WHICH PATIENTS WITH RECTAL CANCER CAN BE MANAGED WITHOUT SURGERY?

SOUTH FLORIDA
GI CANCER SYMPOSIUM

April 11-12, 2025

The Diplomat Beach Resort | Hollywood, Florida

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COLUMBIA

NewYork-Presbyterian

ASCRS
American Society of Colon & Rectal Surgeons

Clinical Practice Guidelines: #RectalCancer (1/3)

Protocolized **MRI** is **preferred staging** method *(ERUS ok for T1/2 or if MRI contraindicated)* 1B

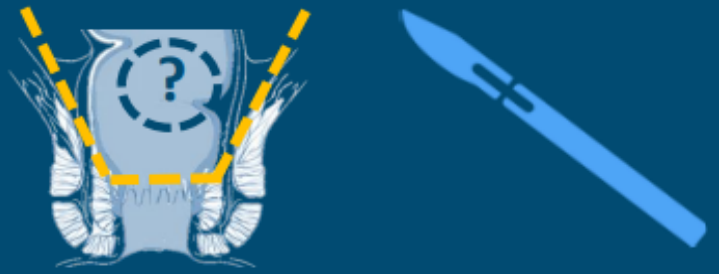
Treatment Plan should be discussed at multidisciplinary tumor (MDT) board (1C)

Neoadjuvant ChemoXRT for T3 or N+ patients based on MDT(1A)

Restaging should be **considered after neoadjuvant** CXRT with locally advanced tumors (1C)

11-15% have altered Tx plan

Patients with complete clinical response should be **offered radical resection.**



"Watch & Wait" can be considered for ***highly select patients*** in **protocolized** setting 1B

You N et al. *Dis Colon Rectum* 2020;63

DISEASES OF THE COLON & RECTUM

Principles of Total Mesorectal Excision for Rectal Cancer

Carlos M. Mery, MD, MPH* and Ronald Bleday, MD†,‡

Semin Colon Rectal Surg 16:117-127 © 2005

Study	Years	N	Technique	Local Recurrence (%)	Survival (%)	Notes
Arbman et al[81]	1984–1986	134	Conventional	14	35‡	In the combined group 65% of patients had TME
	1990–1992	128	Combined	6	23‡	
Bokey et al[84]	1971–1991	322	Conventional	14*		
		274	TME	8*		
Kapiteijn et al[93]	1987–1990	269	Conventional	16†	77†	CRAB trial compared with Dutch TME trial
	1996–1999	661	TME	9†	86†	
Martling et al[77]	1994–1997	686	Conventional	15	85†,§	Stockholm I and II trials compared with Swedish TME project. ~50% patients received XRT
		481	Conventional	14	84†,§	
		381	TME	6	91†,§	

ACS NSQIP® Surgical Risk Calculator — ACS American College of Surgeons

Home | About | FAQ | ACS Website | ACS NSQIP Website

Procedure: 45111 - Proctectomy; partial resection of rectum, transabdominal approach
Risk Factors:

Change Patient Risk Factors

Note: Your Risk has been rounded to one decimal point.

Outcomes	Your Risk	Average Risk	Chance of Outcome
Serious Complication	7.4%	16.5%	Below Average
Any Complication	9.8%	19.0%	Below Average
Pneumonia	0.3%	1.7%	Below Average
Cardiac Complication	0.0%	0.7%	Below Average
Surgical Site Infection	7.0%	11.5%	Below Average
Urinary Tract Infection	2.1%	3.0%	Below Average
Venous Thromboembolism	0.7%	1.6%	Below Average
Renal Failure	0.1%	1.0%	Below Average
Readmission	5.8%	12.2%	Below Average
Return to OR	2.6%	4.3%	Below Average
Death	0.0%	0.6%	Below Average
Discharge to Nursing or Rehab Facility	0.6%	3.7%	Below Average
Sepsis	1.3%	3.9%	Below Average
T Proctectomy Ileus	9.9%	16.4%	Below Average

Predicted Length of Hospital Stay: 4 days

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Procedure: 45110 - Proctectomy; complete, combined abdominoperineal, with colostomy
Risk Factors:

Change Patient Risk Factors

Note: Your Risk has been rounded to one decimal point.

Outcomes	Your Risk	Average Risk	Chance of Outcome
Serious Complication	11.5%	24.5%	Below Average
Any Complication	15.4%	28.4%	Below Average
Pneumonia	0.2%	1.8%	Below Average
Cardiac Complication	0.0%	0.9%	Below Average
Surgical Site Infection	10.8%	17.7%	Below Average
Urinary Tract Infection	2.8%	4.4%	Below Average
Venous Thromboembolism	0.6%	1.6%	Below Average
Renal Failure	0.1%	0.9%	Below Average
Readmission	7.1%	15.2%	Below Average
Return to OR	4.5%	7.6%	Below Average
Death	0.0%	0.5%	Below Average
Discharge to Nursing or Rehab Facility	1.4%	7.7%	Below Average
Sepsis	1.7%	5.3%	Below Average
T Proctectomy Ileus	13.7%	22.5%	Below Average

Predicted Length of Hospital Stay: 5 days

Anterior Resection Syndrome and Quality of Life with Long-term Follow-up After #RectalCancer Resection

Methods:

Leaks excluded

Stoma free

n=311 TME pts 6.5 years post-LAR

2003-2016

No: 21.5%
Minor: 23.5%
Major: 53.4%

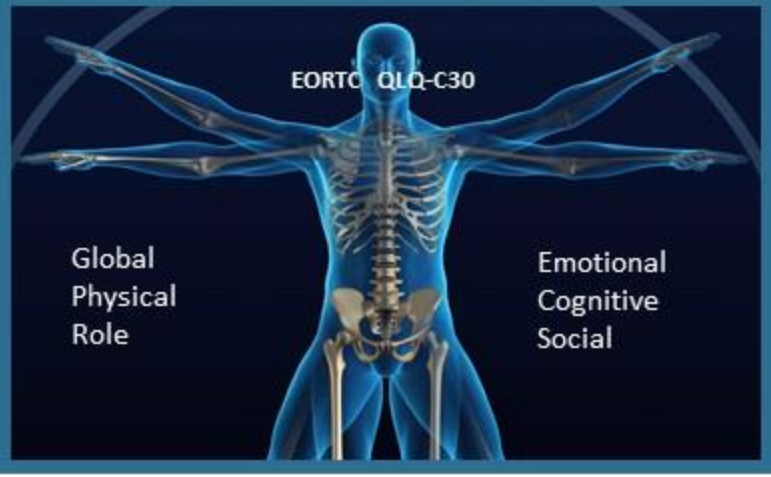
LAR pts vs. general population

Major LARS 53%
Any LARS 77%

XRT

NO CHANGE

Neoadjuvant chemo 19%



Results:

2.4%/yr major LARS

LAR pts vs. general population

better

Global health
Physical function
Role
Emotional
Cognitive

Social

worse

Major LARS vs. no LARS

Physical
Cognitive

Global health
Role
Emotional
Social

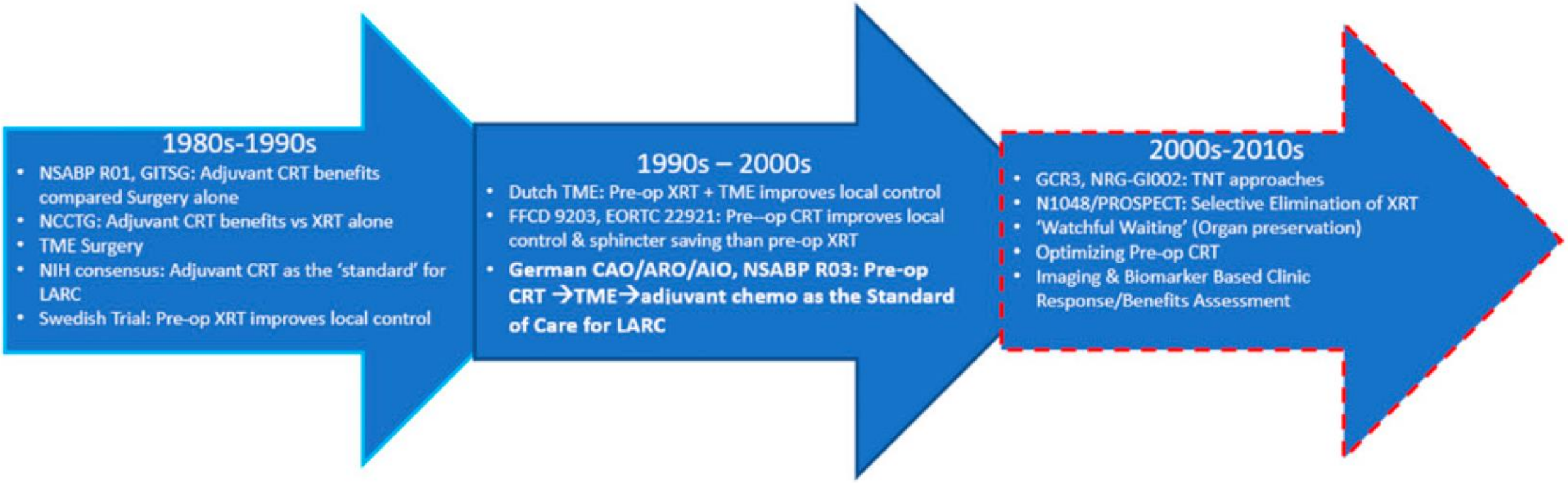
Dilke et al. *Dis Colon Rectum* 2022;65(10):1251-63

DISEASES OF THE COLON & RECTUM
ASCRS

2020 ASCO EDUCATIONAL BOOK | asco.org/edbook

Controversies in Rectal Cancer Treatment and Management

Weijing Sun, MD, FACP[1]; Raed Al-Rajabi, MD[1]; Rodrigo O. Perez, MD, PhD[2]; Saquib Abbasi, MD[1]; Ryan Ash, MD[3]; and Angelita Habr-Gama, MD, PhD[2]

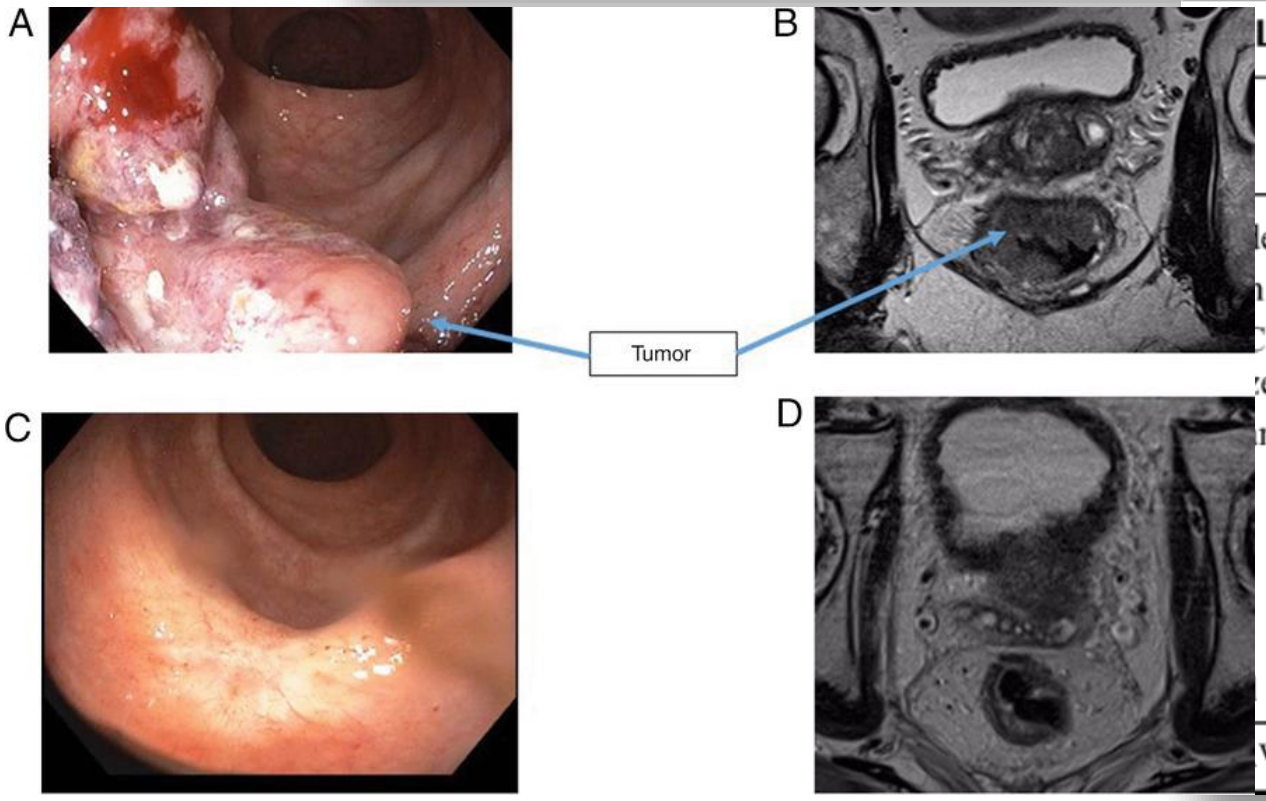


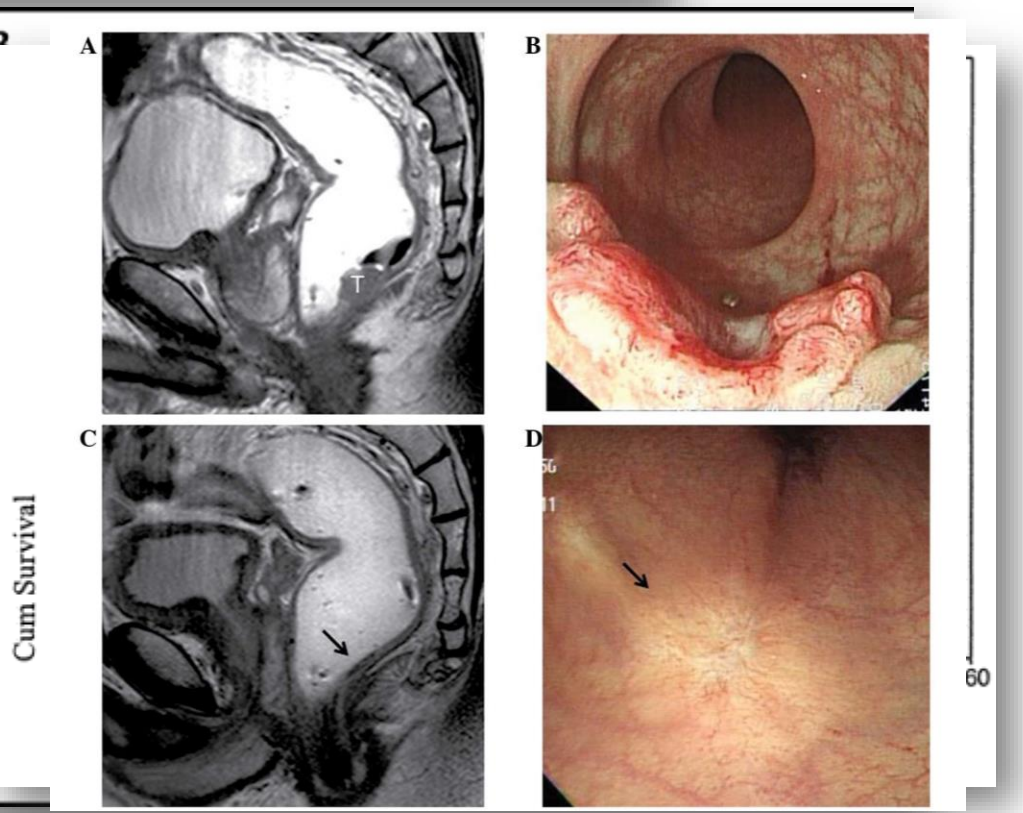
Annals of Surgery • Volume 240, Number 4, October 2004

Operative Versus Nonoperative Treatment for Stage 0 Distal Rectal Cancer Following Chemoradiation Therapy

Long-term Results

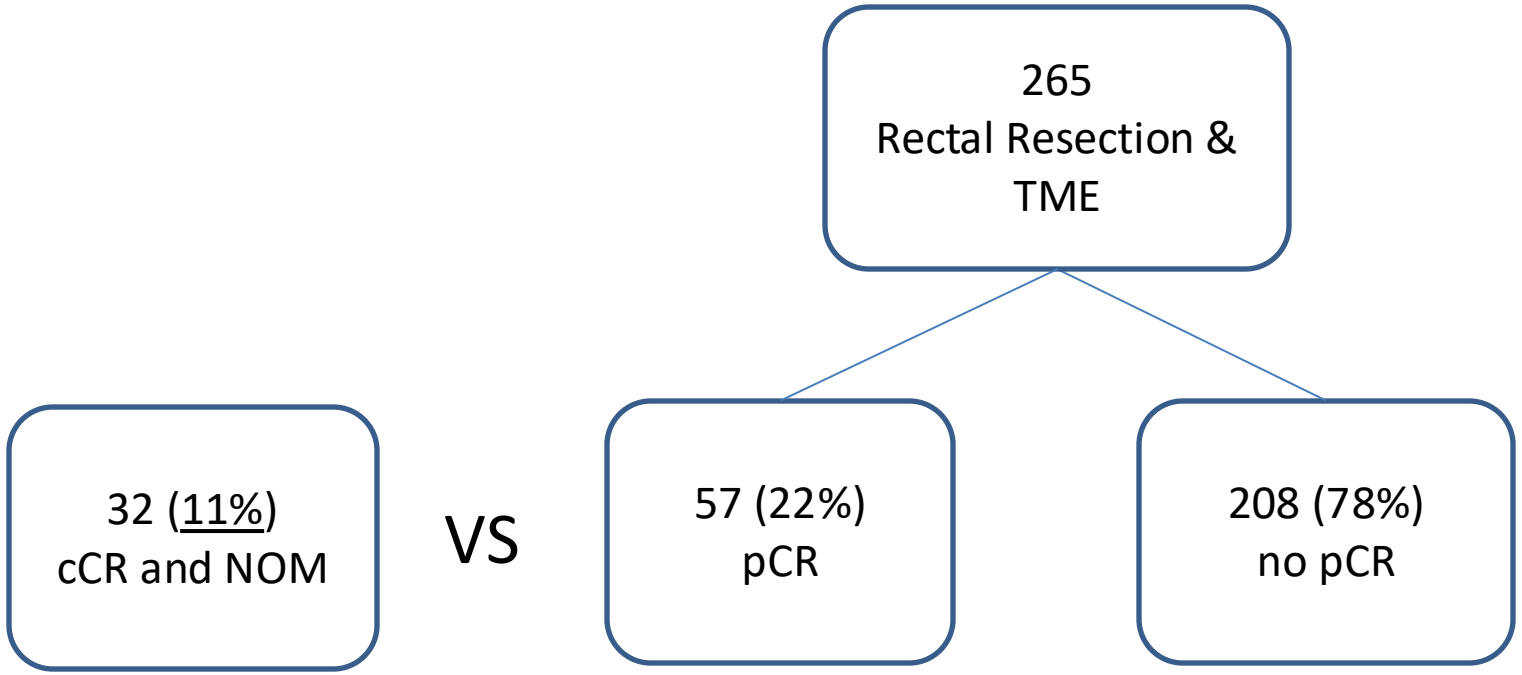
Angelita Habr-Gama, MD, Rodrigo Oliva Perez, MD,* Wladimir Nadalin, MD,†*
*Jorge Sabbaga, MD,† Ulysses Ribeiro Jr, MD,‡ Afonso Henrique Silva e Sousa Jr, MD,**
Fábio Guilherme Campos, MD, Desidério Roberto Kiss, MD,* and Joaquim Gama-Rodrigues, MD‡*





Nonoperative Management of Rectal Cancer With Complete Clinical Response After Neoadjuvant Therapy

James D. Smith, MD, Jeannine A. Ruby, MD,* Karyn A. Goodman, MD,† Leonard B. Saltz, MD,‡ José G. Guillem, MD,* Martin R. Weiser, MD,* Larissa K. Temple, MD,* Garrett M. Nash, MD,* and Philip B. Paty, MD**

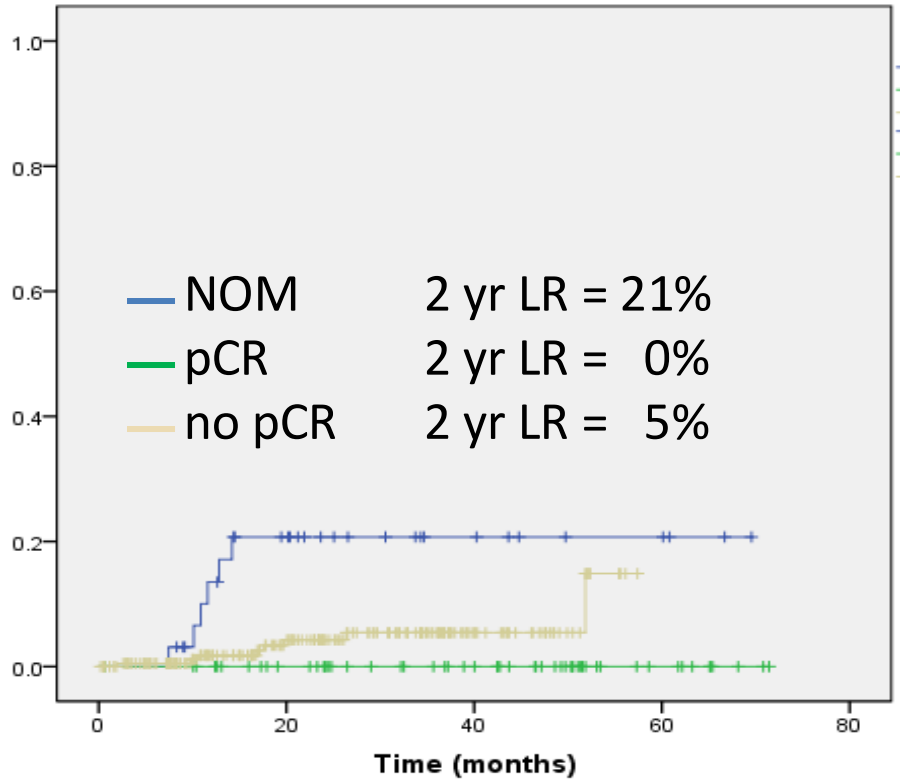


32 pts selectively treated with NOM by agreement of patient and treating physicians

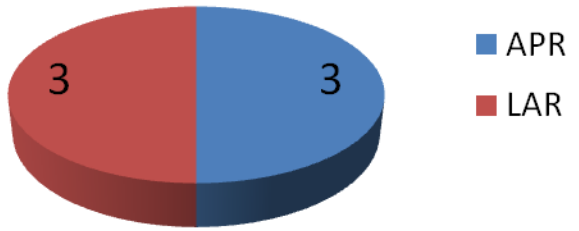
MSKCC Experience: Local Recurrence

No pCR patients developed local recurrence

6 (21%) NOM patients recurred locally at 11 (4-14) months post CRT



All 6 had Salvage Surgery



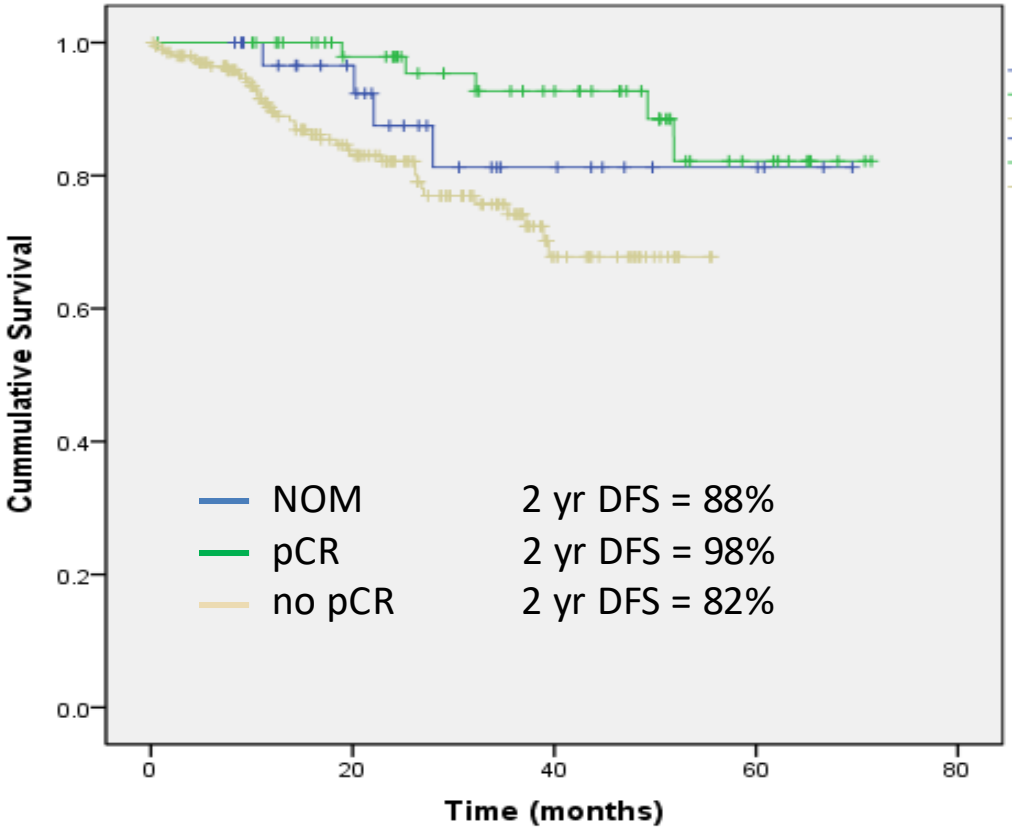
No local recurrences after 17m

MSKCC Experience: Survival

There were 3 distant recurrences in each group

NOM: 1 DOD & 2 AWD

pCR: 2 DOD & 1 NED



Surveillance

Table 3. Proposed Schedule of Follow-Up

of Patients Achieving cCR

examination.

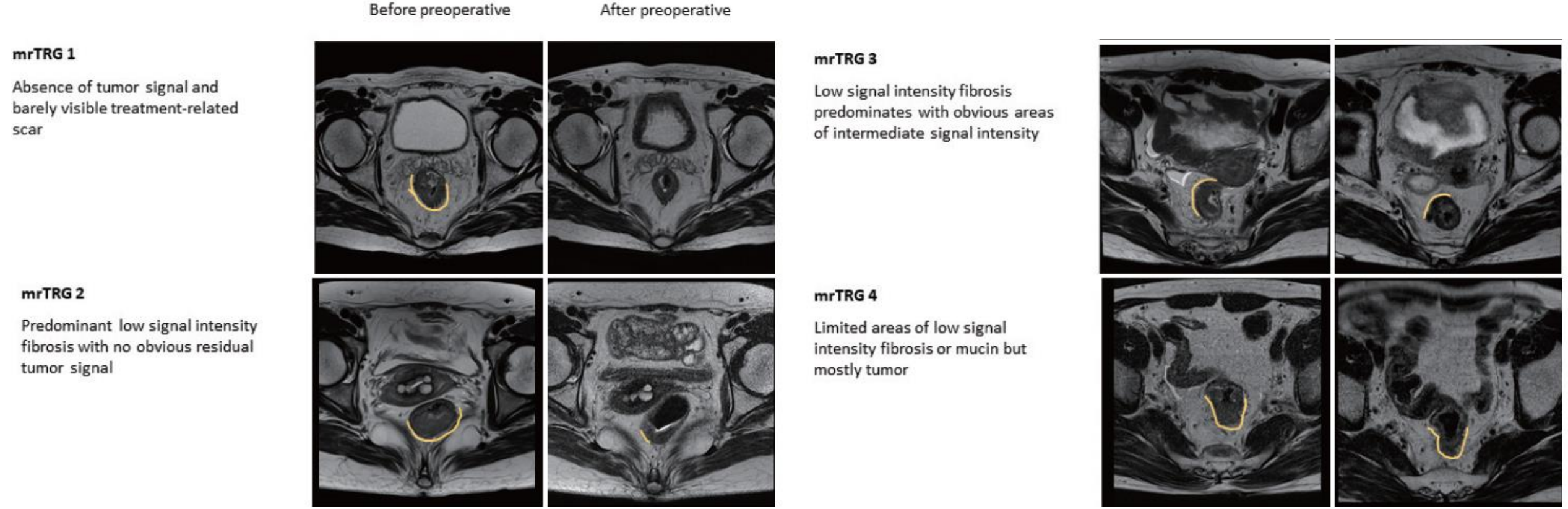
Information from Maas et al. J Clin Oncol. 2011.[46]

TABLE 1 OPRA trial clinical response criteria.

	Clinical Complete Response	Near Complete Clinical Response	Incomplete Clinical Response
DRE	• Normal	• Smooth induration	• Palpable tumor
Endoscopy	• Flat, white scar • Telangiectasias • No ulceration • No nodularity	• Superficial ulceration • Small nodules • Irregular mucosa • Mild erythema of the scar	• Visible tumor
MRI	• Only dark T2 signal • Invisible or very few lymph nodes <5mm in SAD • Absent restricted diffusion	• Mostly dark T2 signal with 1-2 foci of intermediate T2 signal • Partially regressed lymph nodes (≥ 5mm in SAD) • Significant regression of restricted diffusion	• More intermediate than dark T2 signal • Persistently enlarged lymph nodes • Persistent restricted diffusion

DRE, digital rectal exam; MRI, magnetic resonance imaging; SAD, short axis diameter.

Tumor response assessment: MRI



mrTRG categorized tumor regression extent using tumor characteristics and degree of fibrosis, similar to the pathologic tumor regression grade system.

Pooled analysis: 75% accuracy, 95% sensitivity, 31% specificity, 83% positive predictive values, and 47% negative predictive values to detect cCR → MRI more useful in ruling out cCR rather than determining cCR

Surgery 2016;159:688-99

Assessment of Clinical Complete Response After Chemoradiation for Rectal Cancer with Digital Rectal Examination, Endoscopy, and MRI: Selection for Organ-Saving Treatment

Monique Maas, MD, PhD[1], Doenja M. J. Lambregts, MD, PhD[1], Patty J. Nelemans, MD, PhD[2], Luc A. Heijnen, MD[1,3], Milou H. Martens, MD[1,3], Jeroen W. A. Leijtens, MD[4], Meindert Sosef, MD, PhD[5], Karel W. E. Hulsewé, MD, PhD[6], Christiaan Hoff, MD[7], Stephanie O. Breukink, MD, PhD[3], Laurents Stassen, MD, PhD[3], Regina G. H. Beets-Tan, MD, PhD[1], and Geerard L. Beets, MD, PhD[3]

Ann Surg Oncol (2015) 22:3873–3880

Parameter	Clinical assessment	T2W-MRI and DWI	All
Sensitivity	53 %	35 %	71 %
Specificity	97 %	94 %	97 %
PPV	90 %	75 %	NA
NPV	80 %	74 %	NA
AUC	0.88 (0.78–0.99)	0.79 (0.66–0.92)	0.89 (0.79–0.99)
LR positive	17.67	5.83	–
LR negative	0.48	0.69	–
Positive posttest probability	90 %	75 %	98 %
Negative posttest probability	20 %	26 %	15 %

Positive posttest probability is the probability of CR when both tests have positive results (indicate CR) and negative posttest probability is the probability of CR when both tests have negative results (indicate residual tumor). Diagnostic parameters were calculated on the basis of predefined cutoff in confidence levels between 2 and 3

Tumor response assessment: optimal timing

Table 1 Time between completion of neoadjuvant therapy and first reassessment in watch and wait clinical studies

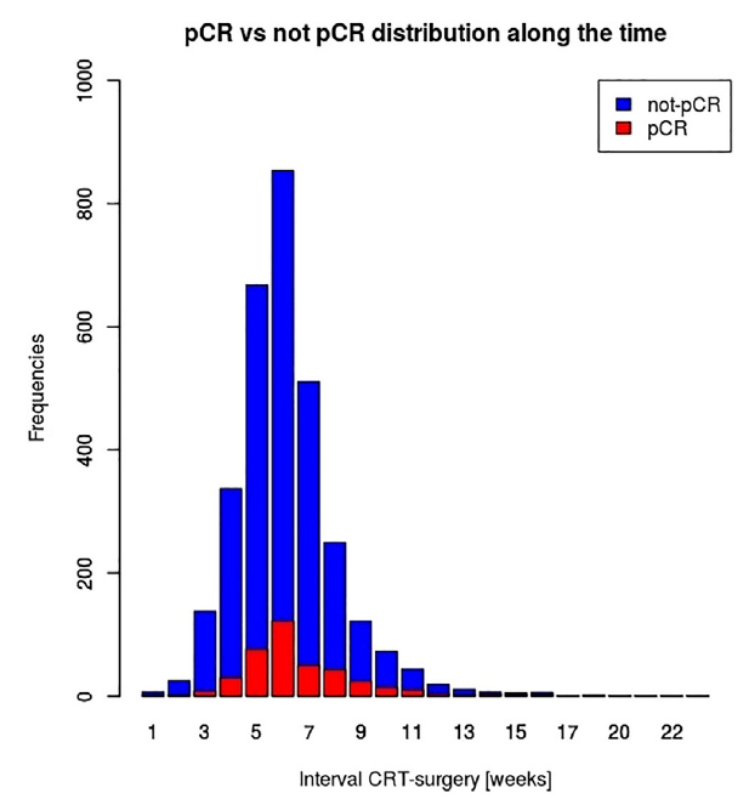
Study	Patients (*n*)	Neoadyuvant therapy		Timing of assessment after CRT
		Radiotherapy schedule	Chemotherapy regimen	
Habr-Gama *et al*[107], 2013	70	54Gy/30	CRT: 5-FU/LV CNCT: 5-FU/LV x3	10 wk
Araujo *et al*[128], 2015	51	45 Gy/25 or 50, 40 Gy/28	CRT: 5-FU or capecitabine	NS
Smith *et al*[129], 2012	32	50,4 Gy/28	CRT: 5-FU or capecitabine	4-10 wk
Dalton *et al*[127], 2012	12	45 Gy/25	CRT: capecitabine	8 wk
Renehan *et al*[99], 2016	259	45 Gy/25	CRT: 5-FU or capecitabine	≥ 8 wk
Appelt *et al*[5], 2015	51	60 Gy/30 to tumor + 50 Gy/30 to LNs	Tegafur-uracil (UFT)	6 wk
Vaccaro *et al*[130], 2016	204	50.4 Gy/28	CRT: 5-FU/LV	8-12 wk
Lai *et al*[131], 2016	267	45 Gy/25 or 54 Gy/30	CRT: 5-FU/LV	8-12 wk
Martens *et al*[98], 2016	141	50.4 Gy/28 or 5 Gy/5	CRT: 5-FU	8-20 wk
Creavin *et al*[132],	362	50-54 Gy/30	CRT: 5-FU	6-8 wk

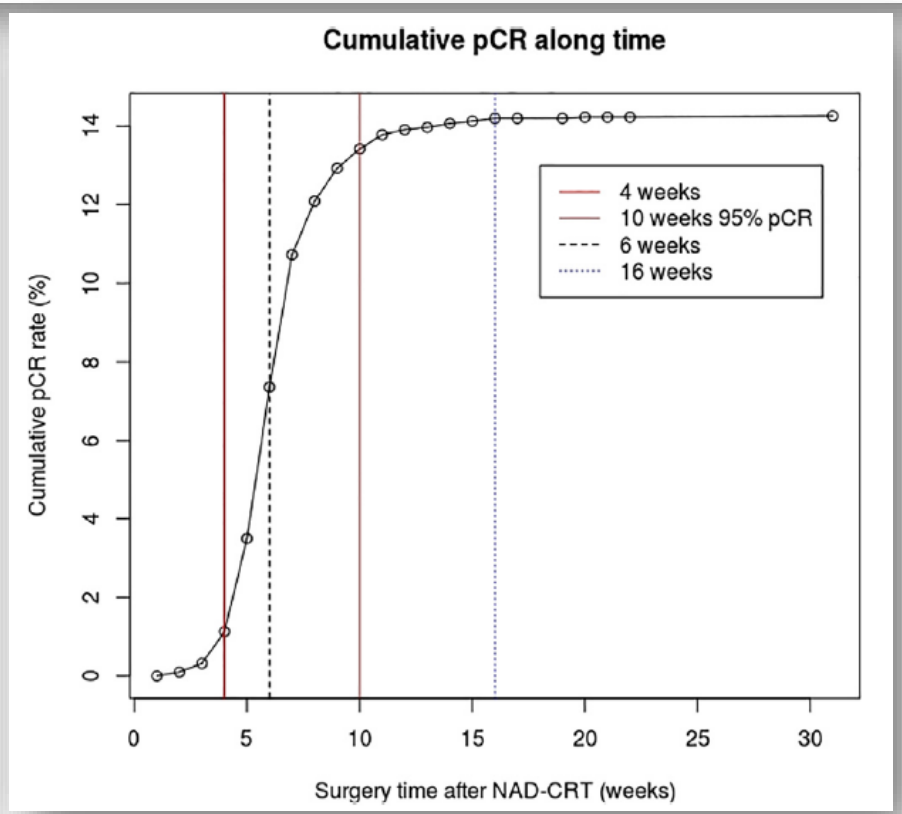
Tumor response assessment: optimal timing

Radiotherapy and Oncology 154 (2021) 154–160

Timing to achieve the highest rate of pCR after preoperative radiochemotherapy in rectal cancer: a pooled analysis of 3085 patients from 7 randomized trials

Maria Antonietta Gambacorta [a,b,1], Carlotta Masciocchi [a,1], Giuditta Chiloiro [a,b,*], Elisa Meldolesi [a], Gabriella Macchia [c], Johan van Soest [d], Fenke Peters [e], Laurence Collette [f], Jean-Pierre Gérard [g], Samuel Ngan [h], C. Claus Rödel [i], Andrea Damiani [a], Andre Dekker [d], Vincenzo Valentini [a,b]





95% of pCR events within 10 weeks after completion of CRT.

Systematic review

BJS 2019; **106**: 1298–1310

Meta-analysis of the effect of extending the interval after long-course chemoradiotherapy before surgery in locally advanced rectal cancer

É. J. Ryan[1,4], D. P. O'Sullivan[1], M. E. Kelly[2,4], A. Z. Syed[1], P. C. Neary[1,3], P. R. O'Connell[2,4], D. O. Kavanagh[1,3], D. C. Winter[2,4] and J. M. O'Riordan[1,3]

Fig. 2

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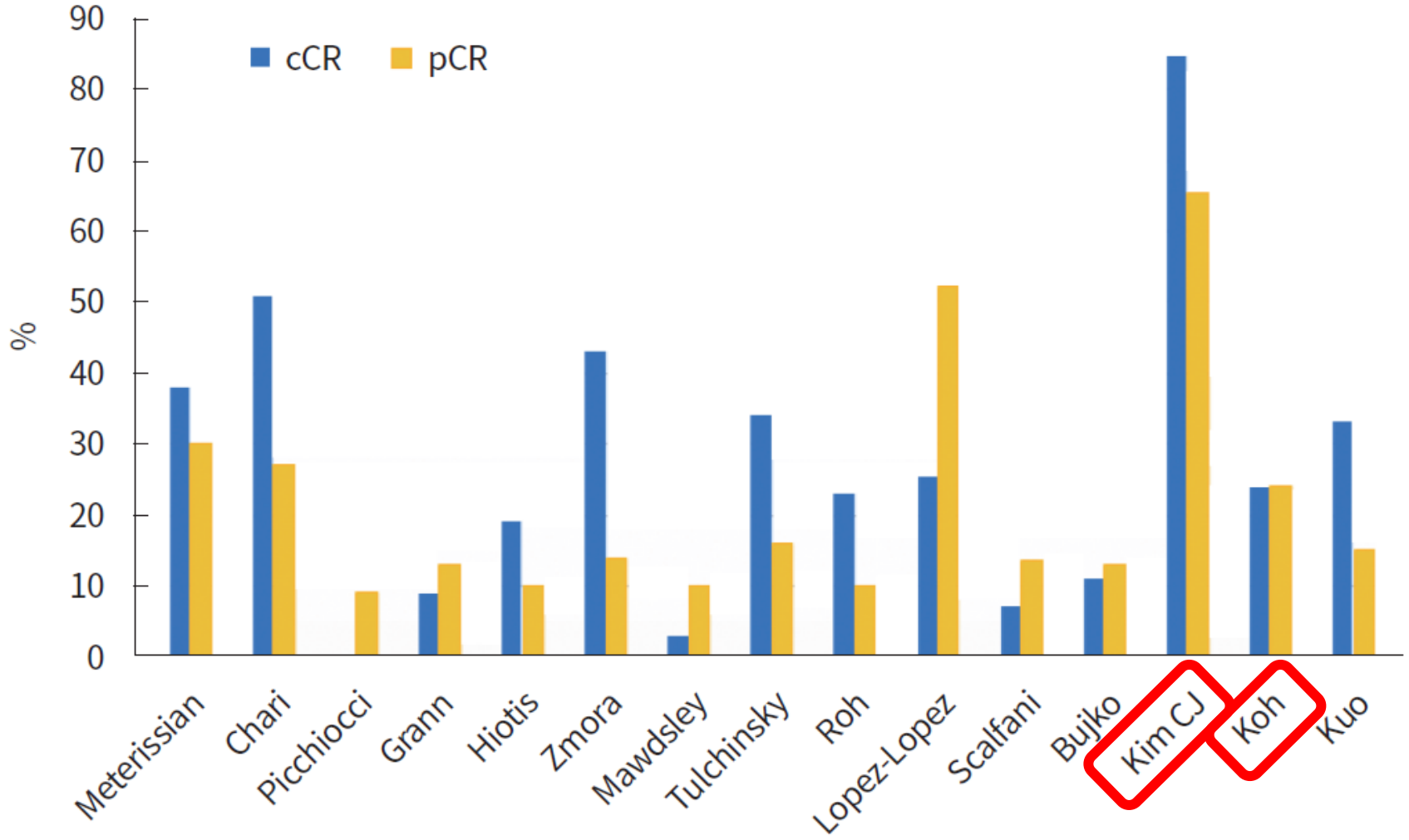
Table 2 Pooled odds ratios for selected secondary outcomes

	Anastomotic leak		SSI/wound complications		Ileus/bowel obstruction		Urological injury		VTE		Major morbidity (Clavien–Dindo grade > IIIa)		Postoperative mortality	
Group	≥8	<8	≥8	<8	≥8	<8	≥8	<8	≥8	<8	≥8	<8	≥8	<8
n	974	977	655	648	605	592	335	315	525	498	777	840	5166	7161
Pooled OR	0·87 (0·60, 1·25)		0·91 (0·53, 1·57)		0·94 (0·61, 1·44)		0·94 (0·28, 3·08)		1·73 (0·57, 5·32)		0·99 (0·72, 1·37)		1·13 (0·75, 1·71)	
Overall *P*	0·44		0·73		0·78		0·91		0·34		0·97		0·56	
I^2 statistic (%)	0		27		0		0		0		0		0	
Heterogeneity *P*	0·89		0·19		0·99		0·66		0·95		0·57		0·66	

100

Tumor response assessment



Reported rate of lymph node metastasis after pCRT in patients with cCR of the primary tumor **up to 16%**

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

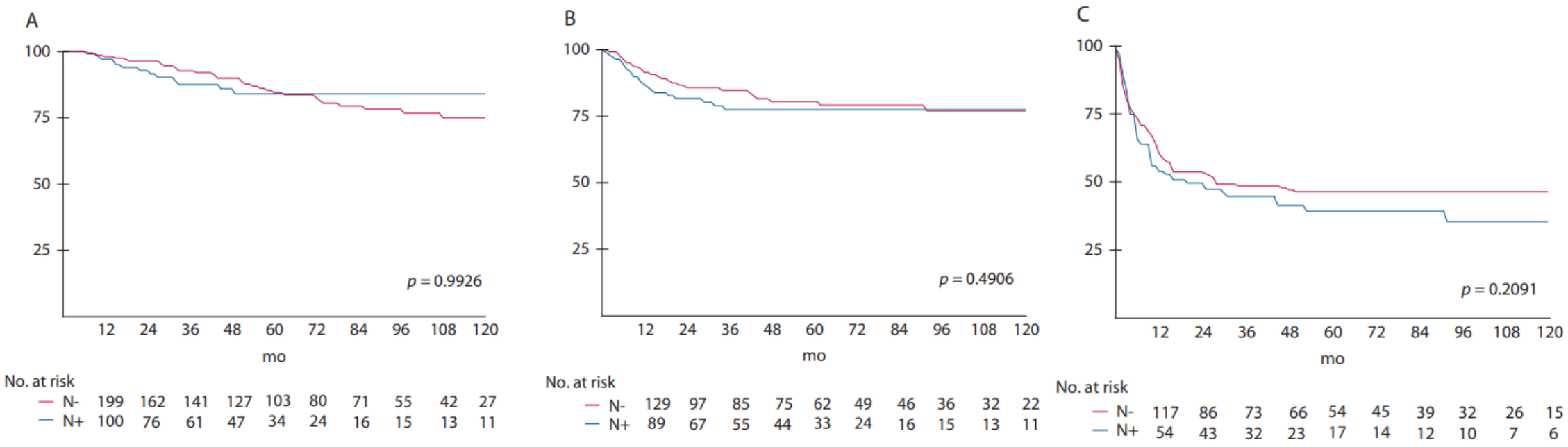
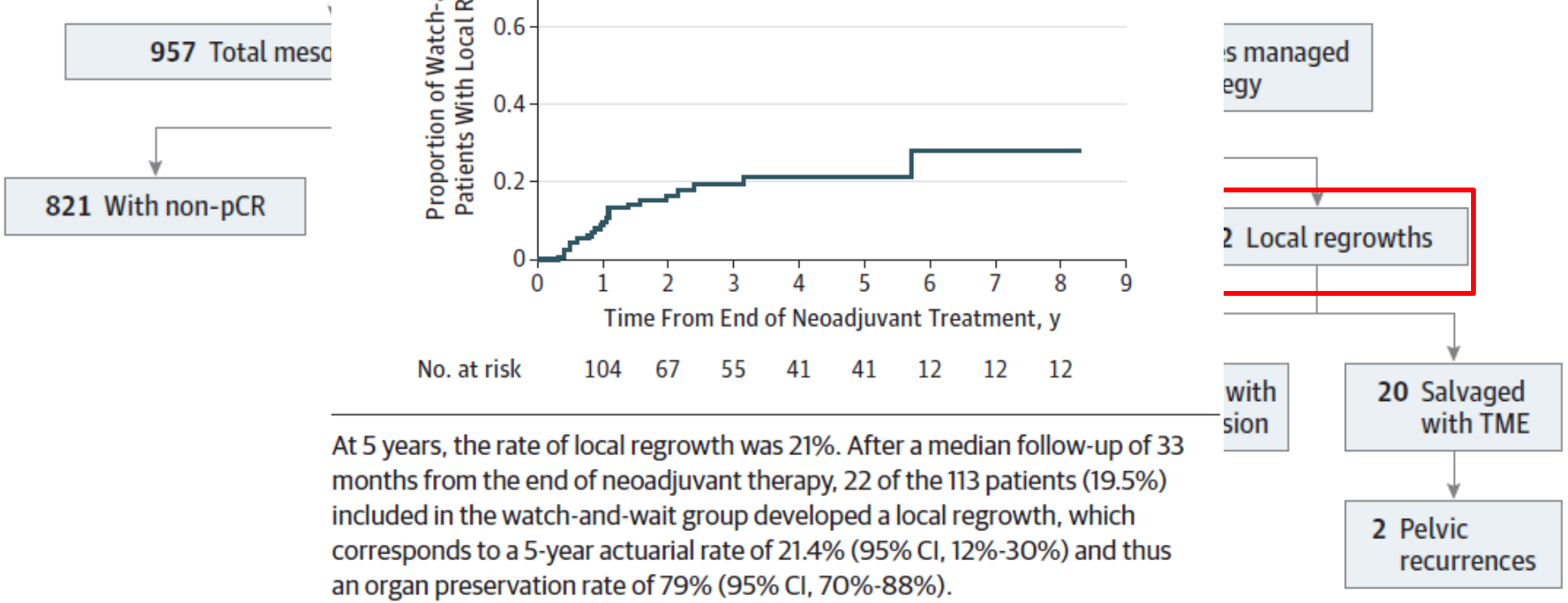


FIGURE 1. There were no significant differences in 5-year (A) overall cancer-specific (83.9% vs 84.5%; $p = 0.99$); (B) distant metastases–free (77.5% vs 80.5%; $p = 0.49$); or (C) surgery-free (organ-preservation) survival (39.7% vs 46.8%; $p = 0.20$) between cN+ and cN0 patients.

MSKCC Updated Experience

Figure 2. Local Regrowth and Rectal Preservation in the Watch-and-Wait Cohort



At 5 years, the rate of local regrowth was 21%. After a median follow-up of 33 months from the end of neoadjuvant therapy, 22 of the 113 patients (19.5%) included in the watch-and-wait group developed a local regrowth, which corresponds to a 5-year actuarial rate of 21.4% (95% CI, 12%-30%) and thus an organ preservation rate of 79% (95% CI, 70%-88%).

Smith JJ JAMA Oncol. 2019 Jan 10:e185896

MSKCC Updated Experience

Patient	Pattern of Regrowth	Salvage Operation	Height From AV, cm	Initial Clinical Staging[a]	Surgical Pathology Staging[a]	CRM	Pelvic Recurrence	Distant Metastases	Disease Status
1	Extraluminal	LAR	6.0	cT3N2	ypT3N0	Negative	No	No	NED
2	Endoluminal	LAR	6.5	cT2N0	ypT2N0	Negative	No	No	NED
3	Endoluminal	LAR	6.0	cT3N1	ypT2N0	Negative	No	No	NED
4	Endoluminal	LAR	4.0	cT2N0	ypT3N0	Negative	No	Yes (lung)	AWD
5	Endoluminal	LAR	6.5	cT3N0	ypT1N0	Negative	No	No	NED
6	Endoluminal	TAE	10.0	cT3N1	NA[b]	NA	No	Yes (liver, SBRT)	DOC
7	Endoluminal	LAR	12.0	cT3N1	ypT3N0	Negative	No	Yes (liver)	DOD
8	Endoluminal	PR[c]	5.0	cT3N0	ypT2N0	Negative	No	Yes (lung/liver)	DOD
9	Endoluminal	APR	7.5	cT2N1	ypT2N0	Negative	No	No	NED
10	Endoluminal	APR	5.5	cT3N1	ypT2N0	Negative	No	No	NED
11	Extraluminal	APR	4.0	cT3N1	ypT3N0	Negative	No	No	NED
12	Extraluminal	LAR	7.0	cT3N1	ypT3N1	Negative	No	No	NED
13	Endoluminal	APR	7.0	cT3N0	ypT2N0	Negative	No	Yes (lung)[d]	NED
14	Endoluminal	APR	8.0	cT3N0	ypT3N1	Negative	Yes	Yes (lung/liver)	DOD
15	Endoluminal	APR	0.5	cT2N0	ypT3N0	Negative	No	Yes (lung)	DOD
16	Endoluminal	LAR	10.0	cT3N1	ypT3N0	Negative	No	No	NED
17	Endoluminal	APR[c]	3.0	cT2N0	ypT2N2	Positive	Yes	Yes (lung)	DOD
18	Endoluminal	APR	5.0	cT3N0	ypT3N0	Negative	No	No	NED
19	Endoluminal	LAR	5.5	cT3N1	ypT2N0	Negative	No	No	NED
20	Endoluminal	TAE	5.0	cT3N0	ypT1Nx	NA	No	No	NED
21	Endoluminal	APR	4.0	cT3N1	ypT2N0	Negative	No	No	NED
22	Endoluminal	APR	5.0	cT3N0	ypT3N0	Negative	No	No	NED

Smith JJ JAMA Oncol. 2019 Jan 10:e185896

Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium*

Lancet 2018; 391: 2537–45

- Distant metastasis was diagnosed in 71 (8%) of 880 patients
- 5-year OS rate was 85% (95% confidence interval [CI], 80.9% to 87.7%)
- 5-year DFS rate was 94% (95% CI, 91% to 96%).
- 2-year cumulative incidence of local regrowth was 25.2%.
- Patients who sustained a cCR for 3 years had a less than 2% risk of developing systemic recurrence thereafter during the median long-term follow-up of 55.2 months

Oncologic outcomes: WW vs radical surgery

Study	Year	Number		FU duration (mo)		Local recurrence (%)		Distant metastasis (%)		Cancer-related death (%)	
		WW	RS	WW	RS	WW	RS	WW	RS	WW	RS
Habr-Gama et al. [18]	2004	71	22	57.3	48	2.8	0	4.2	13.6	0	9.1
Maas et al. [22]	2011	21	20	25	35	4.7	0	0	5	-	-
Smith et al. [24]	2012	32	57	28	43	18.8	0	9.3	5.3	3.2	0
Ayloor Seshadri et al. [16]	2013	23	10	72	72	30.4	0	13	20	-	-
Lee et al. [20]	2015	8	28	41	41	25	3.5	0	10.7	0	10.7
Li et al. [21]	2015	147	51	58	58						
Araujo et al. [15]	2015	42	69	47.7	46.7	19	4.7			62[a)]	82.7[a)]
Renehan et al. [23]	2016	129	109	33	33	-	-	-	-	96[b)]	87[b)]
Lai et al. [19]	2016	18	26	49	42	11.1	0	-	-	-	-
Yeom et al. [26]	2019	15	129	60	60	40	12.4	26.7	3.8	-	-
Beard et al. [17]	2020	53	42	-	-					95[b)]	100[b)]
Wang et al. [25]	2020	59	179	60	60	11.9	0.5	10.2	9.5	-	-

a)Disease-free survival; b)Overall survival.

Precision and Future Medicine 2022;6(2):91-104

Lancet Gastroenterol Hepatol
2017; 2: 501–13

A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation: a systematic review and meta-analysis

Fahima Dossa, Tyler R Chesney, Sergio A Acuna, Nancy N Baxter

A Disease-free survival for patients treated by surgery with pCR *vs* W&W

	W&W		Surgery with pCR		Weight (%)	HR IV, random (95% CI)
	Events	Total	Events	Total		
Araujo et al (2015)[39]	23	42	22	69	77·4	0·47 (0·26–0·84)
Smith et al (2012)[58]	N/A	32	N/A	57	10·1	0·29 (0·06–1·43)
Maas et al (2011)[50]	1	21	4	20	5·5	1·39 (0·15–12·41)
Smith et al (2015)[60]	2	18	2	30	6·9	0·42 (0·06–2·98)
Total		**113**		**176**	**100·0**	**0·47 (0·28–0·78)**

Heterogeneity: τ^2=0·00; χ^2=1·31, DF=3 (p=0·73); I^2=0%

Test for overall effect: Z=2·89, p=0·004

B Overall survival for patients treated by surgery with pCR *vs* W&W

	W&W		Surgery with pCR		Weight (%)	HR IV, random (95% CI)
	Events	Total	Events	Total		
Araujo et al (2015)[39]	8	42	10	69	59·6	0·62 (0·24–1·58)
Smith et al (2012)[58]	N/A	32	N/A	57	23·5	0·61 (0·14–2·74)
Maas et al (2011)[50]	0	21	2	20	6·9	5·50 (0·34–88·03)
Gossedge et al (2012)[43]	1	15	1	13	6·8	0·23 (0·01–3·81)
Smith et al (2015)[60]	0	18	1	30	3·3	6·89 (0·12–395·98)
Total		**128**		**189**	**100·0**	**0·73 (0·35–1·51)**

Heterogeneity: τ^2=0·01; χ^2=4·03, DF=4 (p=0·40); I^2=1%

Test for overall effect: Z=0·85, p=0·40

Lancet Gastroenterol Hepatol
2017; 2: 501–13

A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation: a systematic review and meta-analysis

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- Local regrowth for watch-and-wait 15.7%
- **No significant difference** in overall survival (HR 0.73)
- Disease-free survival was **better** in the surgery group (HR 0.47)
- **No significant difference** in terms of non-regrowth recurrence (RR 0.58), cancer-specific mortality (RR 0·58), or overall survival (HR 3.91)
- Only three (1.9%) of 157 patients with data available could not have salvage therapy after local regrowth because of the extent of local or systemic disease

Surgical salvage

Study	Year	Patients	Regrowth (%)	Luminal regrowth only (%)	Salvage surgery (%)	Type of salvage surgery (%)	Disease-free survival (%)
Maas et al. [22]	2011	21	4.7	4.7	100	Transanal endoscopic microsurgery	89[a]
Habr-Gama et al. [28]	2014	71	31	92.8	89.2	APR (44), AR (28), local excision (28)	88[b]
Renehan et al. [23]	2016	129	34	93.2	84	APR (49), AR (20), other resection (7)	96 (3-year OS)
Kong et al. [42]	2017	370	28.4	-	83.8	-	
van der Valk et al. [33]	2018	1,000	25.2	97	86	TME (78), local excision (22.3)[c]	85[d]
Chadi et al. [39][e]	2018	602	28	-	89	-	87[d]
Dattani et al. [44][e]	2018	692	22.1	-	88	Sphincter preservation (45.3)	93.5[b]
On et al. [45][e]	2019	248	12.1	80	83.3	APR (40), LAR(20), other resection (8), local excision (28)	-
Smith et al. [31]	2019	113	19.4	86	100	APR (41), LAR (41), local excision (9), other resection (9)	75[d]
Park et al. [14]	2019	42	28.2	77.8	88.9	APR (25), sphincter saving resection (37.5), local excision (25)	-
van der Sande et al. [46]	2020	385	23.1	73	94.4	APR (27.4), LAR (40.5), local excision (30.9), induction CTx+CRT+APR (1.2)	90.3[a]
Beard et al. [17]	2020	53	11.3	-	66.7	APR (50), LAR (50)	95[f]
Wang et al. [40]	2021	94	14.9	92.9	85.7	APR (41.7)	88[g]

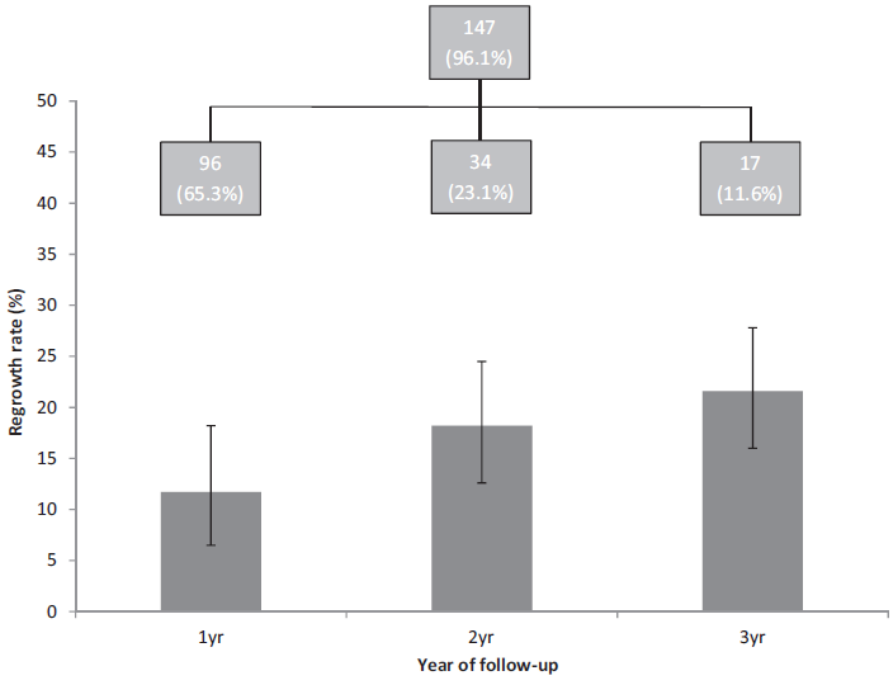
Precision and Future Medicine 2022;6(2):91-104

Oncological and Survival Outcomes in Watch and Wait Patients With a Clinical Complete Response After Neoadjuvant Chemoradiotherapy for Rectal Cancer

A Systematic Review and Pooled Analysis

Mit Dattani, FRCS, Richard J. Heald, FRCS,* Ghaleb Goussous, FRCS,† Jack Broadhurst, FRCS,‡ Guilherme P. São Julião, MD,§ Angelita Habr-Gama, MD,§ Rodrigo Oliva Perez, PhD,§ and Brendan J. Moran, FRCSI‡*

- cCR 22.4%
- 153 (22.1%) local regrowths. 96% in the first 3 years of surveillance.
- 3-year cumulative risk of local regrowth 21.6%
- Salvage surgery 88% of patients, 121 (93%) R0 resection.
- 57 metastases (8.2%), 35 (60%) without synchronous regrowths.
- 3-year distant disease 6.8%
- 3-year OS 93.5%



Ann Surg. 2018 May 9

Surgical salvage

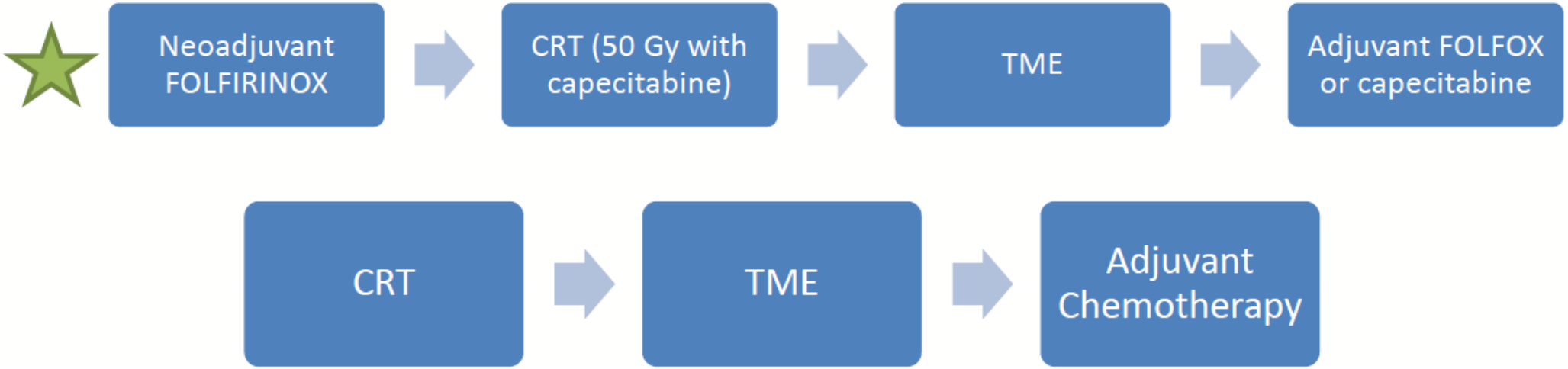
Table 2 Tumor regrowth and salvage surgery in watch and wait clinical studies

Study	Patients (*n*)	Regrowth	Salvage surgery	Distant metastasis	Survival
Habr-Gama *et al*[161]	90	27 (31%)	93%	13 (14%)	3 yr (88%)
Renehan *et al*[99]	129	44 (34%)	84%	5 (4%)	3 yr (96%)
Kong *et al*[162]	370	105 (28.4%)	83.80%		
van der Valk *et al*[102]	1000	250 (25%)	86%	80 (8%)	5 yr (85%)
Chadi *et al*[165]	602	168 (28%)	89%	60 (10%)	5 yr (87%)
Dattani *et al*[100]	692	149 (21.6%)	88%	56 (8.2%)	3 yr (93.5%)
On *et al*[164]	248	37 (15.3%)	68.40%	8 (21%)	92.30%
Nasir *et al*[160]	78	23 (29.5%)	100%	1 (4.35%)	3 yr (96%)

Evidence in favor of TNT

- STELLAR

- **PRODIGE 23**
  - Eligibility: cT3 or cT4 M0 rectal adenocarcinoma



  - 3-year disease-free survival: 76% TNT and 69% standard (p=0.03)

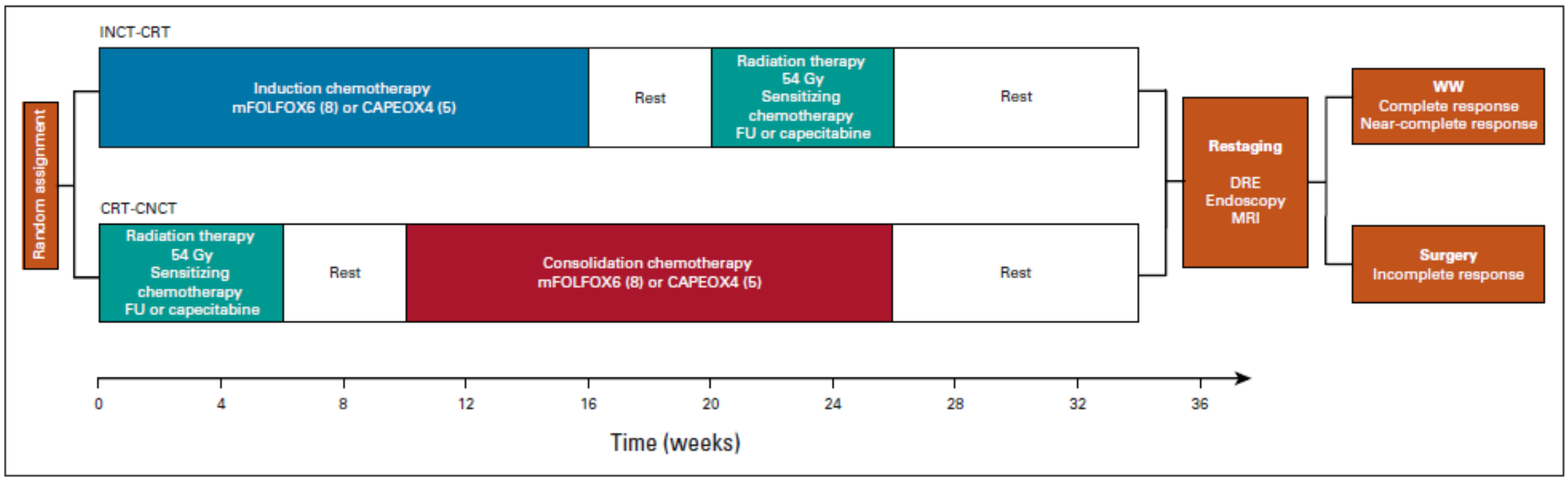
Probability of OS at 5 years improved with TNT (80.5% vs 75.1%)

J Clin Oncol 40:2546-2556. © 2022 by American Society of Clinical Oncology

original reports

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]; Hannah M. Thompson, MD[1]; Floris S. Verheij, MD[1]; Dana M. Omer, MD[1]; Meghan Lee, BS[1]; Richard F. Dunne, MD[4]; Jorge Marcet, MD[5]; Peter Cataldo, MD[6]; Blase Polite, MD[7]; Daniel O. Herzig, MD[8]; David Liska, MD[9]; Samuel Oommen, MD[10]; Charles M. Friel, MD[11]; Charles Ternent, MD[12]; Andrew L. Coveler, MD[13]; Steven Hunt, MD[14]; Anita Gregory, MD[15]; Madhulika G. Varma, MD[16]; Brian L. Bello, MD[17]; Joseph C. Carmichael, MD[18]; John Krauss, MD[19]; Ana Gleisner, MD[20]; Philip B. Paty, MD[1]; Martin R. Weiser, MD[1]; Garrett M. Nash, MD[1]; Emmanouil Pappou, MD[1]; José G. Guillem, MD[21]; Larissa Temple, MD[22]; Iris H. Wei, MD[1]; Maria Widmar, MD[1]; Sabrina Lin, MS[2]; Neil H. Segal, MD, PhD[23]; Andrea Cercek, MD[23]; Rona Yaeger, MD[23]; J. Joshua Smith, MD, PhD[1]; Karyn A. Goodman, MD[24]; Abraham J. Wu, MD[25]; and Leonard B. Saltz, MD[23]



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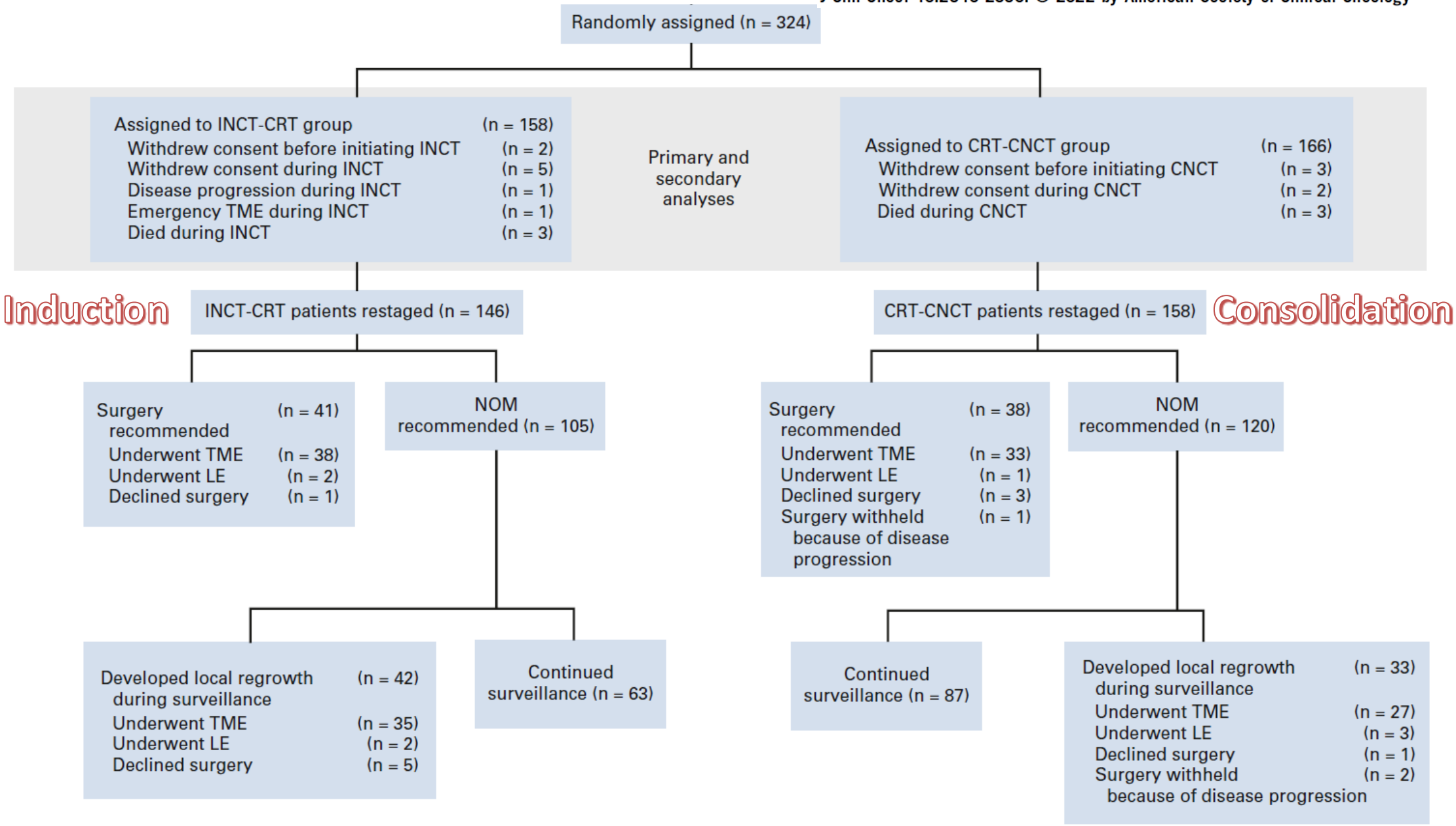


J Clin Oncol 40:2546-2556. © 2022 by American Society of Clinical Oncology

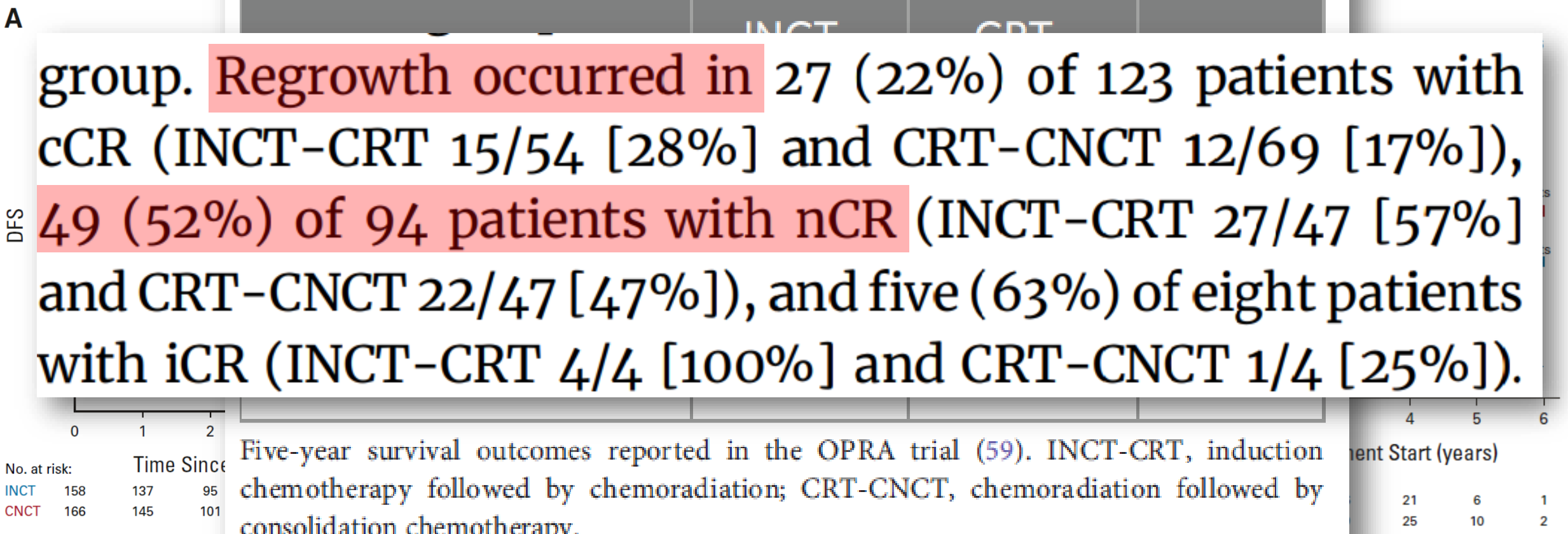
NOM group

Front. Oncol. 14:1477510.

TABLE 2 Five-year survival outcomes from the OPRA trial.

group. Regrowth occurred in 27 (22%) of 123 patients with cCR (INCT-CRT 15/54 [28%] and CRT-CNCT 12/69 [17%]), 49 (52%) of 94 patients with nCR (INCT-CRT 27/47 [57%] and CRT-CNCT 22/47 [47%]), and five (63%) of eight patients with iCR (INCT-CRT 4/4 [100%] and CRT-CNCT 1/4 [25%]).

Five-year survival outcomes reported in the OPRA trial (59). INCT-CRT, induction chemotherapy followed by chemoradiation; CRT-CNCT, chemoradiation followed by consolidation chemotherapy.



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

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

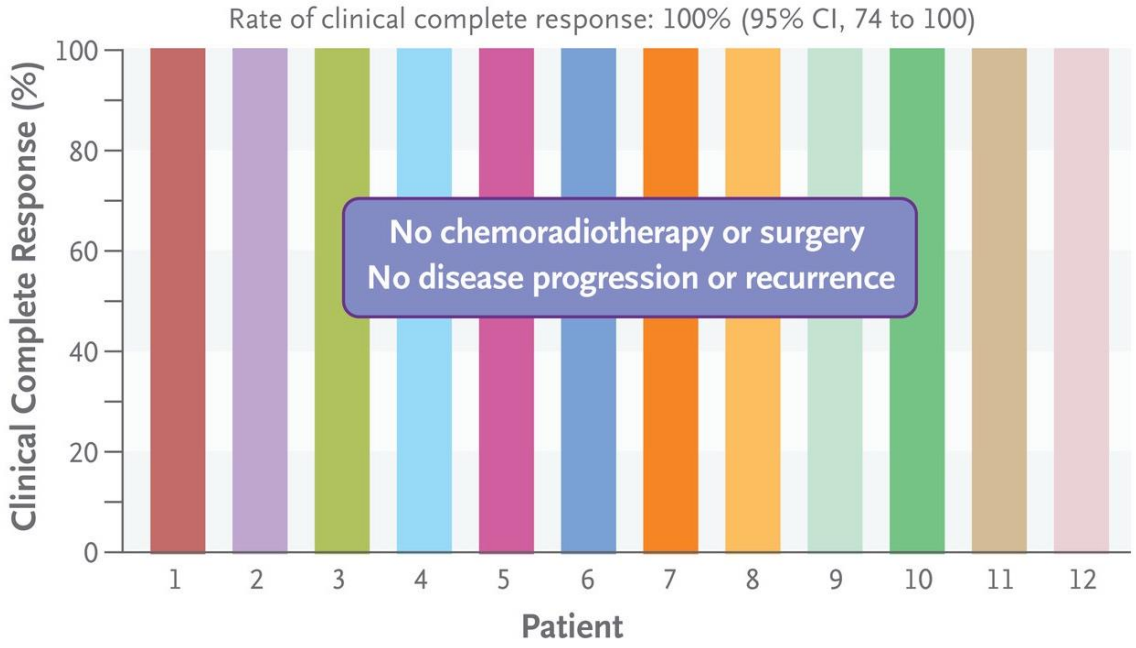
Cercek A et al. DOI: 10.1056/NEJMoa2201445

RESULTS

Efficacy: 12 of 16 enrolled patients have already completed 6 months of dostarlimab. All 12 had a clinical complete response, with no evidence of tumor on any diagnostic test. During a median follow-up of 12 months, no patient received chemoradiotherapy or underwent surgery, and none had disease progression or recurrence.

Safety: No adverse events of grade 3 or higher have occurred. The most common adverse events of grade 1 or 2 included rash or dermatitis, pruritus, fatigue, and nausea.

Overall Response to Dostarlimab in 12 Patients

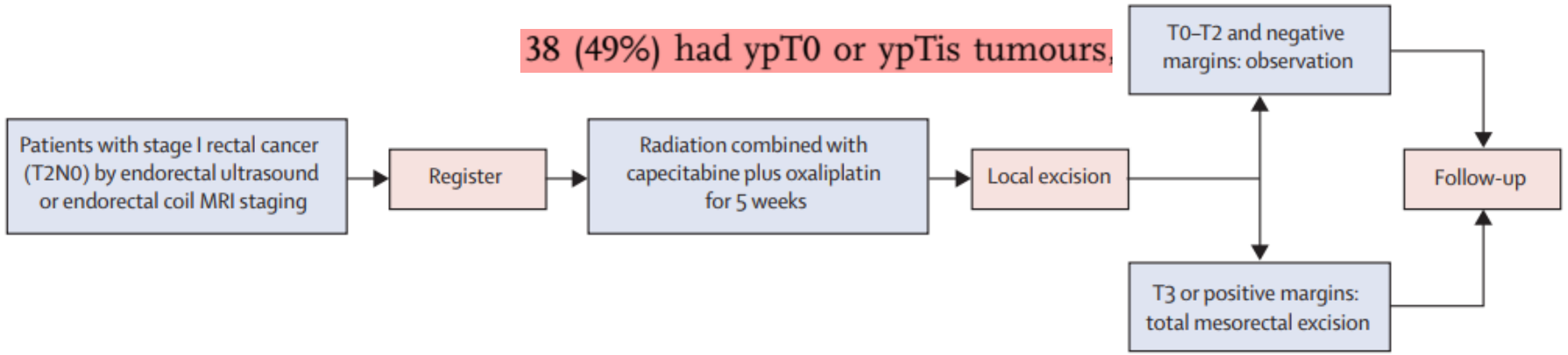


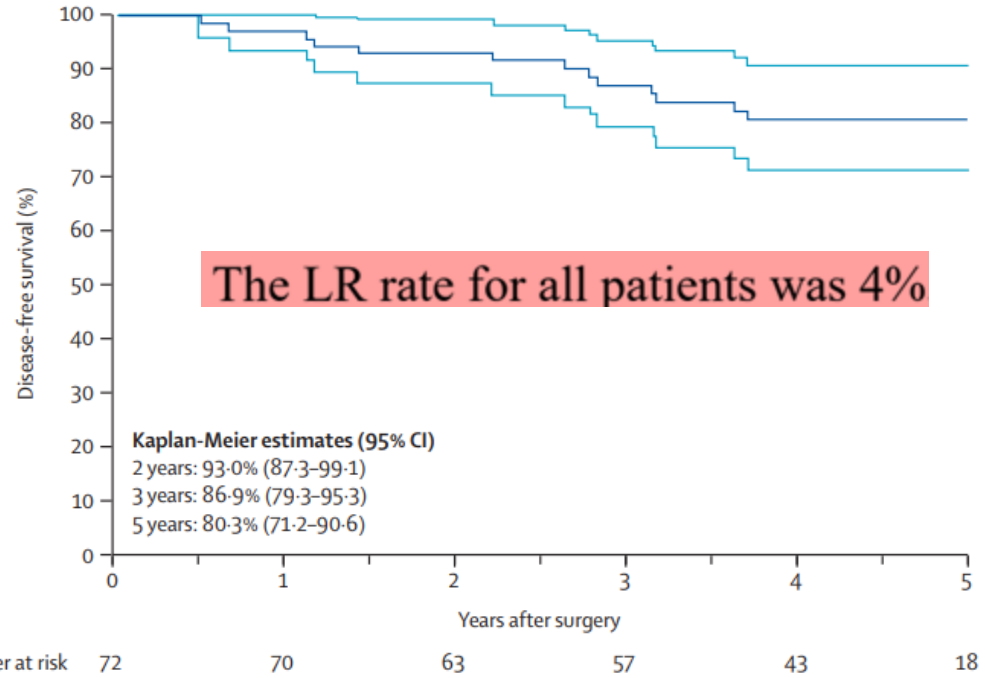
www.thelancet.com/oncology Vol 16 November 2015

Local excision

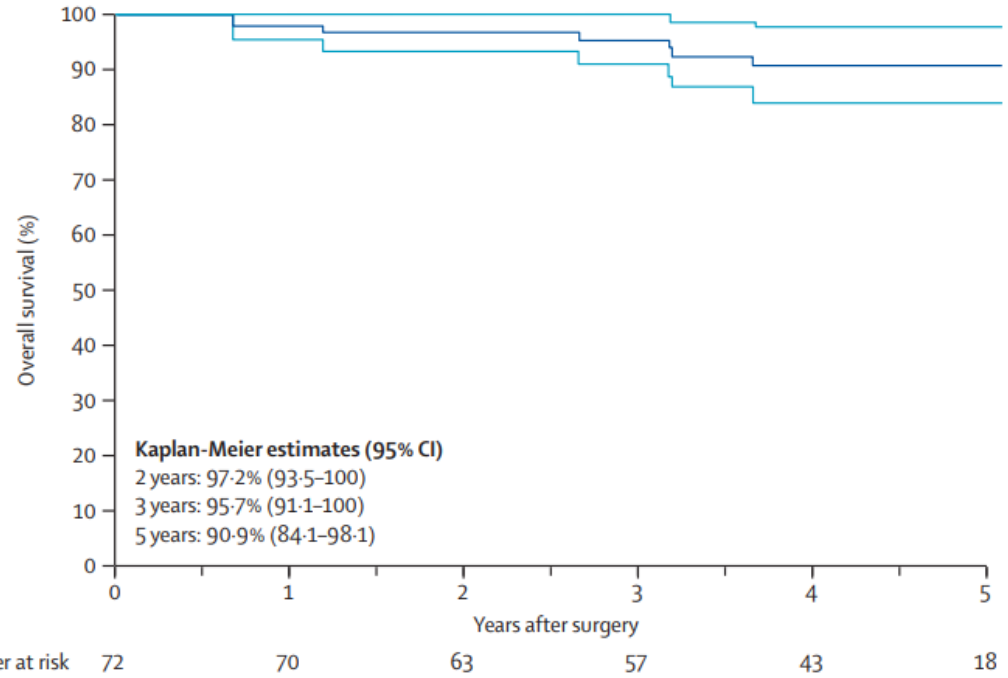
ACOSOG Z6041

38 (49%) had ypT0 or ypTis tumours



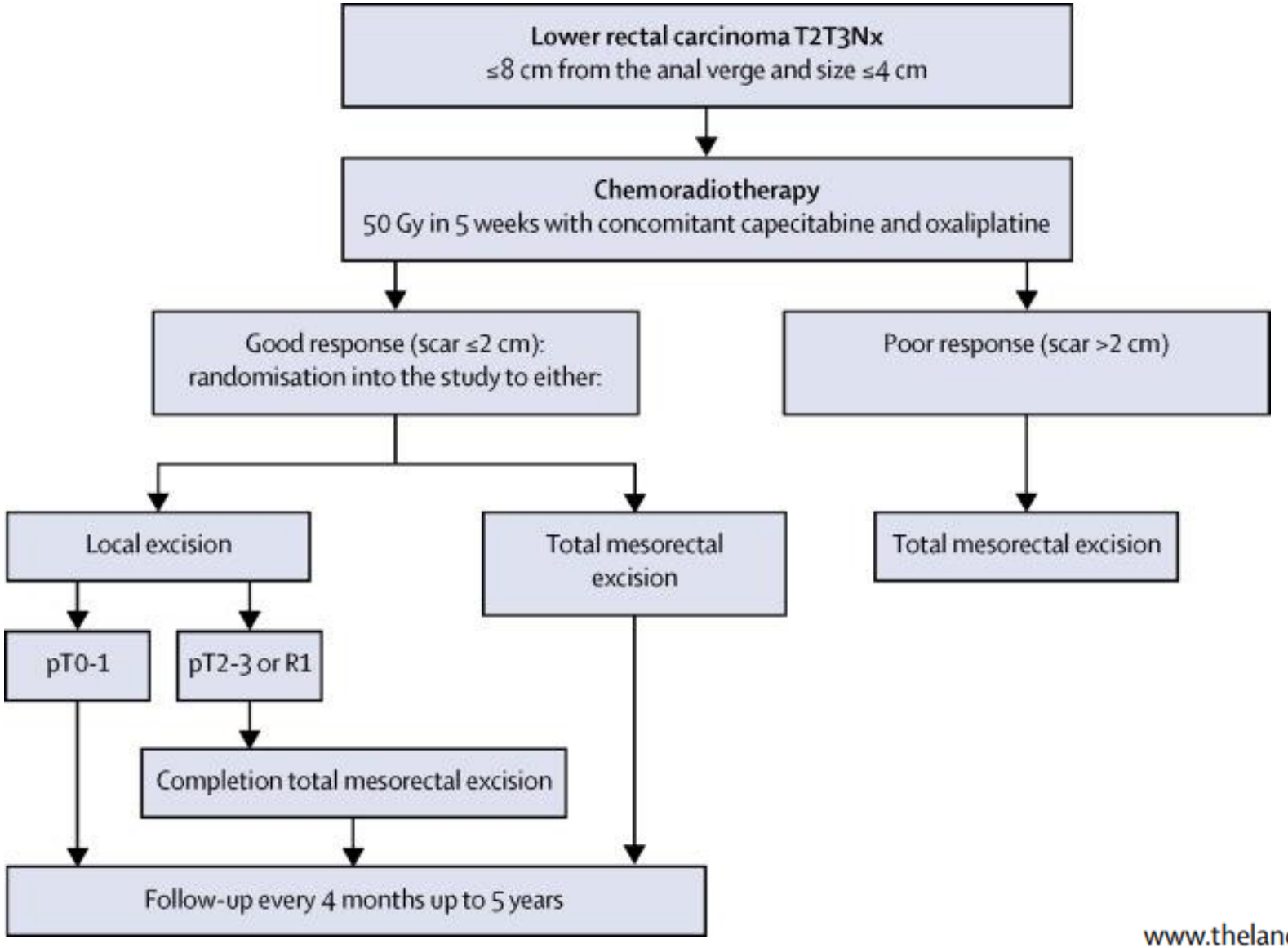


The LR rate for all patients was 4%



Local excision

GRECCAR2



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Local excision

GRECCAR2

	Local excision		Total		Local excision plus completion total mesorectal excision (n=28)*	p value†
	LE	TME	All			
Tumour response	(n=74)	(n=68)	(n=142)*			
ypT0	26	31	57	40%		
ypT1	15	14	29	21%		
ypT2	27	17	44	31%		
ypT3	6	6	12	8%		
Nodal response	(n=27)	(n=62)	(n=89)			
ypN0	23	59	82	92%	7/28 (25%)	0·0178
ypN1	4	3	7	8%	3/22 (14%)	0·0056
Sexual dysfunction			7/53 (13%)		10/58 (17%) 11/27 (41%)	0·0113

	ypN1	% ypN1
ypT0	0/30	0
ypT1	0/13	0
ypT2	3/36	8%
ypT3	4/10	40%

2% in cN0

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Local excision

GRECCAR2

- ✓ The oncologic safety of the strategy is suggested by the similar LR and survival at 2 years between the 2 groups
- ✓ Globally, LE was not superior to TME due to a high rate of completion TME that increased morbidity and after-effects
- ✓ A better patient selection avoiding un necessary completion TME for ypT2/cN0 will give advantage of LE

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Local excision

GRECCAR2
5y outcomes

Pathologic stage	10 LR	Surgery performed
ypT0	2	LE, LE

	LE N=74	TME N=71	All patients N=145
Lung	13	9	22
Liver	5	12	17
Lymphatic	5	3	8
Peritoneum	1	1	2
Bone	3	0	3
Brain	0	4	4
Number of patients	13	13	26
Number of sites of metastasis	28	29	57

	Stage	Initial Surgery	Recurrence	Salvage TME	Resection
	T2	LE	Local	LAR	R0
	T2	TME	Local	APR	R2
	T2	LE	Local + lung	No	-
	T3	LE	Local + méta	No	-
10	T3	W&W	Local + méta	No	-

	Local recurrence	Metastases
ypT0-1	6%	11%
ypT2-3	5%	26%

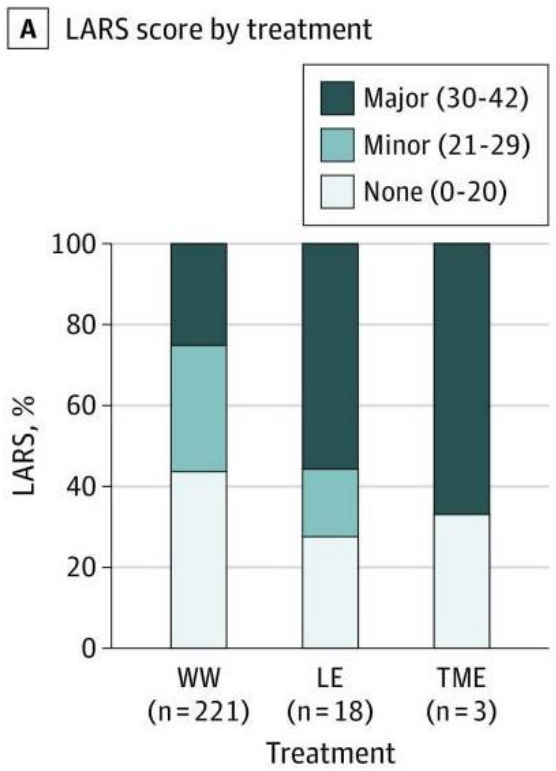
www.thelancet.com/gastrohep Vol 5 May 2020

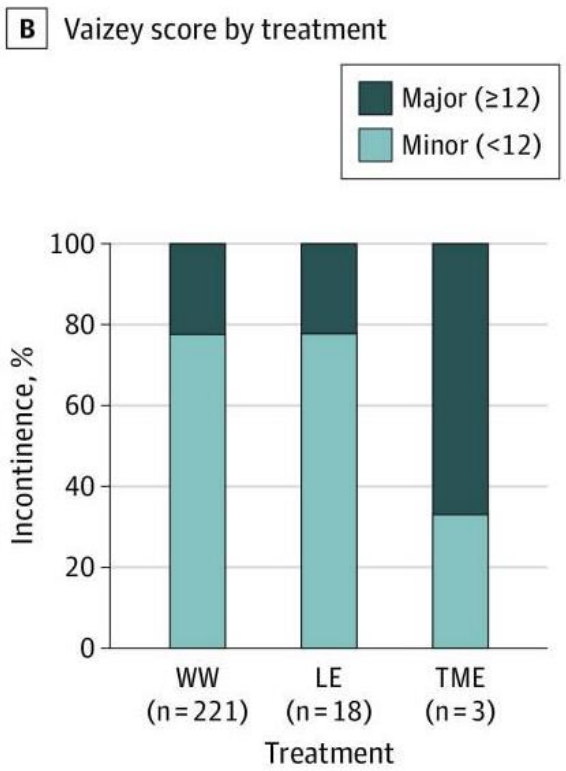
JAMA Surgery | Original Investigation

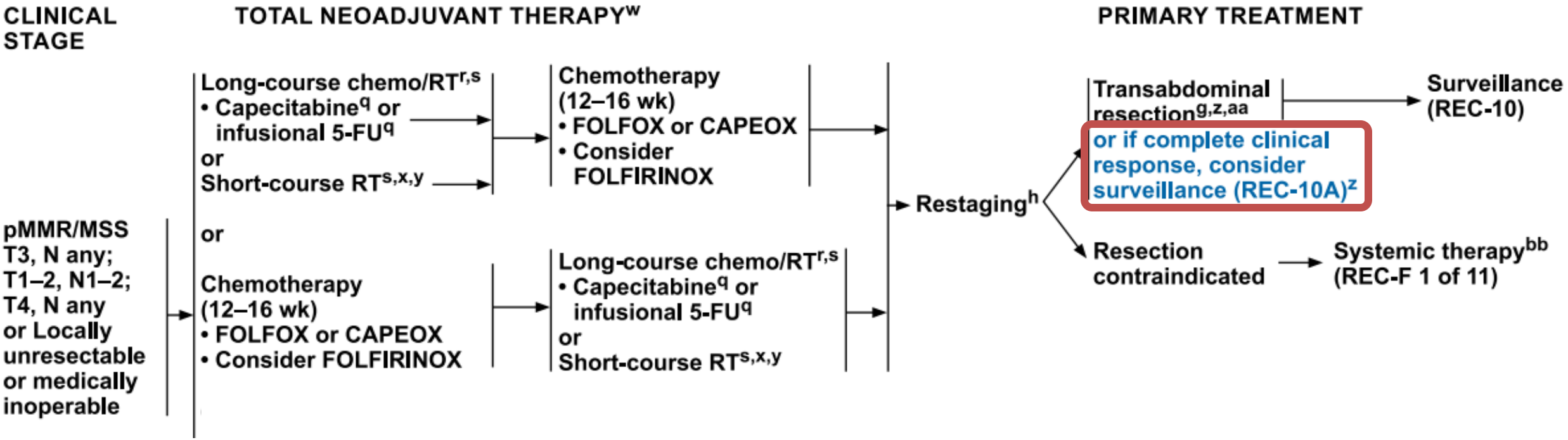
JAMA Surgery May 2023 Volume 158, Number 5

Long-term Quality of Life and Functional Outcome of Patients With Rectal Cancer Following a Watch-and-Wait Approach

Petra A. Custers, MD; Marit E. van der Sande, MD; Brechtje A. Grotenhuis, MD, PhD; Femke P. Peters, MD, PhD; Sander M. J. van Kuijk, PhD; Geerard L. Beets, MD, PhD; Stéphanie O. Breukink, MD, PhD; for the Dutch Watch-and-Wait Consortium







[z] In those patients who achieve a complete clinical response with no evidence of residual disease on digital rectal examination (DRE), rectal MRI, and direct endoscopic evaluation, a "watch and wait," nonoperative (chemotherapy and/or RT) management approach may be considered in centers with experienced multidisciplinary teams. The degree to which risk of local and/or distant failure may be increased relative to standard surgical resection has not yet been adequately characterized. Decisions for nonoperative management (NOM) should involve a careful discussion with the patient of their risk tolerance. See Principles of Nonoperative Management (REC-H).

Conclusions

- WW has become an acceptable alternative to TME after neo-adjuvant CRT in a subgroup of LARC patients with cCR
- Surveillance modalities are still less than perfect in assessing cCR
- 1/3 of WW patients will experience local regrowth, most within 2 years; the majority of these can be salvaged
- A small percentage of patients will recur systemically
- Local excision may be an option in high-risk surgical patients

Future directions:

- Identification of genetic and molecular markers
- Triplet (mFOLFIRINOX) therapy? -> Janus Trial
- WW for Stage 1? -> STAR-TREC trial