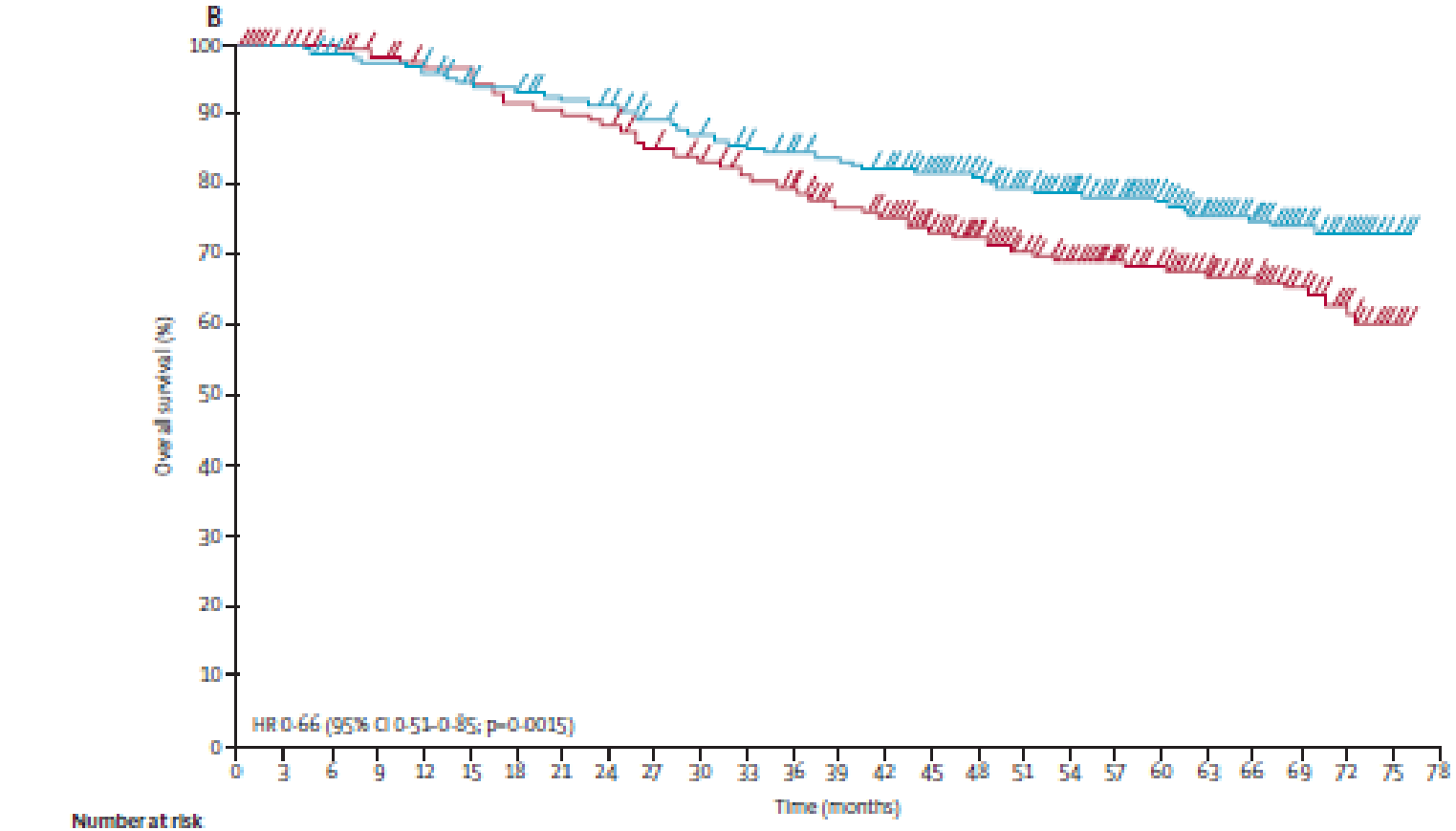
Lancet 2023; 402: 1272–81

Zev A Wainberg, Davide Melisi, Teresa Macarulla, Roberto Pazo Cid, Sreenivasa R Chandana, Christelle De La Fouchardière, Andrew Dean, Igor Kiss,



Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial

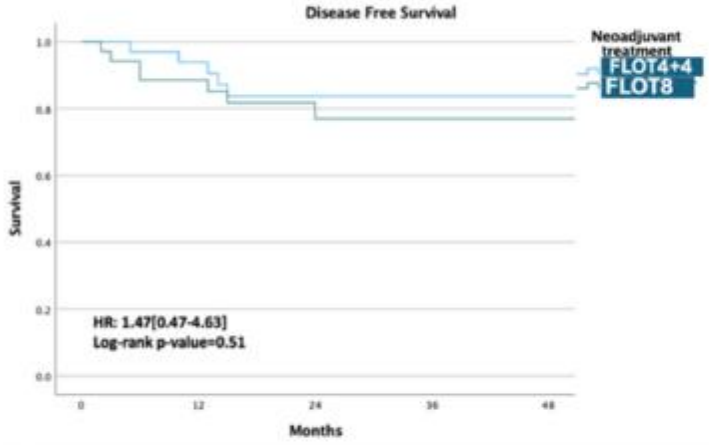
Prof Yung-Jue Bang, MD [a,‡] · Young-Woo Kim, MD [c] · Prof Han-Kwang Yang, MD [b] · Prof Hyun Cheol Chung, MD [e] ·



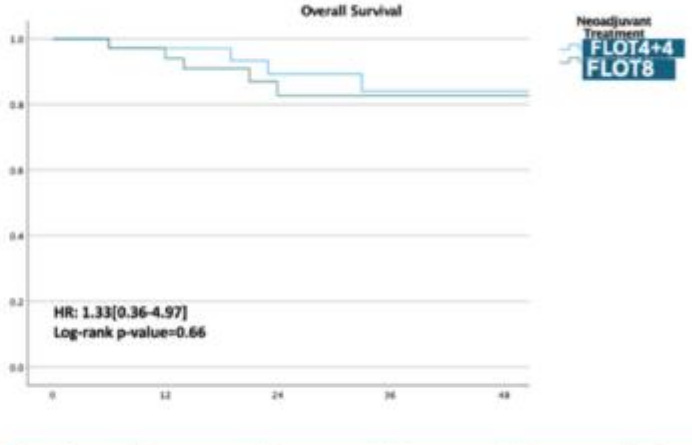
The New Era of Total Neoadjuvant FLOT Therapy for Locally Advanced, Resectable Gastric Cancer: A Propensity-Matched Comparison With Standard Perioperative Therapy

Ahmet Rencuzogullari[1] | Salih Nafiz Karahan[1] | Fatih Selcukbiricik[2] | Sahin Lacin[2] | Orhun Cig Taskin[3] | Burcu Saka[3] | Duygu Karahacioglu[4] | Bengi Gurses[4] | Emre Ozoran[1] | Derya Salim Uymaz[1] | Ibrahim Halil Ozata[1] | Sezer Saglam[5] | Dursun Bugra[1,6] | Emre Balik[1]

the median follow-up of 36 months, DFS and OS rates also showed no significant differences, with DFS rates at 83.7% for the FLOT 4+4 group and 76.9.3% for the FLOT x8 group ($p = 0.51$, HR: 1.47 [0.47–4.63]) and OS rates of 84.1% and 82.6%, respectively ($p = 0.66$, HR: 1.33 [0.36–4.97]) (Figure 2).



Months	0	12	24	36	48
FLOT4+4	37	29	20	12	8
FLOT8	37	26	16	6	3



Months	0	12	24	36	48
FLOT4+4	37	31	22	14	9
FLOT8	37	30	19	7	3

J Cancer Res Clin Oncol
DOI 10.1007/s00432-014-1816-y

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Adjuvant chemoradiotherapy after D2 resection in gastric cancer: a single-center observational study

Esra Kaytan Saglam · Serap Yucel · Emre Balik · Sezer Saglam · Oktar Asoglu · Sumer Yamaner · Dursun Bugra · Ethem N. Oral · Ahmet Kizir · Yersu Kapran · Burak Sakar · Ali Akyuz · Mine Gulluoglu

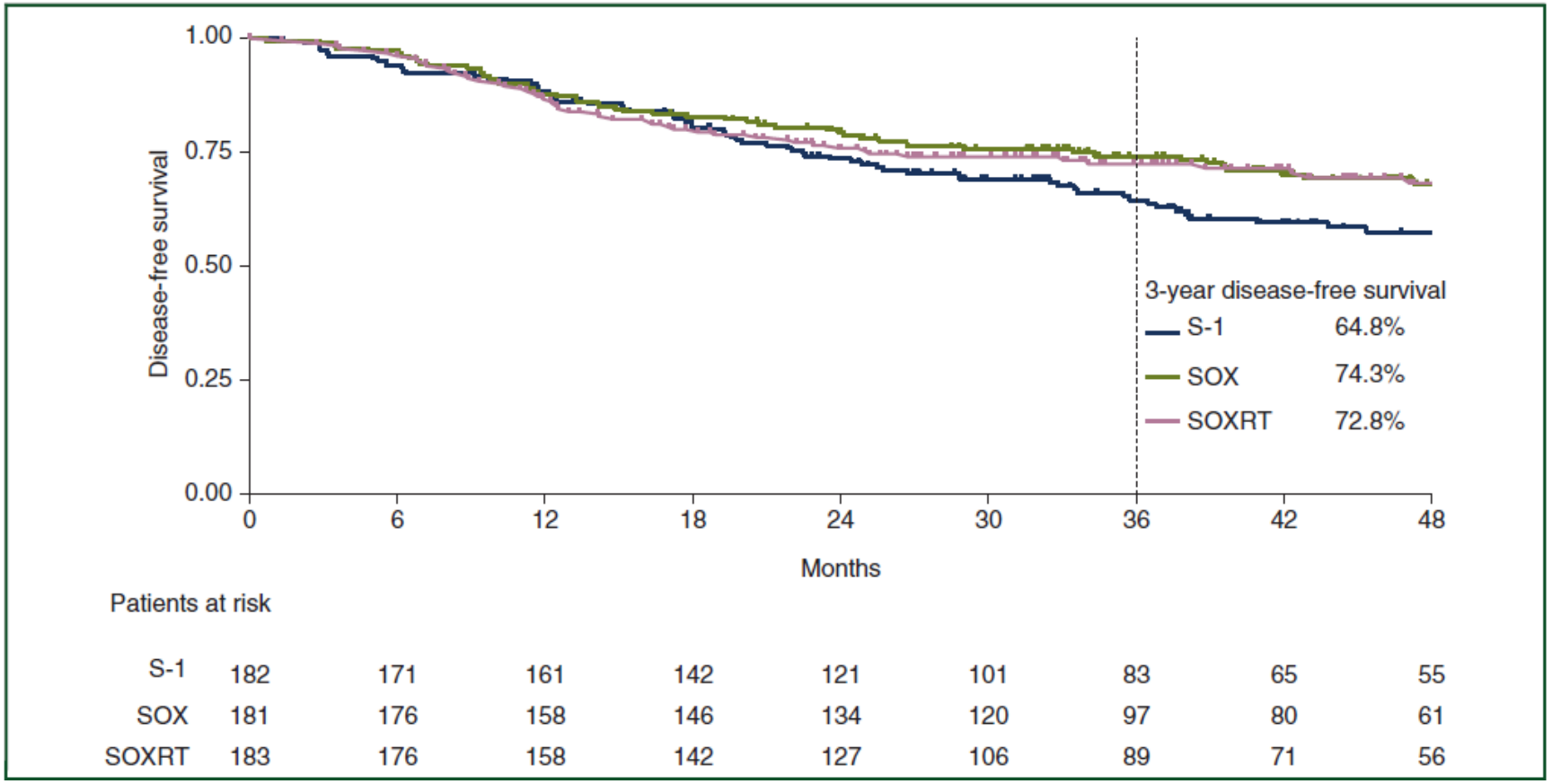
Table 4 Previous studies on the treatment of gastric cancer with D2 surgery and adjuvant chemoradiotherapy, in reference to the INT-0116 trial

Study	Design	No. of patients	Surgery type	% of T3/T4 patients	% with (+) nodes	No. of removed nodes	Median follow-up (m)	Overall 5-year survival
Macdonald et al. (2001)[a]	Prospective randomized	281	D0–D1	68	85	≤15	60	50 % (3-year)
Kim et al. (2005)	Retrospective	544	D2	48	94.1	≥25 (87 %)	66	57.1 %
Leong et al. (2008)	Retrospective	70	D2	60	91	>15 (86 %)	27	60.6 % (3-year)
Zhu et al. (2012)	Prospective randomized	186	D2	70	85	?	54	48.8 %
Lee et al. 2012[b]	Prospective randomized	230	D2	?	88.3	40	53.2	78.3 % (DFS)
Jacome et al. (2013)	Retrospective	104	D2	88	63	?	30.8	64.4 % (3-year)
This study	Prospective observational	288	D2	87	87	20–28	47	57.2 % (5-year)

[a] INT-0116 trial, [b] ARTIST trial. For comparative studies, only data of radiochemotherapy arm is given

A randomized phase III trial comparing adjuvant single-agent S1, S-1 with oxaliplatin, and postoperative chemoradiation with S-1 and oxaliplatin in patients with node-positive gastric cancer after D2 resection: the ARTIST 2 trial☆

S. H. Park[1†], D. H. Lim[2†], T. S. Sohn[3†], J. Lee[1†], D. Y. Zang[4†], S. T. Kim[1], J. H. Kang[5], S. Y. Oh[6], I. G. Hwang[7], J. H. Ji[8],

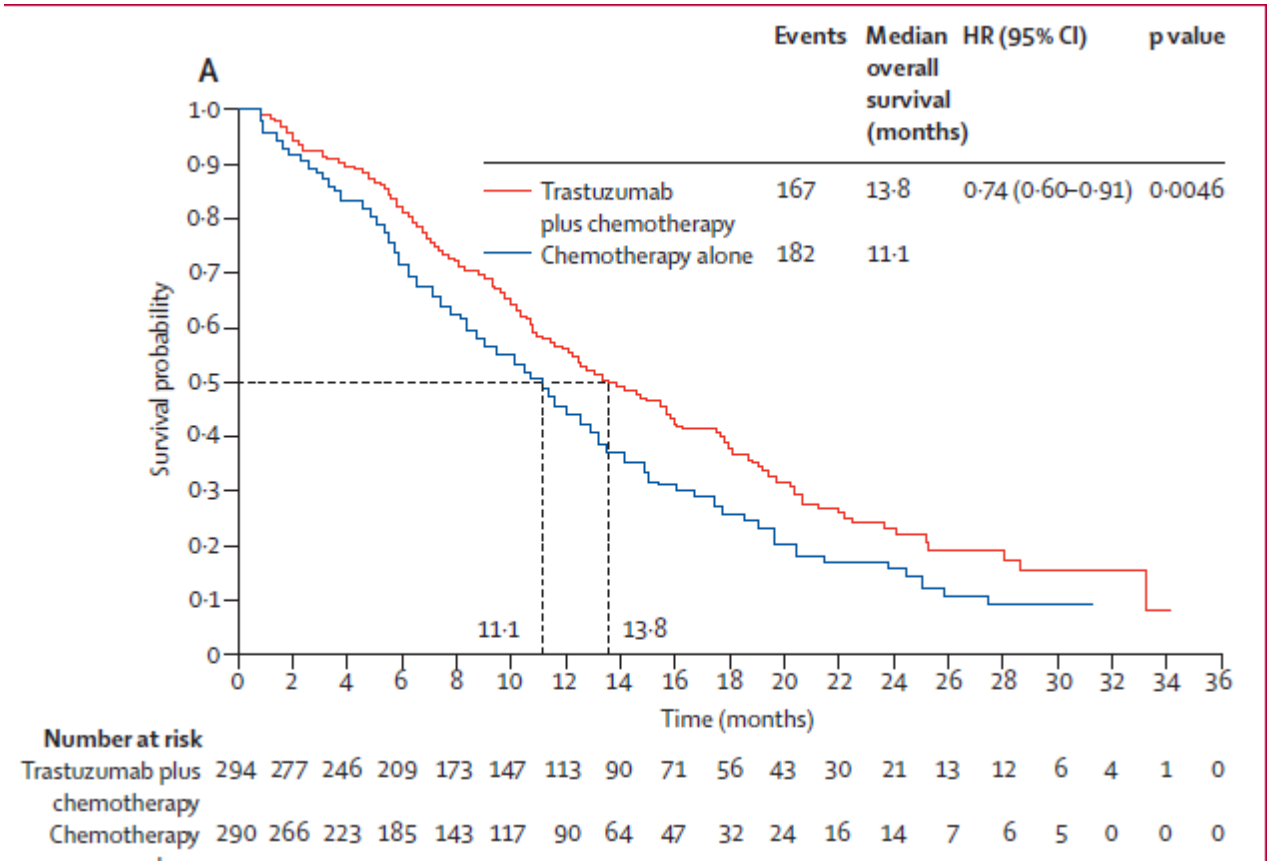


Patients at risk

S-1	182	171	161	142	121	101	83	65	55
SOX	181	176	158	146	134	120	97	80	61
SOXRT	183	176	158	142	127	106	89	71	56

Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial

Yung-Jue Bang, Eric Van Cutsem,* Andrea Feyereislova, Hyun C Chung, Lin Shen, Akira Sawaki, Florian Lordick, Atsushi Ohtsu, Yasushi Omuro,*

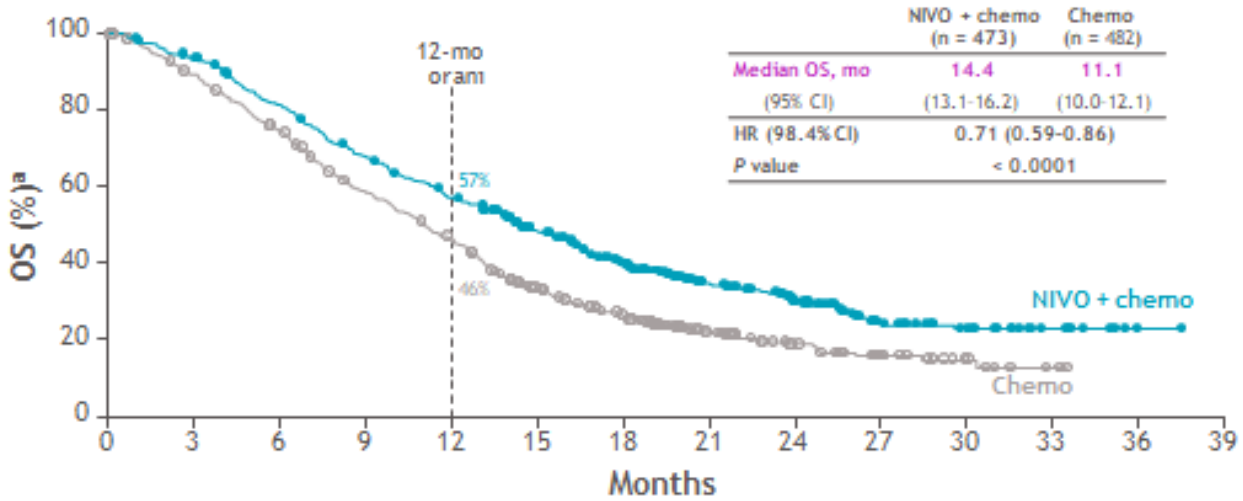


First-line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial

CheckMate 649

Genel Sağkalım / İlk Sonuçlar (min 12 ay takip)

Primary endpoint (PD-L1 CPS ≥ 5)



	NIVO + chemo (n = 473)	Chemo (n = 482)
Median OS, mo	14.4	11.1
(95% CI)	(13.1-16.2)	(10.0-12.1)
HR (98.4% CI)	0.71 (0.59-0.86)	
P value	< 0.0001	

No. at risk

NIVO + chemo	473	438	377	313	261	198	149	96	65	33	22	9	1	0
Chemo	482	421	350	271	211	138	98	56	34	19	8	2	0	0

- Superior OS, 29% reduction in the risk of death, and a 3.3-month improvement in median OS with NIVO + chemo versus chemo in patients whose tumors expressed PD-L1 CPS ≥ 5

[a]Minimum follow-up 12.1 months.

1. Moehler, M., et al. "LBA6_PR Nivolumab (nivo) plus chemotherapy (chemo) versus chemo as first-line (1L) treatment for advanced gastric cancer/gastroesophageal junction cancer (GC/GEJC)/esophageal adenocarcinoma (EAC): First results of the CheckMate 649 study." Annals of Oncology 31 (2020): S1191.

nature medicine

Article

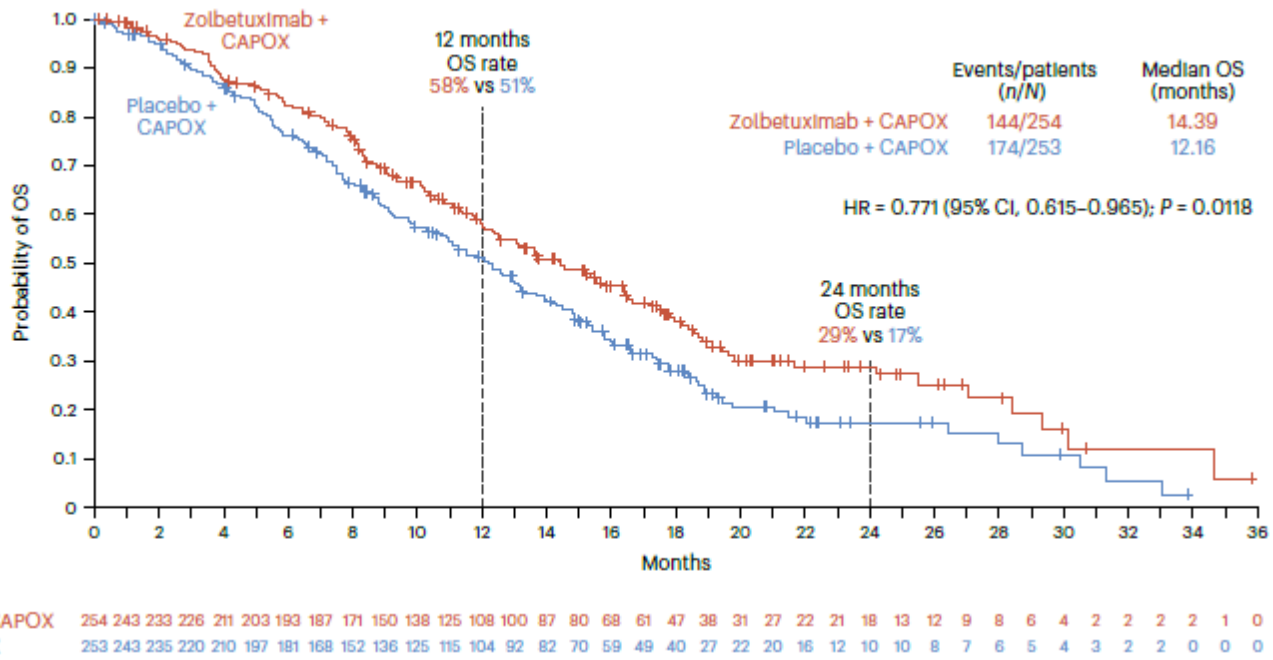
https://doi.org/10.1038/s41591-023-02465-7

Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial

Received: 5 May 2023

Manish A. Shah[1], Kohei Shitara[2], Jaffer A. Ajani[3], Yung-Jue Bang[4],

a



JAMA Oncology | Original Investigation

FOLFOXIRI Plus Bevacizumab as Conversion Therapy for Patients With Initially Unresectable Metastatic Colorectal Cancer

A Systematic Review and Pooled Analysis

Gianluca Tomasello, MD; Fausto Petrelli, MD; Michele Ghidini, MD; Alessandro Russo, MD; Rodolfo Passalacqua, MD; Sandro Barni, MD

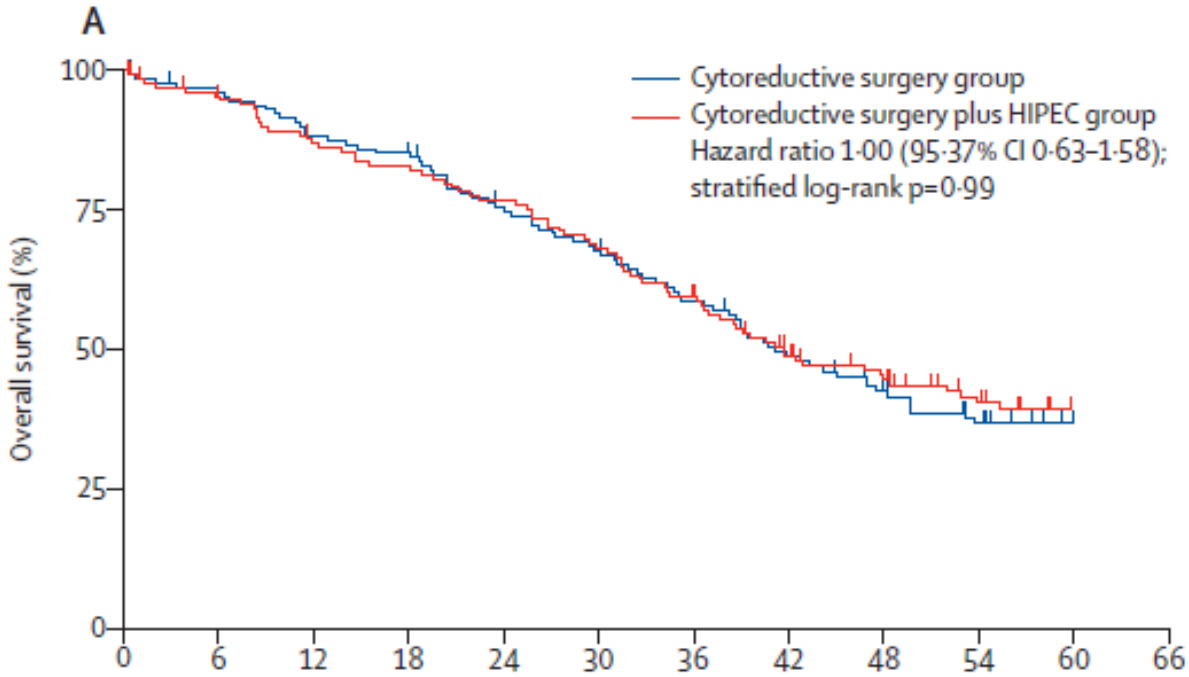
RESULTS Eleven FOLFOXIRI-Bev studies published between 2010 and 2016 met the inclusion criteria and were pooled for analysis. The studies included 889 patients, with 877 patients clinically evaluable for overall response rates. The objective response rate to FOLFOXIRI-Bev was 69% (95% CI, 65%-72%; I^2 = 25%). The rate of overall surgical conversions was 39.1% (95% CI, 26.9%-52.8%), and the rate of R0 surgical conversions was 28.1% (95% CI, 18.1%-40.8%). Median pooled overall survival was 30.2 months (95% CI, 26.5-33.7 months) in 6 trials with data available, and progression-free survival was 12.4 months (95% CI, 10.0-14.3 months) in 9 trials with data available. In meta-regression analysis, variables significantly associated with conversion surgery were disease limited to the liver and a higher median number of cycles (close to 12).

Table. Summary Statistics of Pooled Analysis of FOLFOXIRI-Bev Efficacy

Characteristic	Range of Raw Values Between the Studies	Weighted Pooled Mean
Median OS, mo	24.1-32.2	30.2
Median PFS, mo	9.2-18.6	12.4
Response rate, %	51-82	69
Resection rate, %	15.0-64.2	39.1
R0 resection rate, %	15.0-64.2	28.1

Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy versus cytoreductive surgery alone for colorectal peritoneal metastases (PRODIGE 7): a multicentre, randomised, open-label, phase 3 trial

François Quénet, Dominique Elias, Lise Roca, Diane Goéré, Laurent Ghouti, Marc Pocard, Olivier Facy, Catherine Arvieux, Gérard Lorimier,



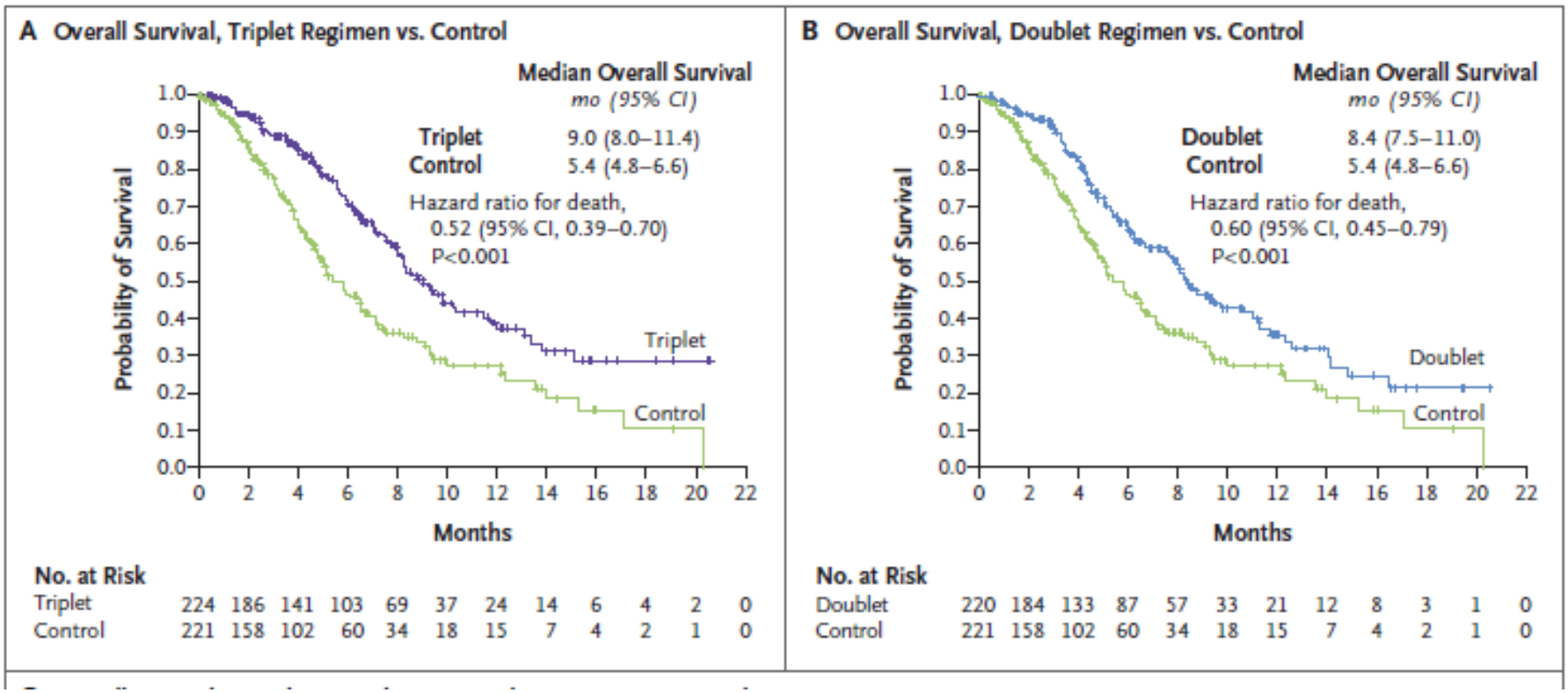
Findings Between Feb 11, 2008, and Jan 6, 2014, 265 patients were included and randomly assigned, 133 to the cytoreductive surgery plus HIPEC group and 132 to the cytoreductive surgery alone group. After median follow-up of 63·8 months (IQR 53·0–77·1), median overall survival was 41·7 months (95% CI 36·2–53·8) in the cytoreductive surgery plus HIPEC group and 41·2 months (35·1–49·7) in the cytoreductive surgery group (hazard ratio 1·00 [95·37% CI 0·63–1·58]; stratified log-rank p=0·99). At 30 days, two (2%) treatment-related deaths had occurred in

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Encorafenib, Binimetinib, and Cetuximab in *BRAF* V600E–Mutated Colorectal Cancer

S. Kopetz, A. Grothey, R. Yaeger, E. Van Cutsem, J. Desai, T. Yoshino, H. Wasan,



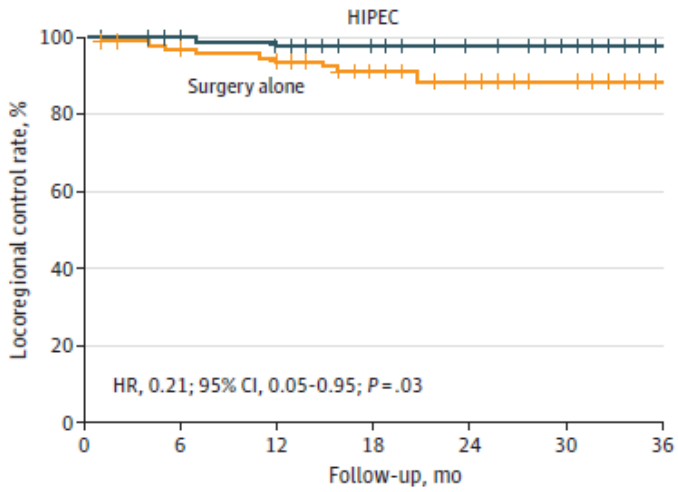
JAMA Surgery | Original Investigation

Efficacy and Safety of Intraoperative Hyperthermic Intraperitoneal Chemotherapy for Locally Advanced Colon Cancer
A Phase 3 Randomized Clinical Trial

Alvaro Arjona-Sánchez, MD, PhD; Esther Espinosa-Redondo, MD; Alberto Gutiérrez-Calvo, PhD; Juan J. Segura-Sampedro, PhD; Estibalitz Pérez-Viejo, PhD;

CONCLUSIONS AND RELEVANCE In this randomized clinical trial, the addition of HIPEC to complete surgical resection for locally advanced colon cancer improved the 3-year LC rate compared with surgery alone. This approach should be considered for patients with locally advanced colorectal cancer.

Figure 2. Kaplan-Meier Estimates of Locoregional Control Rate in the Surgery Plus Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and Surgery Alone Groups



No. at risk (censored)

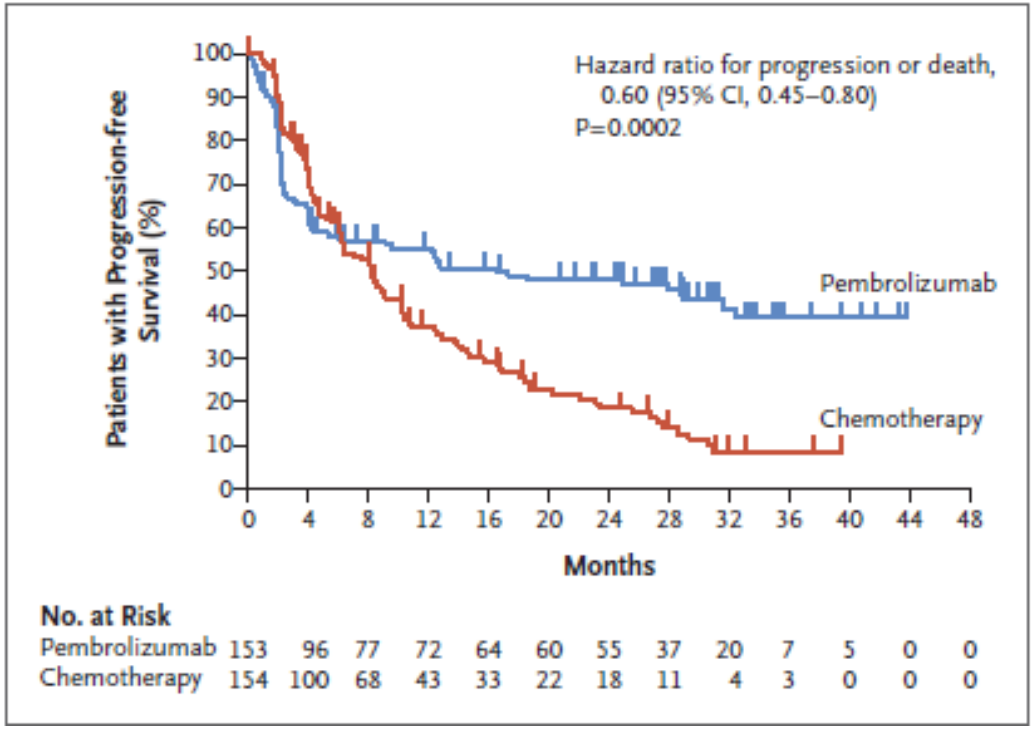
Surgery alone	95	86 (4)	66 (15)	47 (19)
HIPEC	89	82 (5)	65 (17)	49 (16)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2020 VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides,

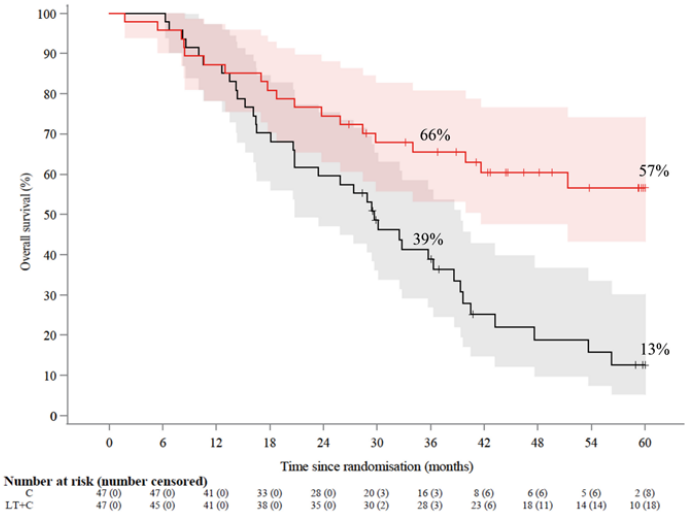


Liver transplantation plus chemotherapy versus chemotherapy alone in patients with permanently unresectable colorectal liver metastases (TransMet): results from a multicentre, open-label, prospective, randomised controlled trial

Prof René Adam, PhD [a,q] · Céline Piedvache, PhD [b] · Prof Laurence Chiche, MD [c] · Jean Philippe Adam, MD [c] ·

Results

Primary endpoint: **Intention to treat overall survival**



LT + C group: median not reached

C alone group: median 29·7 (95% CI: 20·8–39·4)

HR 0.37 (95%CI 0.21-0.65) Log Rank p= 0.0003

The estimated RMST up to 60 months was 43·9 months (95% CI: 38·0–49·9) for the LT+C group and 31·3 (95% CI: 26·3–36·3) (p=0·0014)

Cut-off date: January 18th, 2024. At median follow-up: 59 months (IQR 42–60)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma

Richard S. Finn, M.D., Shukui Qin, M.D., Masafumi Ikeda, M.D., Peter R. Galle, M.D.,

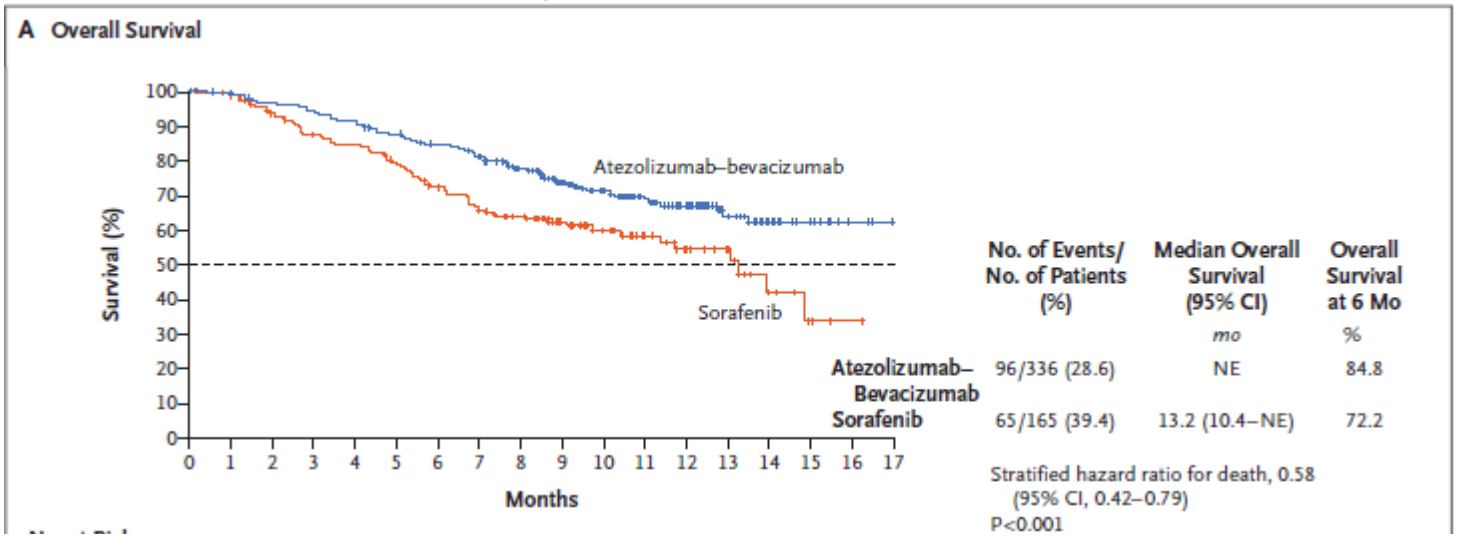


Table 2. Secondary Efficacy Outcomes.*

Variable	RECIST 1.1			HCC-Specific mRECIST		
	Atezolizumab–Bevacizumab (N=326)	Sorafenib (N=159)	Difference (P Value)†	Atezolizumab–Bevacizumab (N=325)	Sorafenib (N=158)	Difference (P Value)†
Confirmed objective response — no. (% [95% CI])‡	89 (27.3 [22.5–32.5])	19 (11.9 [7.4–18.0])	15.4 (<0.001)	108 (33.2 [28.1–38.6])	21 (13.3 [8.4–19.6])	19.9 (<0.001)
Complete response — no. (%)	18 (5.5)	0		33 (10.2)	3 (1.9)	
Partial response — no. (%)	71 (21.8)	19 (11.9)		75 (23.1)	18 (11.4)	