VIII CONGRESO ALATRO
Asociación Ibero Latinoamericana de Terapia Radiante Oncológica

LIMA - PERÚ

Congreso ALATRO 2022

16 - 18 de Noviembre de 2022

Hipofraccionamiento en Recto

Dr. Sebastián Solé
Director Médico - Clínica IRAM
Director Programa Radioterapia - UDP
Santiago, Chile

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Asociación Ibero Latinoamericana de Terapia Radiante Oncológica

Clínica IRAM
Expertos en oncología

udp
UNIVERSIDAD DIEGO PORTALES

ARÁN

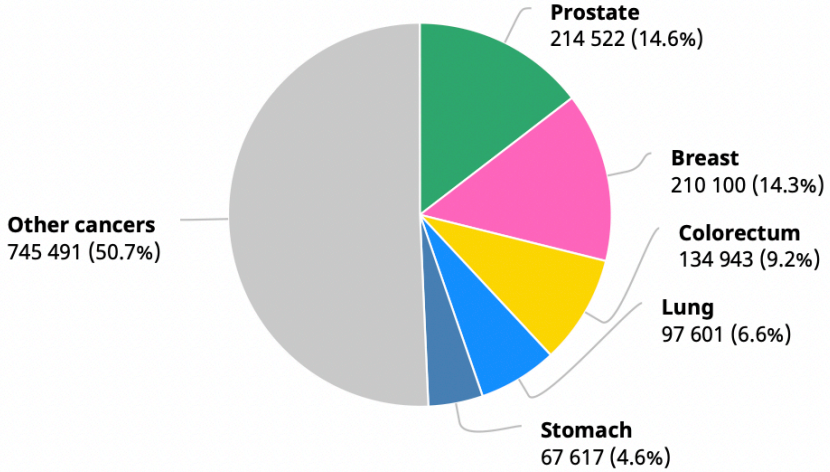
International Agency for Research on Cancer
World Health Organization

Latin America and the Caribbean

Source: Globocan 2020

GCO

Number of new cases in 2020, both sexes, all ages



Total: 1 470 274

Geography

Cáncer de recto localmente avanzado: es necesario hacer tratamientos adyuvantes

The New England
Journal of Medicine

Volume 312 JUNE 6, 1985 Number 23

PROLONGATION OF THE DISEASE-FREE INTERVAL IN SURGICALLY TREATED RECTAL CARCINOMA

GASTROINTESTINAL TUMOR STUDY GROUP

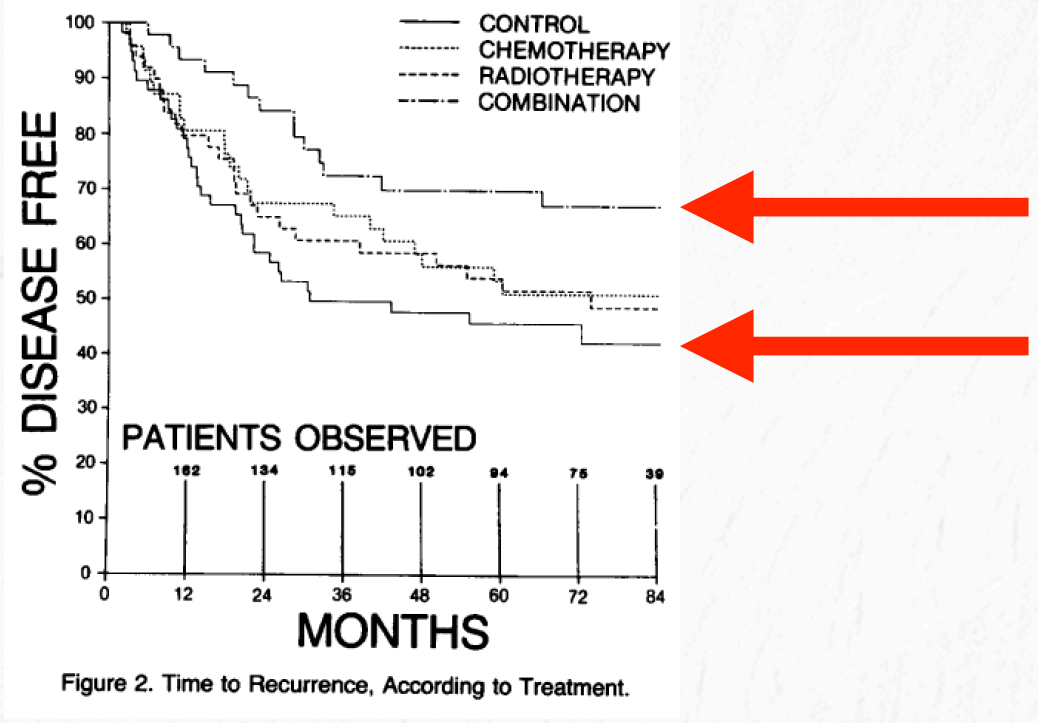


Figure 2. Time to Recurrence, According to Treatment.

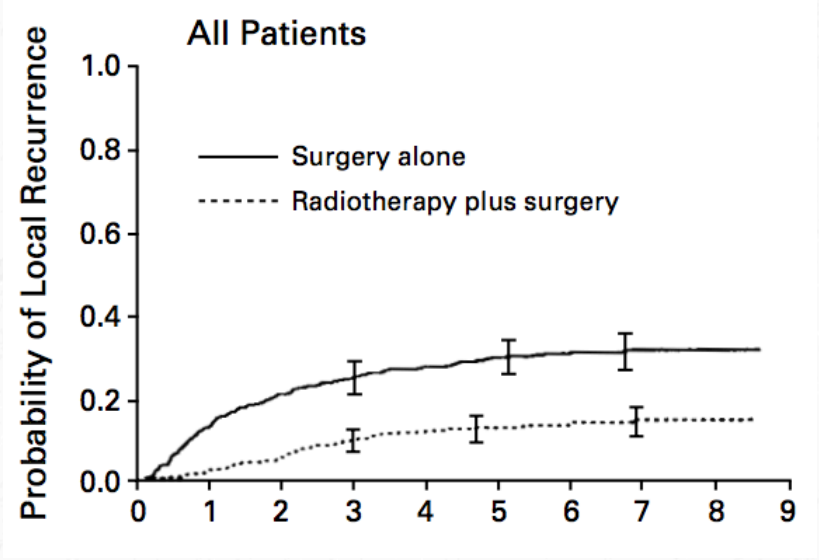
GTSG, NEJM 1985

Neoadyuvancia con Rt Hipofraccionada

The New England Journal of Medicine

IMPROVED SURVIVAL WITH PREOPERATIVE RADIOTHERAPY IN RESECTABLE RECTAL CANCER

SWEDISH RECTAL CANCER TRIAL*



RT hipofraccionada 5x5 (1 semana) sin QT

Pahlman, NEJM 1997

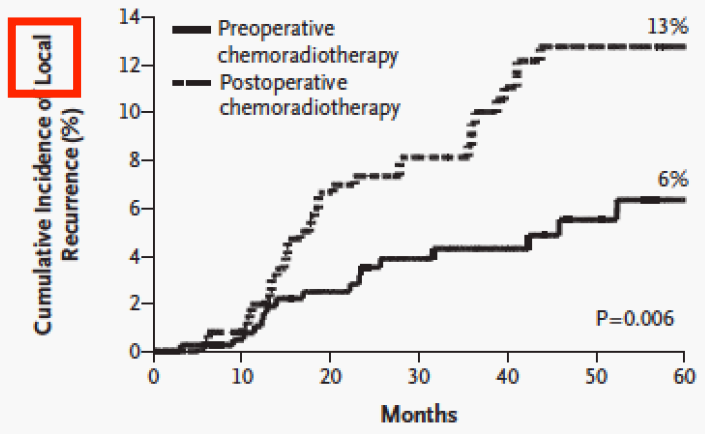
Neoadyuvancia mejor que adyuvancia

ORIGINAL ARTICLE

Preoperative versus Postoperative Chemoradiotherapy for Rectal Cancer

Rolf Sauer, M.D., Heinz Becker, M.D., Werner Hohenberger, M.D., Claus Rödel, M.D., Christian Wittekind, M.D., Rainer Fietkau, M.D., Peter Martus, Ph.D., Jörg Tschmelitsch, M.D., Eva Hager, M.D., Clemens F. Hess, M.D., Johann-H. Karstens, M.D., Torsten Liersch, M.D., Heinz Schmidberger, M.D., and Rudolf Raab, M.D., for the German Rectal Cancer Study Group*

A



No. at Risk							
Preoperative chemoradiotherapy	397	368	312	250	190	133	97
Postoperative chemoradiotherapy	384	351	299	240	184	135	85

RT convencional
1,8-2x25-30 (5-6 semanas)
+ Qt concomitante

Sauer, NEJM 2004

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Rt hipofraccionada vs convencional

Randomized clinical trial

Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer

K. Bujko[1], M. P. Nowacki[2], A. Nasierowska-Guttmejer[3], W. Michalski[4], M. Bebenek[5] and M. Kryj[6] for the Polish Colorectal Study Group

Departments of [1]Radiotherapy, [2]Colorectal Cancer, [3]Pathology and [4]Biostatistics, Maria Sklodowska-Curie Memorial Cancer Centre, Warsaw, [5]Department of Surgery, Silesian Oncological Centre, Wroclaw and [6]Department of Surgery, Maria Sklodowska-Curie Memorial Cancer Centre, Gliwice, Poland
Correspondence to: Dr K. Bujko, The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, W. K. Roentgena 5, 02 781 Warsaw, Poland (e-mail: bujko@coi.waw.pl)

Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial

David Sebag-Montefiore, Richard J Stephens, Robert Steele, John Monson, Robert Grieve, Subhash Khanna, Phil Quirke, Jean Couture, Catherine de Metz, Arthur Sun Myint, Eric Bessell, Gareth Griffiths, Lindsay C Thompson, Mahesh Parmar, on behalf of all the trial collaborators*

VOLUME 30 · NUMBER 31 · NOVEMBER 1 2012
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Trial of Short-Course Radiotherapy Versus Long-Course Chemoradiation Comparing Rates of Local Recurrence in Patients With T3 Rectal Cancer: Trans-Tasman Radiation Oncology Group Trial 01.04

Samuel Y. Ngan, Richard J. Fisher, Bev McClure, Sue-Anne McLachlan, Trevor Leong, John Zalcberg, and John Mackay, Peter MacCallum Cancer Centre; Sue-Anne McLachlan, St

Samuel Y. Ngan, Bryan Burmeister, Richard J. Fisher, Michael Solomon, David Goldstein, David Joseph, Stephen P. Ackland, David Schache, Bev McClure, Sue-Anne McLachlan, Joseph McKendrick, Trevor Leong, Cris Hartopeanu, John Zalcberg, and John Mackay

Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
Annals of Oncology 30: 1298–1303, 2019
doi:10.1093/annonc/mdz186
Published online 13 June 2019

ORIGINAL ARTICLE

Long-course preoperative chemoradiation versus 5 × 5 Gy and consolidation chemotherapy for clinical T4 and fixed clinical T3 rectal cancer: long-term results of the randomized Polish II study

B. Ciseł[1], L. Pietrzak[2], W. Michalski[3], L. Wyrwicz[4], A. Rutkowski[5], E. Kosakowska[5], A. Cencelewicz[5], M. Spałek[2], W. Polkowski[1], M. Jankiewicz[1,6], R. Styliński[7], M. Bębenek[8], B. Kapturkiewicz[8], A. Maciejczyk[9], J. Sadowski[10], J. Zygulska[11], W. Zegarski[12], M. Jankowski[12], M. Las-Jankowska[13], Z. Toczko[14], U. Żelazowska-Omiotek[15], L. Kępka[16], J. Socha[16,17], E. Wasilewska-Tesluk[18,19], W. Markiewicz[20], J. Kładny[21], A. Majewski[22], W. Kapuściński[23], R. Suwiński[24] & K. Bujko[2*], for the Polish Colorectal Study Group

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

Renu R Bahadoer*, Esmée A Dijkstra*, Boudewijn van Etten†, Corrie A M Marijnen†, Hein Putter, Elma Meershoek-Klein Kranenbarg, Annet G H Roodvoets, Iris D Nagtegaal, Regina G H Beets-Tan, Lennart K Blomqvist, Tone Fokstuen, Albert J ten Tije, Jaume Capdevila, Mathijs P Hendriks, Ibrahim Edhemovic, Andrés Cervantes, Per J Nilsson†‡, Bengt Glimelius†‡, Cornelis J H van de Velde†‡, Geke A P Hospers†‡, and the RAPIDO collaborative investigators§

OXFORD
BJS, 2021, 1–10
DOI: 10.1093/bjs/znab020
Randomized Clinical Trial

Short-course radiotherapy with consolidation chemotherapy *versus* conventionally fractionated long-course chemoradiotherapy for locally advanced rectal cancer: randomized clinical trial

D. Chakrabarti [1,*], S. Rajan [2], N. Akhtar [2], S. Qayoom [3], S. Gupta[2], M. Verma [1], K. Srivastava[1], V. Kumar [2], M. L. B. Bhatt[1] and R. Gupta[1]

original reports

Multicenter, Randomized, Phase III Trial of Short-Term Radiotherapy Plus Chemotherapy Versus Long-Term Chemoradiotherapy in Locally Advanced Rectal Cancer (STELLAR)

Jing Jin, MD[1,2]; Yuan Tang, MD[1]; Chen Hu, PhD[3]; Li-Ming Jiang, MD[4]; Jun Jiang, MD[4]; Ning Li, MD[1]; Wen-Yang Liu, MD[1]; Si-Lin Chen, MD[1]; Shuai Li, MD[5]; Ning-Ning Lu, MD[1]; Yong Cai, MD[5]; Yong-Heng Li, MD[5]; Yuan Zhu, MD[6]; Guang-Hui Cheng, MD[7]; Hong-Yan Zhang, MD[8]; Xin Wang, MD[9]; Su-Yu Zhu, MD[10]; Jun Wang, MD[11]; Gao-Feng Li, MD[12]; Jia-Lin Yang, MD[13]; Kuan Zhang, MD[14]; Yihebali Chi, MD[15]; Lin Yang, MD[15]; Hai-Tao Zhou, MD[16]; Ai-Ping Zhou, MD[15]; Shuang-Mei Zou, MD[17]; Hui Fang, MD[1]; Shu-Lian Wang, MD[1]; Hai-Zeng Zhang, MD[16]; Xi-Shan Wang, MD[16]; Li-Chun Wei, MD[18]; Wen-Ling Wang, MD[19]; Shi-Xin Liu, MD[20]; Yuan-Hong Gao MD[21]; and Ye-Xiong Li, MD[1]

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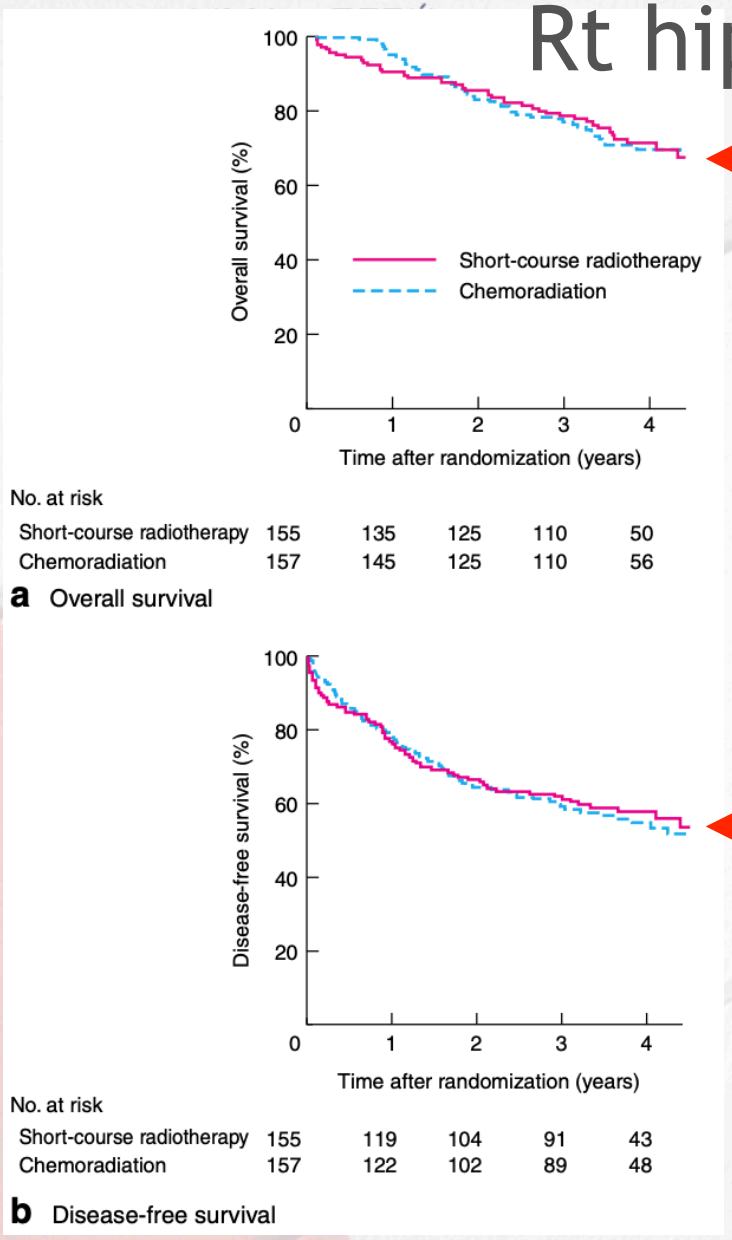
Rt hipofraccionada vs convencional



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Correspondence to: Dr K. Bujko, The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, W. K. Roentgena 5, 02 781 Warsaw, Poland (e-mail: bujko@coi.waw.pl)

Results: Early radiation toxicity was higher in the chemoradiation group

1. Bujko, Br J Surg 2006

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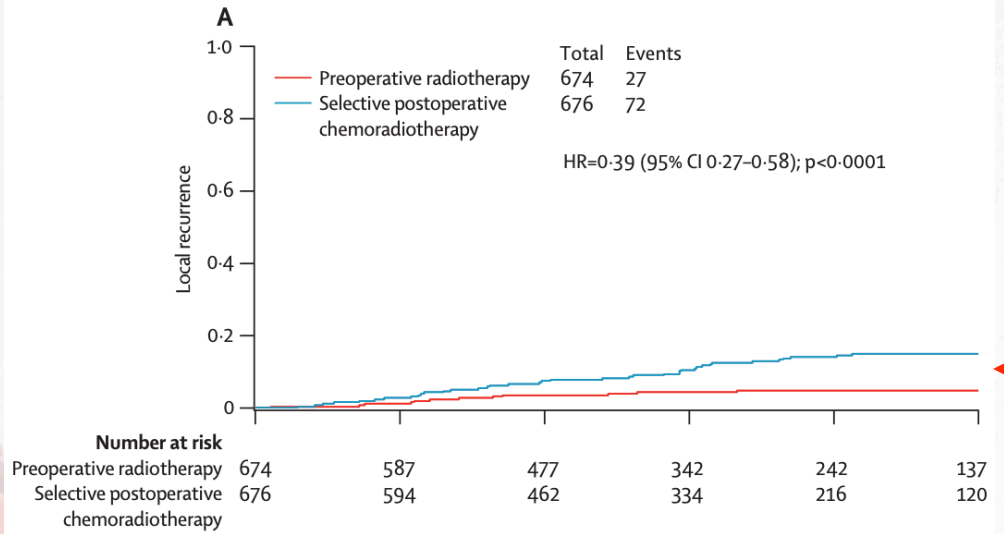
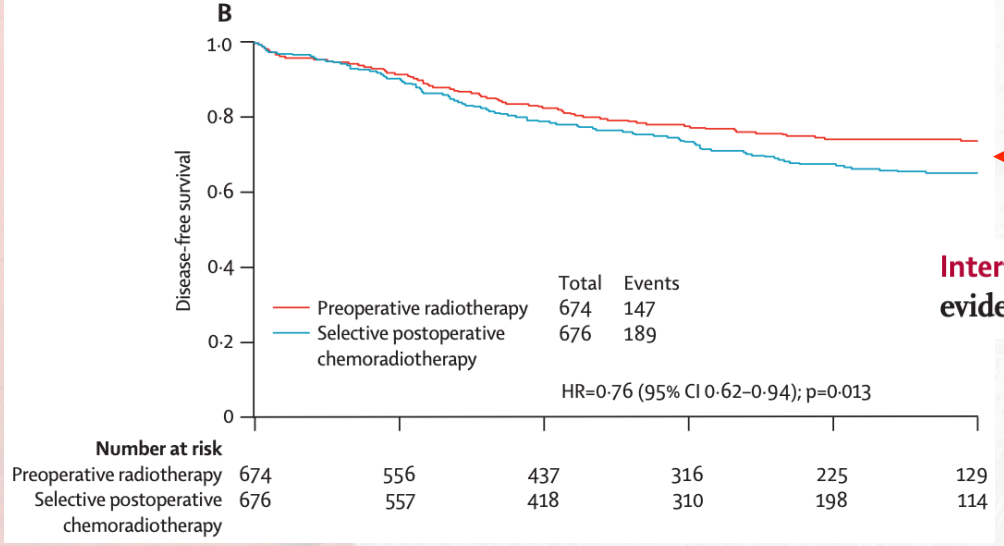
Rt hipofraccionada vs convencional





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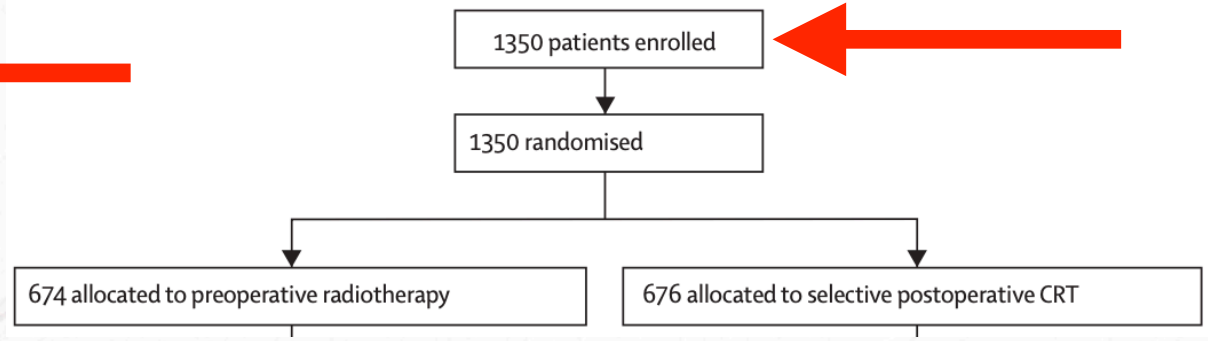
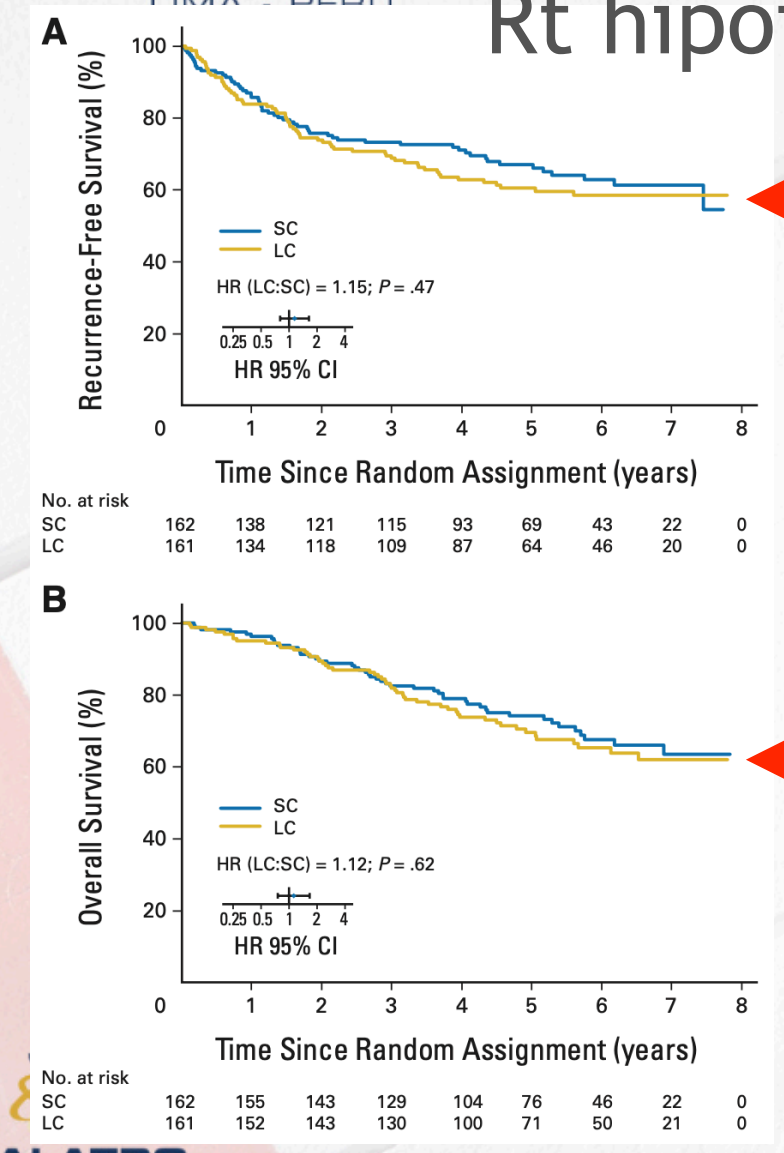


Interpretation Taken with results from other randomised trials, our findings provide convincing and consistent evidence that short-course preoperative radiotherapy is an effective treatment for patients with operable rectal cancer.

2. Sebag-Montefiore, Lancet 2009

ARÁN

Rt hipofraccionada vs convencional



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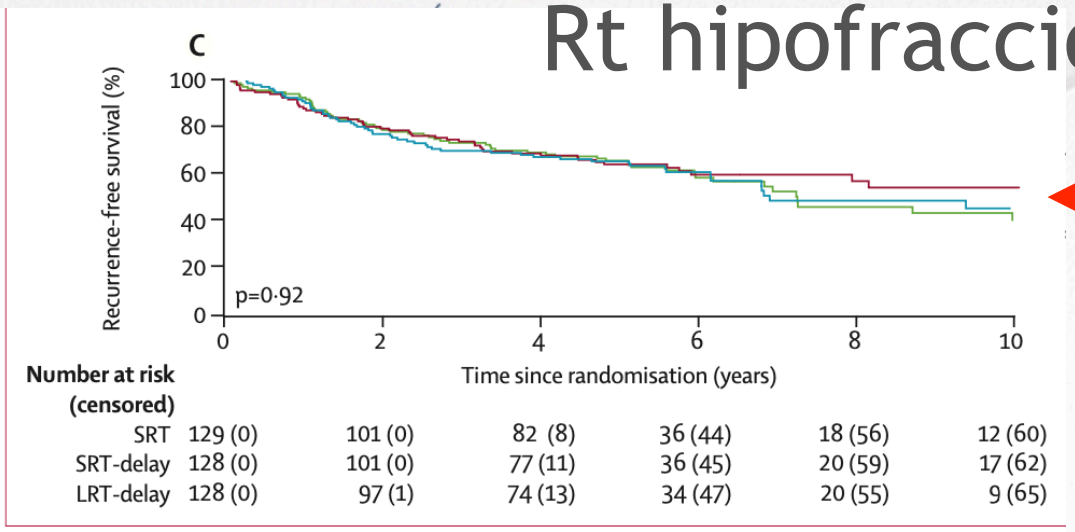
3. Ngan, JCO 2012

Rt hipofraccionada vs convencional



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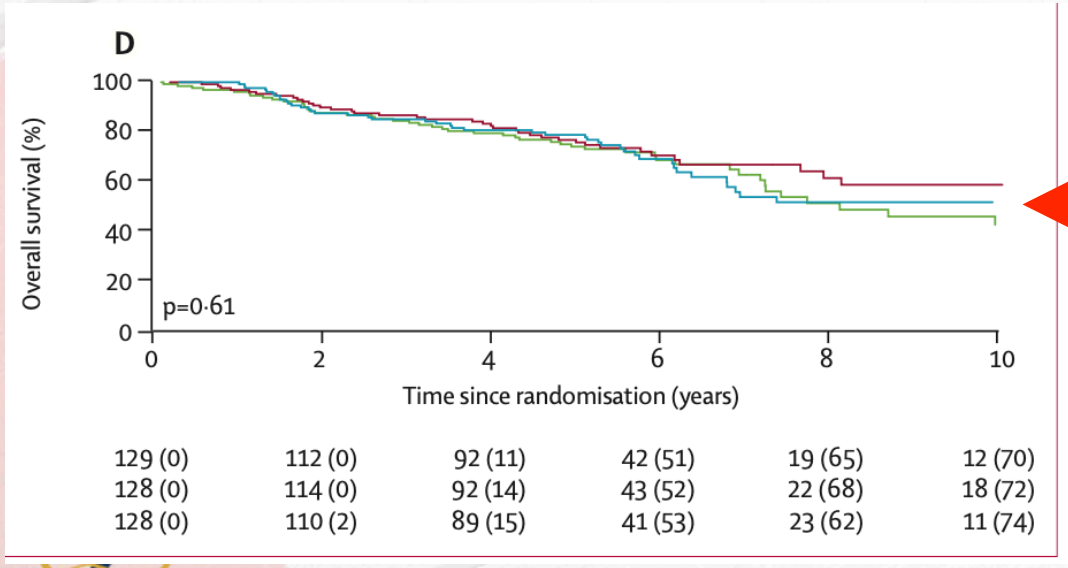
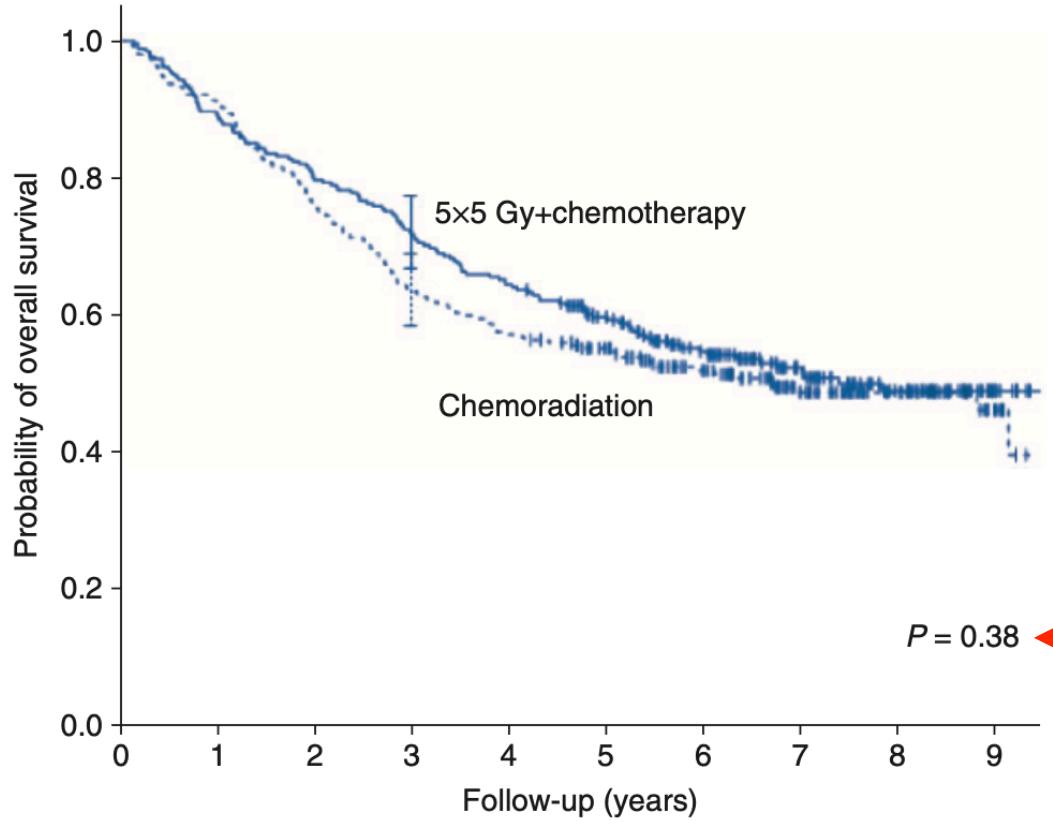


Long-course radiotherapy with delay seems to be no different than short-course radiotherapy with delay, but prolongs the treatment time substantially.

4. Erlandsson, Lancet Oncol 2017

Rt hipofraccionada vs convencional



Number at risk

5×5 Gy+chemotherapy	261	209	168	106	45	15
Chemoradiation	254	193	146	100	38	14

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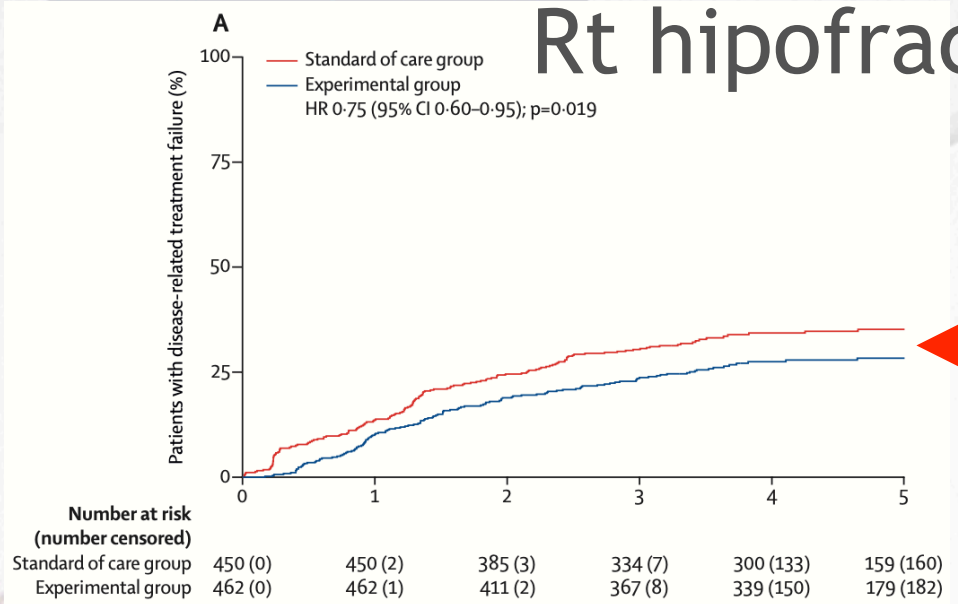
identical in both groups (12.4 weeks). Acute toxicity of preoperative treatment was lower in the short-course/CCT group than in the chemoradiation group, $P = 0.006$. Pelvic tumours were not

5. Cisel, Ann Oncol 2019

Rt hipofraccionada vs convencional



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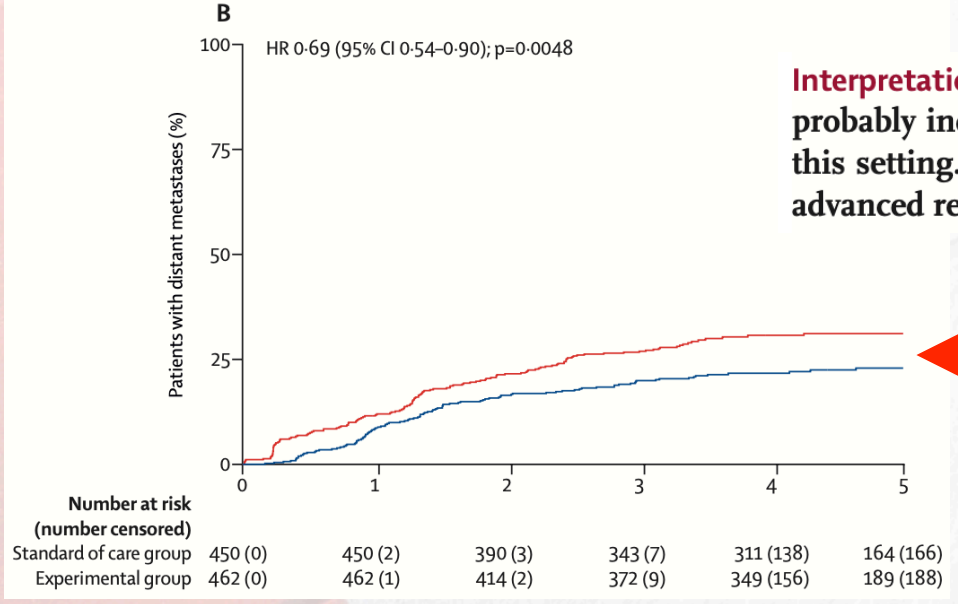

Interpretation The observed decreased probability of disease-related treatment failure in the experimental group is probably indicative of the increased efficacy of preoperative chemotherapy as opposed to adjuvant chemotherapy in this setting. Therefore, the experimental treatment can be considered as a new standard of care in high-risk locally advanced rectal cancer.

6. Badahoer, Lancet Oncol 2020

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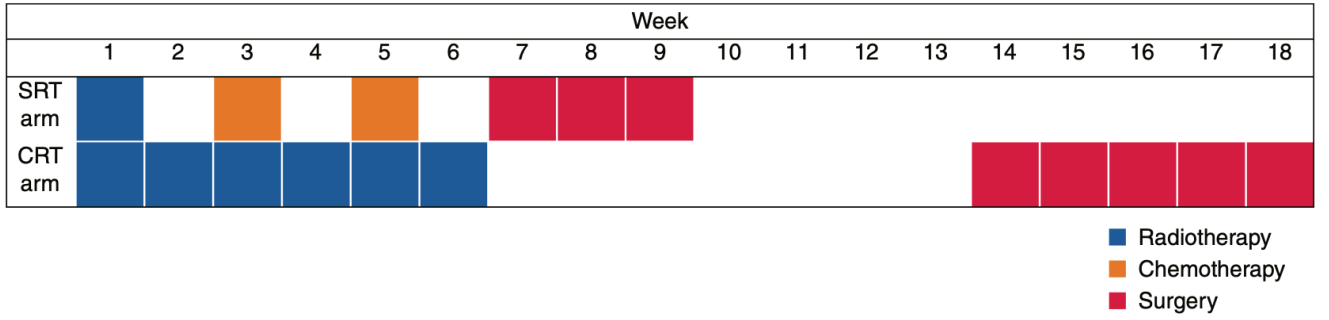

Table 3 Surgical outcomes

	Short-course radiotherapy ($n = 69$)	Chemoradiotherapy ($n = 71$)	P[§]	Hazard ratio[†]	Difference in proportions[†]
Type of surgery					
Low/ultralow anterior resection	39 (57)	38 (54)	0.517	1.09 (0.83, 1.44)[‡]	
Abdominoperineal resection	21 (30)	26 (37)			
No resection	9 (13)	7 (10)			
No. of lymph nodes dissected*	13 (3)	14 (4)	0.120[¶]		
R0 resection	60 of 69 (87)	64 of 71 (90)	0.554	0.96 (0.86, 1.09)	
Sphincter preservation	13 of 41 (32)	17 of 48 (35)	0.708	0.89 (0.50, 1.61)	
Pathological complete response	8 of 69 (12)	7 of 71 (10)	0.740	1.[illegible] (0.45, 3.07)	
yp tumour category			0.044		
ypT0	8 (12)	7 (10)			2 (–9, 13)
ypT1	14 (20)	4 (6)			14 (3, 25)
ypT2	32 (46)	46 (65)			19 (2, 34)
ypT3	6 (9)	7 (10)			1 (–9, 11)
ypT4	0 (0)	0 (0)			
No tumour resection	9 (13)	7 (10)			

require us to be flexible and adapt accordingly. SRT may reflect a better alternative to conventional CRT owing to its oncological equivalence and improved resource utilization[67]. Therefore, there is a need for widespread adoption of this treatment approach and a need to change practice in the light of best evidence.

7. Chakrabarti, BJS 2021

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Rt hipofraccionada vs convencional

original reports

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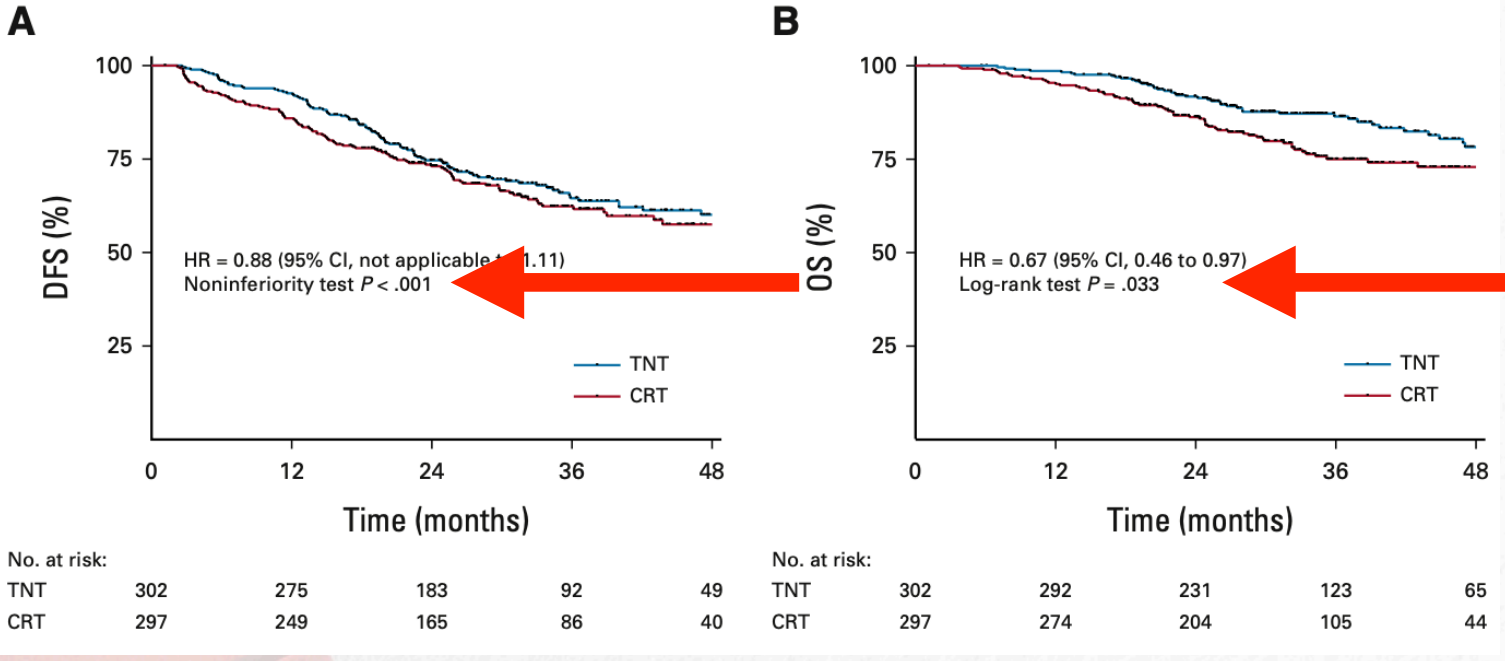
Relevance
This finding provides additional evidence supporting the clinical practice of hypofractionated radiotherapy followed by neoadjuvant chemotherapy for locally advanced rectal cancer.



interval between radiation and surgery. Three-year OS was 86.5% (95% CI, 82.1 to 90.8) in the TNT group compared with 75.1% (95% CI, 69.4 to 80.8) in the CRT group (HR = 0.67, 95% CI, 0.46 to 0.97; log-rank, *P* = .033; Fig

8. Jin, JCO 2022

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Rt hipofraccionada vs convencional

8 estudios randomizados, Rt convencional **NO** mejoró los resultados en ninguno…

Estudio	Diferencia	Mejor hipofraccionamiento	Mejor convencional	Iguales
1. Bujko, Br J Surg 2006	Convencional más toxicidad	+		
2. Sebag-Montefiore, Lancet 2009	Hipofraccionada más sobrevida libre enfermedad	+		
3. Ngan, JCO 2012	Ninguna			+
4. Erlandsson, Lancet Oncol 2017	Ninguna			+
5. Cisel, Ann Oncol 2019	Convencional más toxicidad	+		
6. Badahoer, Lancet Oncol 2020	Hipofraccionada más sobrevida libre de falla	+		
7. Chakrabarti, BJS 2021	Hipofraccionada mejor downstage	+		
8. Jin, JCO 2022	Hipofraccionada mejor sobrevida global	+		

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Rt hipofraccionada vs convencional

Radiobiología

Esquema	Tumor αβ= 5	Tumor c/ corrección de t	Tejido Sano αβ=3
5x5 Gy	35,7 Gy	35,7 Gy	
25x2 Gy	50Gy	50-15,6 =34,4 Gy	

25 Gy en 5 fx > 50 Gy en 25 fx

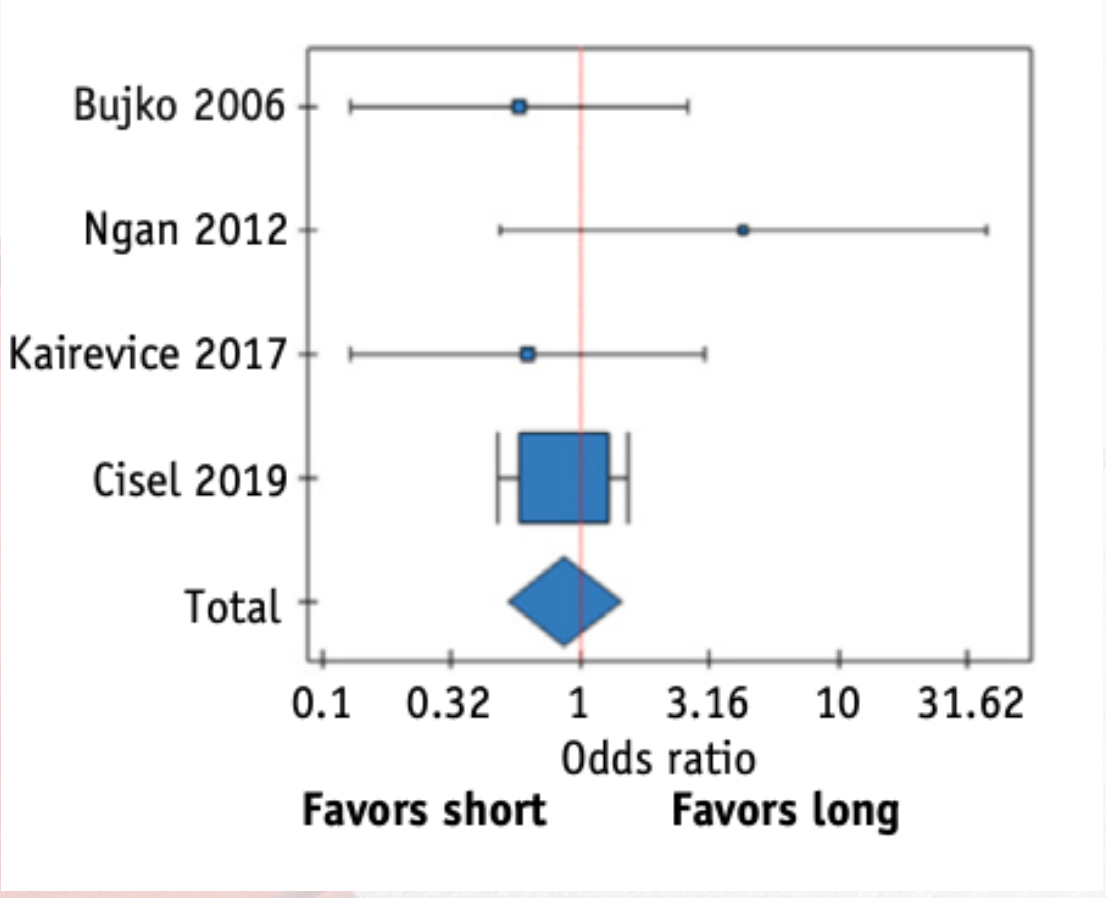
EQD2 (αβ) = (d+αβ) / (2+αβ)
Time correction: EQD2 (αβ) – (OTT-delay) D_{prolif}
Repair rate= D_{prolif}=0,6Gy/day
Proliferation delay: 7 days

Diapositiva Dra. Verónica López
Instituto Nacional del Cáncer - Chile

Guckenberger et al. Radiat Oncol 2009;4:67

Rt hipofraccionada vs convencional

También en los tumores de recto bajo



Clinical Investigation

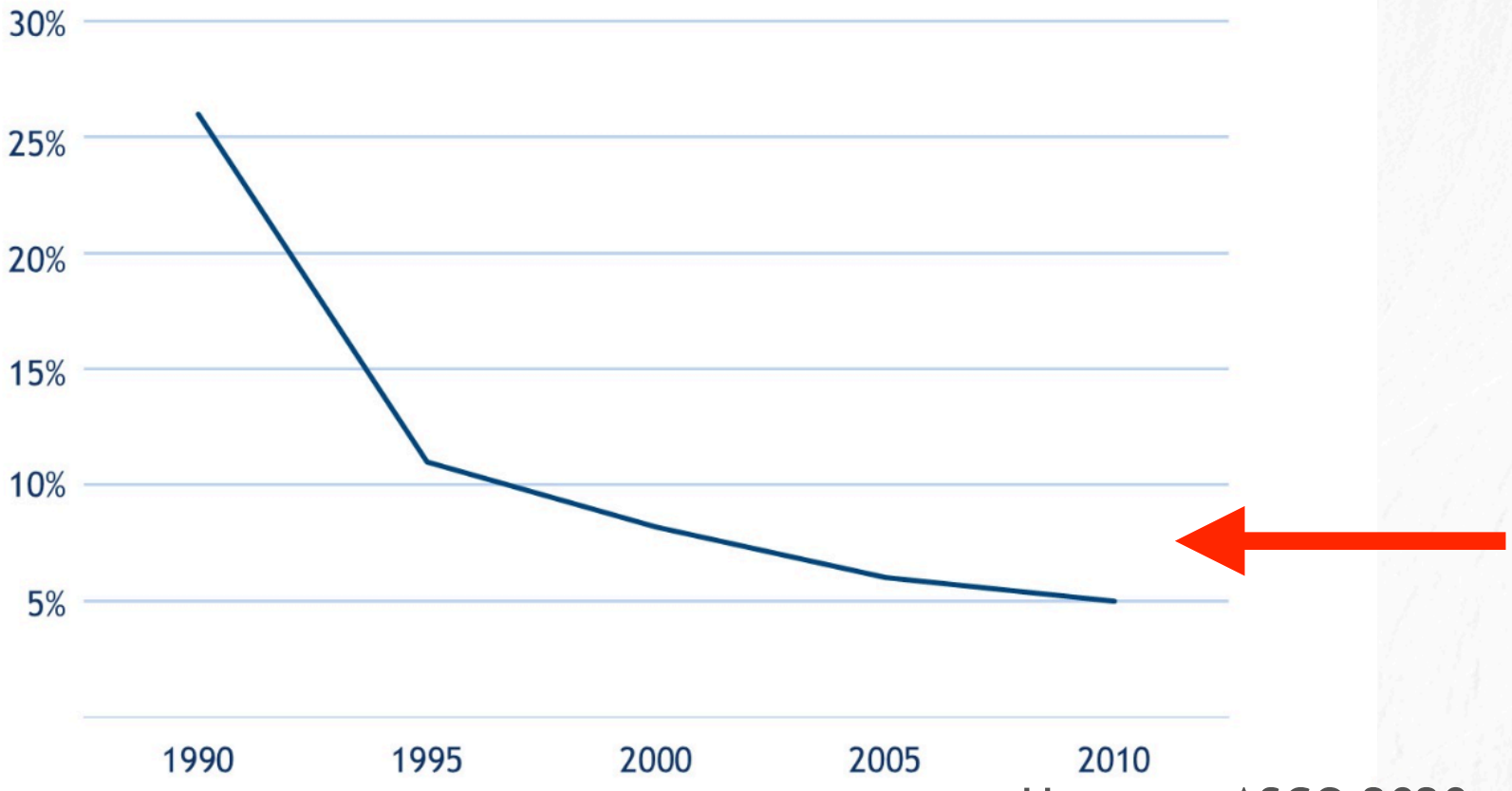
Should Short-Course Neoadjuvant Radiation Therapy Be Applied for Low-Lying Rectal Cancer? A Systematic Review and Meta-Analysis of the Randomized Trials

Joanna Socha, MD, PhD,*,† Laura Kairevice, MD, PhD,‡ Lucyna Kępka, MD, PhD,* Wojciech Michalski, MSc,§ Mateusz Spałek, MD, PhD,‖ Karol Paciorek, MD,¶ and Krzysztof Bujko, MD, PhD¶

This finding and other outcomes of these trials (Table 1) indicate that SC should not be disregarded as a treatment option for low-lying tumors.

Socha, IJROBP 2020

Rectal cancer
Local recurrence no longer a major problem



Hospers, ASCO 2020

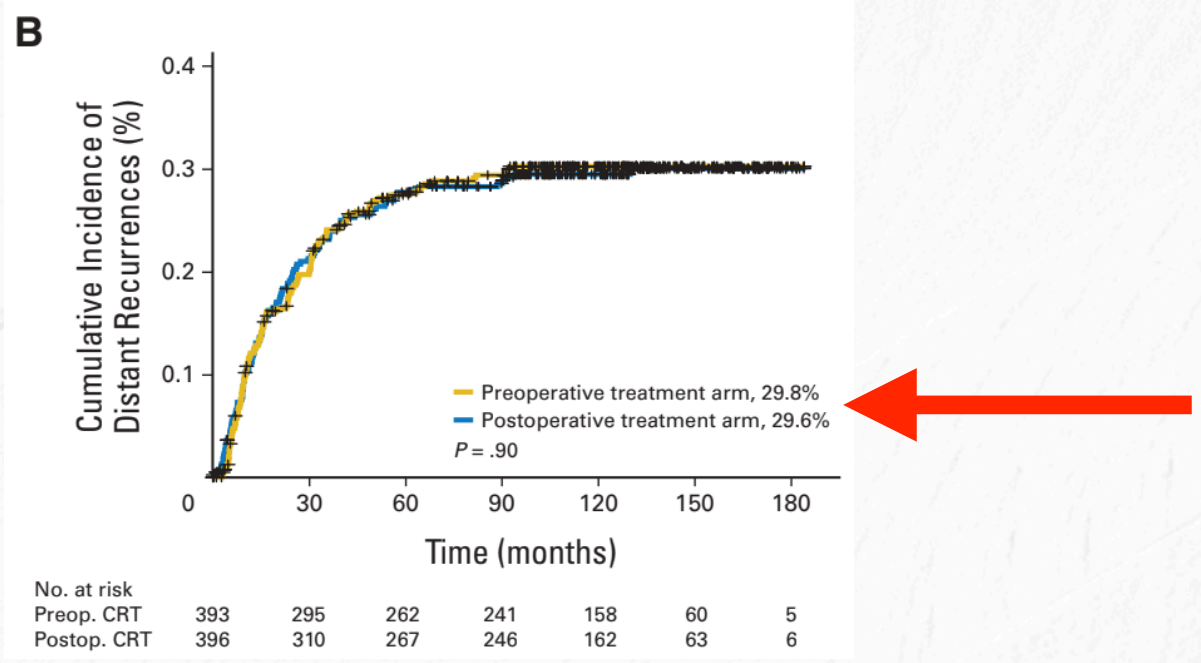
Ahora el mayor problema es el desarrollo de metástasis a distancia

VOLUME 30 · NUMBER 16 · JUNE 1 2012
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Preoperative Versus Postoperative Chemoradiotherapy for Locally Advanced Rectal Cancer: Results of the German CAO/ARO/AIO-94 Randomized Phase III Trial After a Median Follow-Up of 11 Years

Rolf Sauer, Torsten Liersch, Susanne Merkel, Rainer Fietkau, Werner Hohenberger, Clemens Hess, Heinz Becker, Hans-Rudolf Raab, Marie-Therese Villanueva, Helmut Witzigmann, Christian Wittekind, Tim Beissbarth, and Claus Rödel

30% de recurrencia a distancia



Sauer, JCO 2012

Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: Final results of the PRODIGE 23 phase III trial, a UNICANCER GI trial.

Safety: surgery

Restaging before surgery:	TNT	CRT	p-value
Metastatic disease	2 (1%)	10 (4.7%)	0.03
Surgery:	N=213*	N=218	P
Interval preop CRT → surgery	7.9 weeks	7.9 weeks	ns
Non therapeutic laparotomy	0 (0%)	8 (3.7%)	0.007
Due to perop detection of multiple metastases	_	5 (2.3%)	
Unresectable or R2 resection	_	3 (1.4%)	
Median hospital stay (range)	11 days (3-78)	12 days (2-99)	ns
Postoperative morbidity	29.3%	31.2%	ns
Postoperative mortality	0	6 (2.8%)	0.03

* 2 patients in CR after Total Neoadjuvant Treatment refused surgery and are in sustained CR with 59.5 and 62.1 months follow-up with watch-and-wait policy

Conroy, ASCO 2020

Corrie MARIJNEN

Comments on the CAO/ARO/AIO-12 trial

Corrie Marijnen

Chair department Radiation Oncology

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

Rationale for total neoadjuvant treatment

- earlier use of systemic therapy: micrometastases
- maximal downsizing: R0 resections
- potential non-operative approach

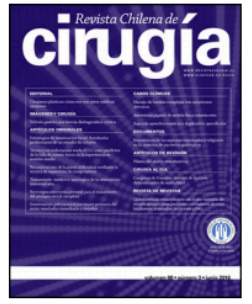
Corrie MARIJNEN

Rt hipofraccionada vs convencional

Rev Chil Cir. 2017;69(2):181–183

Revista Chilena de cirugía

www.elsevier.es/rchic



ARTÍCULO DE REVISIÓN

Nueva estrategia terapéutica en cáncer de recto localmente avanzado

Sebastián Solé Z., Francisco Larsen E.* y Claudio Solé P.

Solé, Rev Chil Cir 2017

Datos Clínica IRAM, Santiago, Chile

RT 25 Gy en 5 fx y 4 ciclos de FOLFOX (2 meses)

total pac 58	n	%
N0	8	13,8
N1	32	55,1
N2	11	18,9
N positivo no clasificado	7	12,1
N +	50	86,2

45 pacientes T3-4 (77,5%)

Gabler, ASTRO 2020

Datos Clínica IRAM, Santiago, Chile

22,4 % de respuesta patológica completa

total pac 58	n	%
pT 0	13	22,4
pT 1	5	8,6
pT2	15	25,9
pT3	22	37,9
pT 4	2	3,4
pT no evaluado	1	1,7

Gabler, ASTRO 2020

Rt hipofraccionada vs convencional
IRAM vs Sauer

Table 3. Postoperative Pathological Tumor Stage, Type of Surgery, and Completeness of Resection, According to Actual Treatment Given.*

Variable	Preoperative Chemoradiotherapy (N=415)	Postoperative Chemoradiotherapy (N=384)	P Value
Histopathological finding (%)			<0.001
Complete response	8	0	
TNM stage			
I	25	18	
II	29	29	
III	25	40	

	IRAM	Sauer
pCR	22,4 %	8 %
Downstage	65,5 %	15 %

Gabler, ASTRO 2020

NAR Score validation in TNT (Total Neoadjuvant treatment) for locally advanced rectal cancer

Ilan Perrot Rosenberg[1-2]; José Solis Campos[1-2]; Gabriel Lazcano Álvarez[2]; Jorge Olivares González[2]
Benjamin Tudela Staub[1-2]; Gabriel Veillon Contreras[1-2]
1. Radiation Oncology Unit, Carlos Van Buren Public Hospital, Valparaíso, Chile.
2. Oncology Department, University of Valparaíso, Valparaíso, Chile.

Introduction

A current management for locally advanced rectal cancer is neoadjuvant radio – chemotherapy and total neoadjuvant treatment (TNT) is one possible approach. The purpose of this study is to analyze the oncological outcomes in survival and the impact of pathologic response in TNT using the *NAR* Score.

$$NAR = \frac{[5ypN - 3\ (cT - ypT) + 12]^2}{9 \cdot 61}$$

Figure 1. Formula used to obtain NAR Score for each histological examination

Materials and Methods

We performed a retrospective cohort study including all locally advanced rectal cancer patients treated with TNT with a curative intention between 2017-2019, receiving 25 Gy in 5 Gy daily fractions followed by FOLFOX Chemotherapy and surgery. Pre-operative and post-operative biopsies were analyzed calculating NAR score for each patient. Survival analysis was performed using the Kaplan Meier method. The study was approved by the local ethics committee.

Results and findings

49 patients were identified. 4 patients cT2 (8.2%); 34 cT3 (69.4%) and 11 cT4 (22.4%). All patients completed radiotherapy with a 7-day median duration (ICR 5-[illegible]). 98% received at least 1 cycle of chemotherapy, median of 3 cycles ([illegible]) radiotherapy and surgery 115 days (ICR 99-144). [illegible] patients (10%) operated within 12 weeks. 34 surgical biopsies were retrieved. 10 patients ypT0 (29.4%); 3 ypT1 (8.8%); 7 ypT2 (20.6%); 11 ypT3 (32.4%); 3 ypT4 (8.8%); 27 ypN0 (79.4%); 4 ypN1 (11.8%) and 3 ypN[illegible] (8.8%). 9 patients showed pathologic complete response (18.4%). [illegible] a 32 month follow up period. Median NAR [illegible]core was 8.4. Considering response to TNT patients with low NAR (<8.4) had 100% Overall survival, while high NAR patients (>8.4) showed 60% overall survival. (p=0.002).

Figure 2. Box plot showing the median NAR score for the entire cohort (8.4)

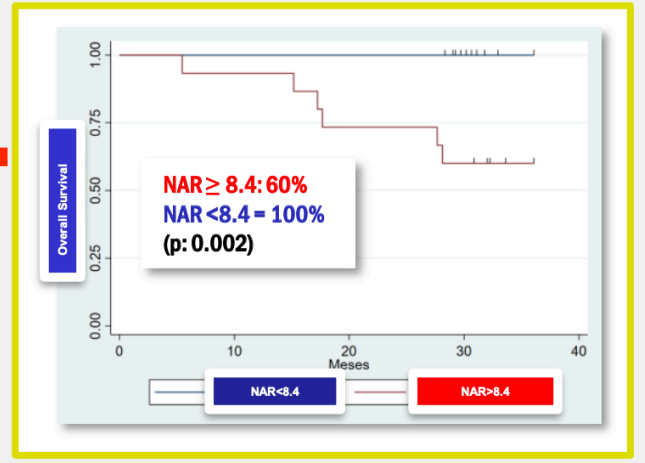


Figure 3. Overall survival according to NAR score value.

Conclusions

In conclusion, our TNT results are comparable to the ones found in the international literature. Although initially validated in extended concomitant neo adjuvant radio chemotherapy trials, we demonstrated NAR score still shows prognostic significance in the context of TNT.

References

1. Glynne-Jones R, Glynne-Jones S. The concept and use of the neoadjuvant rectal score as a composite endpoint in rectal cancer. Lancet Oncol. 2021 Jul;22(7):e314-e326. doi: 10.1016/S1470-2045(21)00053-X. Epub 2021 May 25. PMID: 34048686
2. Keller DS, Berho M, Perez RO, Wexner SD, Chand M. The multidisciplinary management of rectal cancer. Nat Rev Gastroenterol Hepatol. 2020 Jul;17(7):414-429. doi: 10.1038/s41575-020-0275-y. Epub 2020 Mar 12. PMID: 32203400.
3. George TJ Jr, Allegra CJ, Yothers G. Neoadjuvant Rectal (NAR) Score: a New Surrogate Endpoint in Rectal Cancer Clinical Trials. Curr Colorectal Cancer Rep. 2015;11(5):275-280. doi:10.1007/s11888-015-0285-2

Perrot, ESTRO 2022

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TNT nuevo estándar

Invited Commentary ONLINE ONLY

June 14, 2018

Total Neoadjuvant Therapy for Locally Advanced Rectal Cancer—The New Standard of Care?

Theodore S. Hong, MD[1]; David P. Ryan, MD[2]

Author Affiliations

[1]Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

[2]Divison of Hematology-Oncology, Massachusetts General Hospital, Medicine, Harvard Medical School, Boston Massachusetts

JAMA Oncol. 2018;4(6):e180070. doi:10.1001/jamaoncol.2018.0070

Hong, JAMA Oncol 2018

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Guía ASTRO: TNT

Clinical Practice Guideline

Radiation Therapy for Rectal Cancer: Executive Summary of an ASTRO Clinical Practice Guideline

Jennifer Y. Wo, MD,[a] Christopher J. Anker, MD,[b]

For patients with rectal cancer undergoing neoadjuvant therapy ***with*** tumor factors that portend increased recurrence risk, addition of multiagent (FOLFOX or CAPOX) chemotherapy (1) before or after chemoradiation or (2) after short-course RT is conditionally recommended.

Most informed people would choose the recommended course of action, but a substantial number would not.

Wo, PRO 2021

Opciones de TNT en Cáncer de Recto

	T4	Predicted lateral margin <1mm / Mesorectal fascia +	Pathologic complete response	Metastasis free survival
Sauer	6 %	?	8 %	70,2 %
PRODIGE 23	17,8 %	26 %	27,8 %	78,8 %
RAPIDO	31,8 %	61,7	28,4 %	80 %

Opciones de TNT en Cáncer de Recto

	T4	Distance to fascia <1mm / Positive fascia	Pathologic complete response	DFS/DrTF
CAO/ARO/AIO-12 Fase II n=311	18 %	22 %	25 %	73 %
RAPIDO Fase III n=920	31,8 %	61,7 %	28,4 %	76,3 %

Bahadoer, Lancet Oncol 2020

Fokas, JAMA Oncol 2021

Opciones de TNT en Cáncer de Recto

	T4	Enfemedad N0	Seguimiento	DFS/DrTF
OPRA Fase II n=324	11 %	28 %	3 años	76 %
RAPIDO Fase III n=920	31,8 %	9 %	4,6 años	76,3 %

Bahadoer, Lancet Oncol 2020

Garcia-Aguilar, JCO 2022

¿Qué TNT elegir?

- RAPIDO
  - Con peores pacientes logra resultados similares al CAO/ARO/AIO-12, PRODIGE 23, OPRA
  - Partir con Rt produce rápido alivio de síntomas rectales
  - Rt hipofraccionada no produce retraso relevante en administrar Qt
  - Estudio OPRA y CAO/ARO/AIO-12 sugieren partir con Rt (Qt de consolidación mejor que inducción)

¿Qué TNT elegir?

- RAPIDO
  - Más conveniente que PRODIGE 23
    - 9 vs 12 ciclos de Qt
    - 2 vs 3 drogas de Qt
    - 1 vs 5 semanas de Rt

Guía ESMO: Recomendación estándar

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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

CLINICAL PRACTICE GUIDELINES

Clinical Practice Guidelines

Annals of Oncology

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

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

Guía NCCN: Recomendación estándar

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2019
Rectal Cancer

NCCN Guidelines Index
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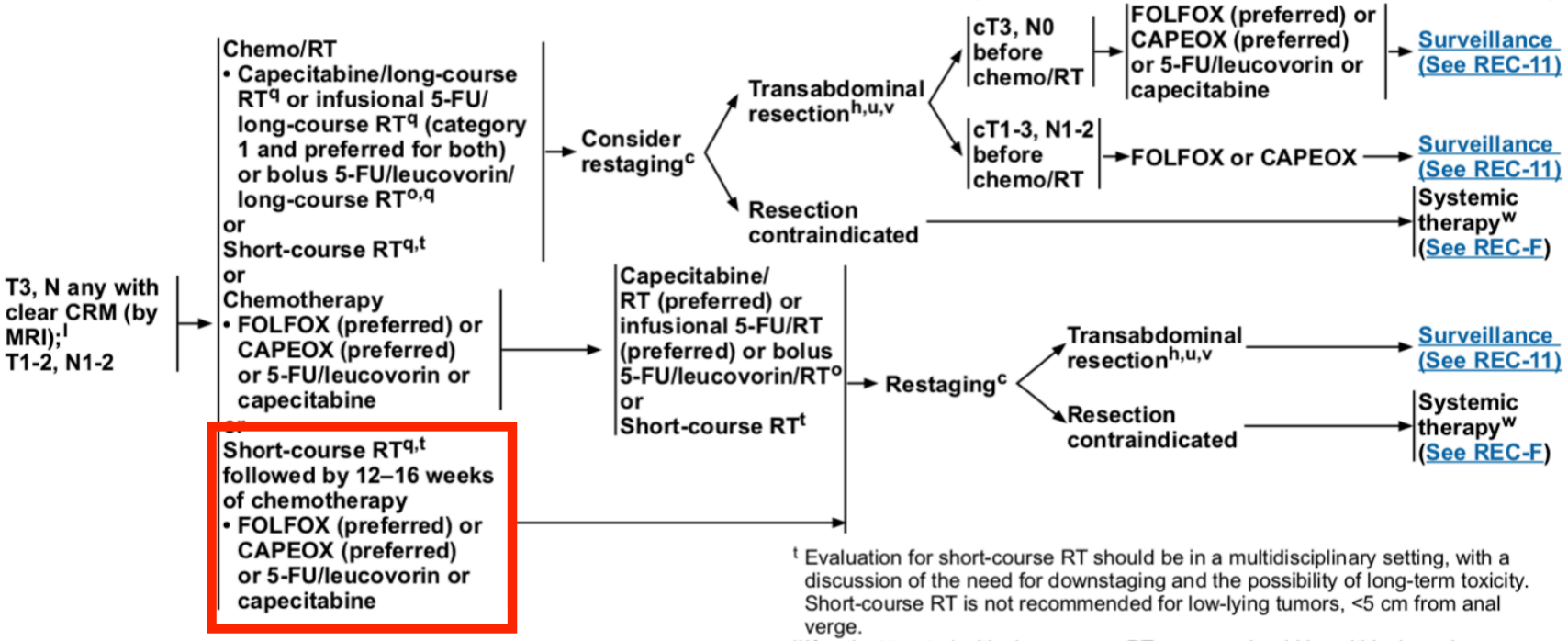

[t] Evaluation for short-course RT should be in a multidisciplinary setting, with a discussion of the need for downstaging and the possibility of long-term toxicity. Short-course RT is not recommended for low-lying tumors, <5 cm from anal verge.

[u] If patient treated with short-course RT, surgery should be within 1 week or

Guía NCCN: Recomendación estándar

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2022
Rectal Cancer

NCCN Guidelines Index
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CLINICAL STAGE

T3, N any with clear CRM (by MRI)[m]; T1–2, N1–2

TOTAL NEOADJUVANT THERAPY (PREFERRED)

- FOLFOX or CAPEOX (12–16 wk) → Long-course chemo/RT[q,r] • Capecitabine[p] or infusional 5-FU[p] or Short-course RT[u] → Restaging[c] (best tumor response 8 wk after completion of RT)
- or
- Long-course chemo/RT[q,r] • Capecitabine[p] or infusional 5-FU[p] or Short-course RT[r,u] → Chemotherapy (12–16 wk) • FOLFOX or CAPEOX → Restaging[c]

PRIMARY TREATMENT

- Transabdominal resection[i,v] → Surveillance (REC-11)
- Resection contraindicated → Systemic therapy[w] (REC-F)

NEOADJUVANT THERAPY

Long-course chemo/RT[q,r] • Capecitabine[p] or infusional 5-FU[p] or Short-course RT[r,u] → Consider restaging[c] (best tumor response 8 wk after completion of RT)

PRIMARY TREATMENT

- Transabdominal resection[i,v] → **ADJUVANT TREATMENT[c,q,r]**: FOLFOX or CAPEOX (12–16 wk) → Surveillance (REC-11)
- Resection contraindicated → Systemic therapy[w] (REC-F)

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Rt hipofraccionada vs convencional

WJCO World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Clin Oncol 2020 December 24; 11(12): 990-995

DOI: 10.5306/wjco.v11.i12.990

ISSN 2218-4333 (online)

EDITORIAL

New standard in locally advanced rectal cancer

Sebastián Solé, Ramón Baeza, Carolina Gabler, Felipe Couñago

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Author contributions: All authors contributed equally to designing and performing this research, and all authors have read and approved the final manuscript.

Conflict-of-interest statement: The authors have no conflicts of interest.

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Solé, WJCO 2020

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¿Qué es lo que quieren los pacientes?

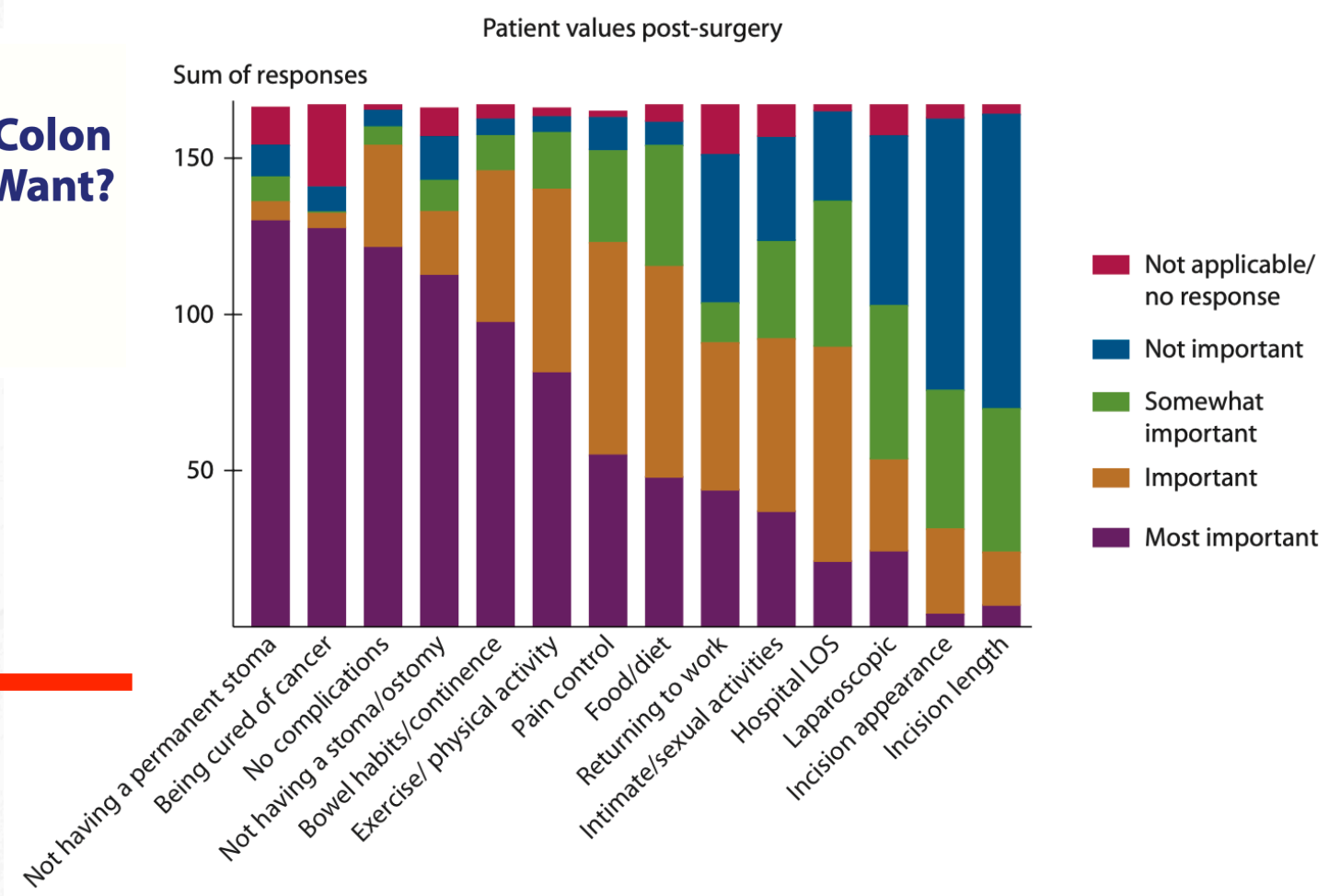
ORIGINAL CONTRIBUTION

Patient Perceptions and Quality of Life After Colon and Rectal Surgery: What Do Patients Really Want?

Sean M. Wrenn, M.D.[1] • Antonio Cepeda-Benito, Ph.D.[2]
Diego I. Ramos-Valadez, M.D.[3] • Peter A. Cataldo, M.D.[1]

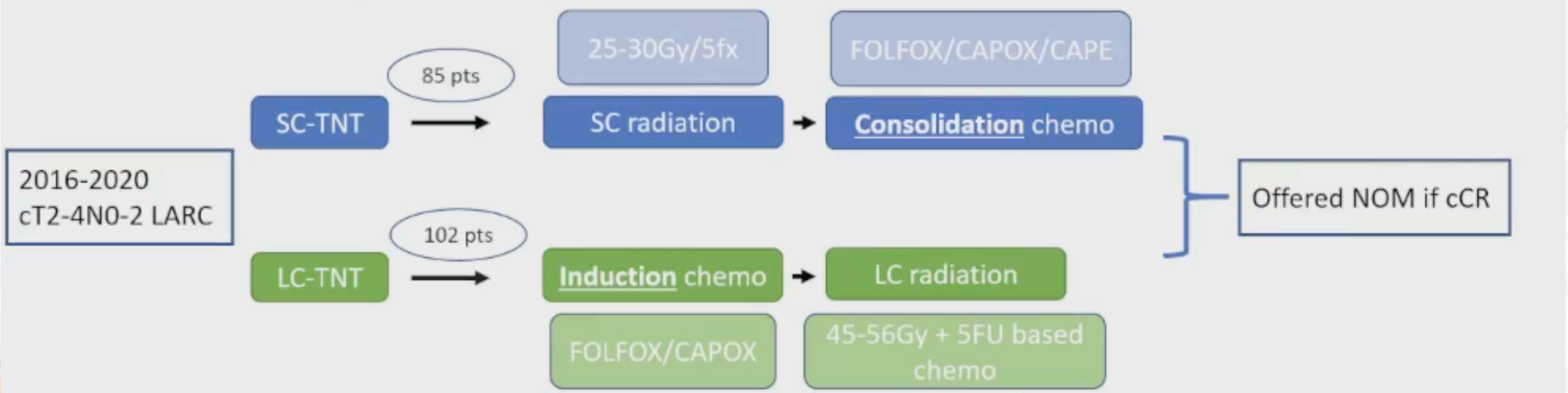
1 Department of Surgery, Robert Larner M.D. College of Medicine, Burlington, Vermont
2 Department of Psychological Science, University of Vermont, Burlington, Vermont
3 Sanford Health, Thief River Falls, Minnesota

"Factors considered most important included being cured of colorectal cancer (76%), not having a permanent stoma (78%)"



Wrenn, Dis Col & Rec 2018

Rt hipofraccionada vs convencional en manejo no operatorio



- Clinical CR rate was higher in the SC-TNT cohort (52.8% vs 20.6%, p<0.001)
- DFS was higher in the LC-TNT cohort on univariate/log rank testing (p=0.023), but without difference on MVA adjusting for other risk factors. 2-year DFS excellent for both groups (95.4 vs. 93.4 % for LC/SC)
- For NOM patients, freedom from local recurrence at 1 year in SC-TNT and LC-TNT was 85.6% vs. 58.9%, p=0.223, respectively
- **SC-TNT demonstrated a greater rate of cCR compared to LC-TNT, without DFS difference on MVA**
- Although unclear if improved outcomes for SC-TNT are due to "short course" or consolidation chemo sequencing, our data support SC-TNT as a suitable regimen for rectal cancer NOM

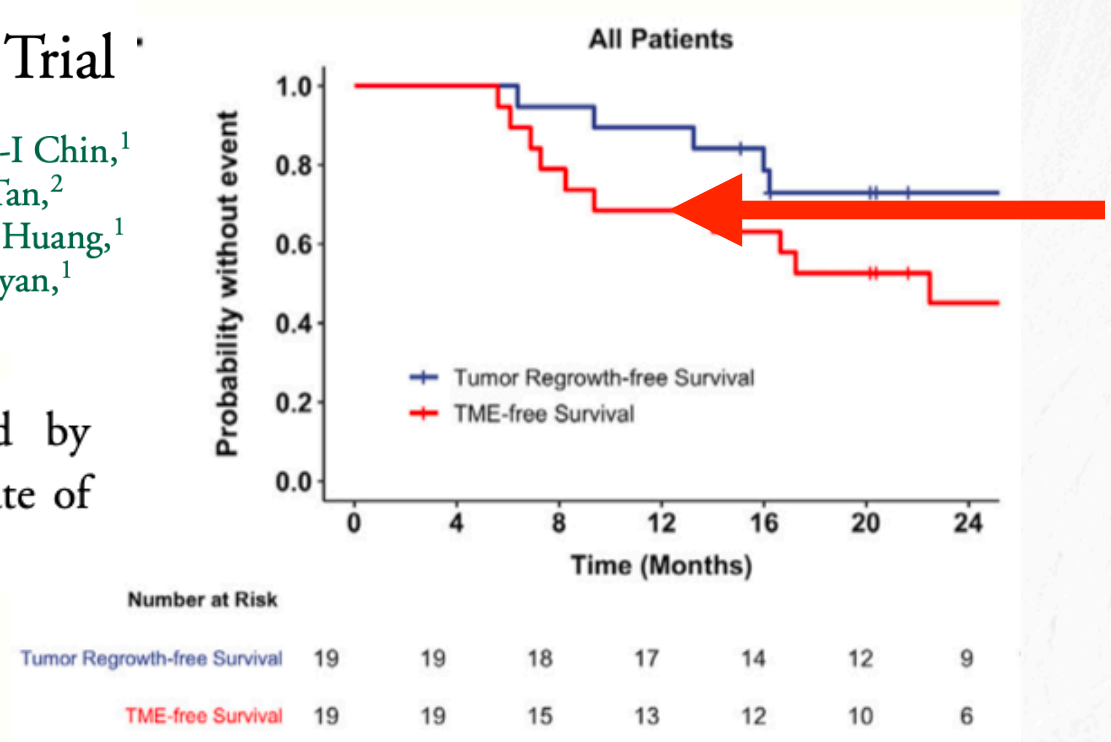
Moskalenko, ASTRO 2021

Hipofraccionamiento en manejo no operatorio

Nonoperative Rectal Cancer Management With Short-Course Radiation Followed by Chemotherapy: A Nonrandomized Control Trial

Hyun Kim,[1] Katrina Pedersen,[2] Jeffrey R. Olsen,[3] Matthew G. Mutch,[4] Re-I Chin,[1] Sean C. Glasgow,[4] Paul E. Wise,[4] Matthew L. Silviera,[4] Benjamin R. Tan,[2] Andrea Wang-Gillam,[2] Kian-Huat Lim,[2] Rama Suresh,[2] Manik Amin,[2] Yi Huang,[1] Lauren E. Henke,[1] Haeseong Park,[2] Matthew A. Ciorba,[5] Shahed Badiyan,[1] Parag J. Parikh,[6] Michael C. Roach,[7] Steven R. Hunt[3]

- In this prospective clinical trial of SCRT followed by chemotherapy, we observed a high initial and 1-year cCR rate of 74% and 68%, respectively.



100% sobrevida libre de metástasis a distancia a 2 años en grupo con cCR

Kim, Clin Col Can 2021

Conclusiones

- Rt hipofraccionada es **al menos** equivalente al curso largo
- Rt hipofraccionada en TNT permite mejorar la **sobrevida libre de metástasis** (Badahoer, Lancet Oncol 2020)
- Rt hipofraccionada en TNT permite mejorar la **sobrevida global** (Jin, JCO 2022)
- TNT es el nuevo estándar y hacerlo con Rt hipofraccionada y FOLFOX secuencial está apoyado por las guías clínicas y es una excelente alternativa de tratamiento (**la mejor en mi opinión**)
- Rt hipofraccionada y FOLFOX secuencial es una excelente alternativa de tratamiento para el **manejo no operatorio**

Futuro

- Identificar pacientes que sobretratamos
- Tratamiento definitivo (no operatorio) en recto bajo:
  - Más Rt hipofraccionada: 3000/5?
  - Más Qt: FOLFOX x 12?
- Rol de marcadores moleculares (dMMR) e inmunoterapia

Caso clínico 1

- 27.12.16
- 62 años
- Rectorragia
- Colonoscopía tumor rectal que impide paso
- Biopsia adenocarcinoma infiltrante
- TC muestra tumor rectal con linfopatías regionales
- CEA 17
- Tacto palpa tumor fijo a 6 cm del margen anal

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Caso clínico 1

- IMRT 2500cGy/5 fx sobre pelvis que finalizó el 11.1.17
- FOLFOX x 4 ciclos

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Caso clínico 1

SERVICIO : CIRUGÍA ADULTO
MUESTRA DE : Arandelas recto-colon - Sigmoides
ANTECEDENTES : Cáncer de recto

INFORME ANATOMO PATOLOGICO

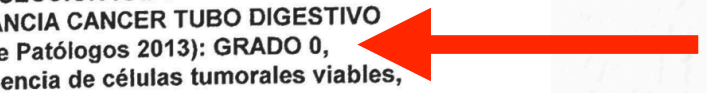
EXAMEN MACROSCÓPICO:
TURNO:12/06/17 DR.FG S.SR
1.Arandela recto-colon: Dos fragmentos tisulares, uno circular con mucosa colónica lisa y pardusca de 2 cm de diámetro mayor. El otro de 2.3 x 0.8 x 0.4 cm, con mucosa pardusca y congestiva.
2.Sigmoides: Colon sigmoides de 22 cm de longitud y 6 cm de diámetro a nivel principal y 8 cm a nivel distal. Por cara posterior segmento de mesosigmoides de 10 x 7 cm de longitud. Superficie serosa lisa y brillante. Superficie mucosa hacia tercio distal con área ulcerada estrellada con convergencia de pliegues de 1.5 x 1 cm, localizada a 4.5 cm del borde quirúrgico distal. La mucosa en esa área se observa lisa, finamente granular. La mucosa remanente muestra pliegues conservados. Al corte, lesión blanquecino-amarillenta que conta el borde quirúrgico profundo, indurada, irregualr de 1.5 x 2 cm.
En tejido adiposo peritumoral no se logran identificar ganglios linfáticos, se incluyen muestras representativas.
En tejido adiposo alejado del tumor se identifican ganglios linfáticos, se incluyen muestras representativas.
En la ligadura arterial se identifican vasos sanguíneos y un ganglio linfático de 0.8 cm de eje mayor.

DIAGNÓSTICO

1.ARANDELA RECTO-COLON:
- PARED COLONICA CON MUCOSA CON LEVE DISTORSION DE LA ARQUITECTURA, INFLAMACION CRONICA ESTROMAL, SIN EVIDENCIAS DE NEOPLASIA.
2.SIGMOIDES:
- COLON SIGMOIDES CON PROCESO INFLAMATORIO CRONICO, CON FIBROSIS CICATRIZAL, CON MUCINA EXTRACELULAR QUE COMPROMETE CAPA MUSCULAR PROPIA Y TEJIDO ADIPOSO PERICOLONICO, SIN COMPROMISO DE BORDE QUIRURGICO.
EL AREA DE MUCINA MIDE 2.3 X 1.4 X 1.0 CM. NO SE IDENTIFICA NEOPLASIA RESIDUAL NI EMBOLOS TUMORALES EN VASOS LINFATICOS NI SANGUINEOS.

9.6.17

- CAMBIOS TISULARES ESTROMALES Y VASCULARES SECUNDARIOS A RADIOTERAPIA.
- INFILTRADO LINFOCITARIO PERILESIONAL AUSENTE.
- DISECCION GANGLIONAR:
· GANGLIOS PERITUMORALES (9 GANGLIOS): GANGLIOS LINFATICOS SIN METASTASIS, CON ARQUITECTURA CONSERVADA.
· GANGLIOS ALEJADOS DEL TUMOR (10 GANGLIOS): GANGLIOS LINFATICOS SIN METASTASIS, CON ARQUITECTURA CONSERVADA.
· GANGLIOS LIGADURA ARTERIAL: NO SE IDENTIFICAN GANGLIOS LINFATICOS.
- BORDES QUIRURGICOS:
· PROXIMAL Y DISTAL EN MUCOSA COLONICA CON CAMBIOS SECUNDARIOS A TERAPIA NEOADYUVANTE.
· RADIAL, EN TEJIDO FIBROSO CICATRIZAL, SIN NEOPLASIA RESIDUAL, MUCINA EXTRACELULAR A 2 CM DEL BORDE DE SECCION RADIAL.
- REGRESION TUMORAL POST NEOADYUVANCIA CANCER TUBO DIGESTIVO (Basado en Protocolo Colegio Americano de Patólogos 2013): GRADO 0, SIN EVIDENCIA DE TUMOR RESIDUAL (Ausencia de células tumorales viables, fibrosis predominante).



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Caso clínico 1

28.10.21

67 años. 57 meses de seguimiento (4 años y 9 meses) desde que recibió IMRT 2500 cGy en 5 fx sobre pelvis que finalizó el 11.1.17, por cáncer de recto T3 N1 M0.

Está bien, hace vida normal, buena calidad de vida. Sin hemorragias, sin colostomía. Dieta normal. Mantiene peso entre 85-90 Kg.

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Caso clínico 2

- 11.9.20
- 46 años
- Rectorragia
- Colonoscopía tumor rectal de 3 cm
- Biopsia adenocarcinoma infiltrante
- RM tumor rectal con compromiso de grasa mesorrectal con al menos 3 linfopatías regionales sospechosas

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Caso clínico 2

- IMRT 2500cGy/5 fx sobre pelvis que finalizó el 25.9.20
- FOLFOX x 9 ciclos
- Por respuesta clínica completa se decide manejo no operatorio

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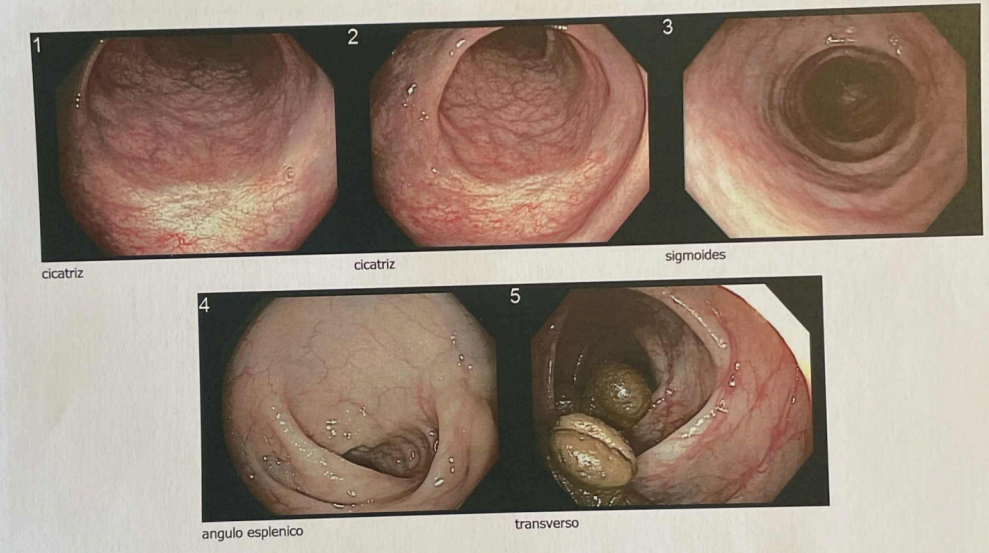
Caso clínico 2

13 meses de seguimiento desde RT

COLONOSCOPIA CORTA



Procedencia	: Dr. Campaña
Premedicación	: Midazolam 3 mg, Fentanyl 0 ug,
Diagnostico	: Ca recto. Neoaduyancia. Control protocolo W
Inspección	: Piel sin lesiones.
Tacto Rectal	: Esfinter de tono normal. Palpación del canal normal. Ampolla rectal vacia. No se palpan masas
Colonoscopía	: Se explora hasta el colon transverso encontrando en ese segmento deposiciones sólidas. En recto medio se observa cicatriz estrellada plana, blanquecina. Retrovisión normal.
Biopsias	: No
Conclusión	: **Colonoscopía izquierda normal. Cicatriz concordante con RCC**

RM de Pelvis Masculina

Antecedente.
Control de neoplasia de recto medio – regresión clínica completa.
Se dispone de estudios previos.

Hallazgos.
Vejiga parcialmente distendida de contenido líquido.
Próstata y vesículas seminales sin alteraciones.
Recto de morfología y señal normal.

En este control no se identifican focos de engrosamiento parietal zonas de realce patológico ni signos de restricción a la difusión.
Vasos ilíacos permeables.
No hay adenopatías pelvianas.
No se observa líquido libre en pelvis.

Impresión.
Control de neoplasia de recto en regresión clínica completa sin signos de compromiso neoplásico macroscópico actual.

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Congreso ALATRO 2022

16 - 18 de Noviembre de 2022

Muchas gracias

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Clínica IRAM
Expertos en oncología

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