Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

La conservazione d'organo negli stadi precoci favorevoli

Elisa Palazzari
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Associazione Italiana Radioterapia e Oncologia clinica

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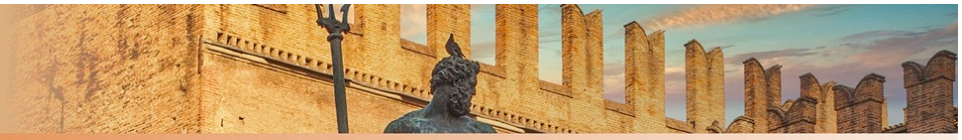


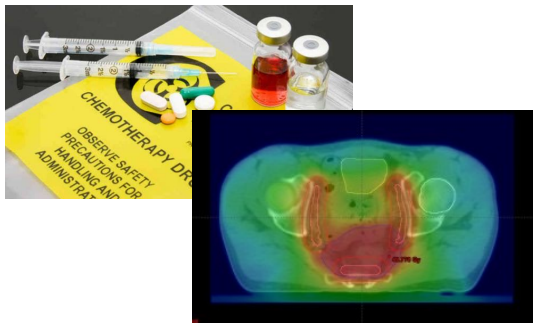
DICHIARAZIONE

Relatore: ELISA PALAZZARI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Consulenza ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazione ad Advisory Board NIENTE DA DICHIARARE
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario NIENTE DA DICHIARARE
- Altro

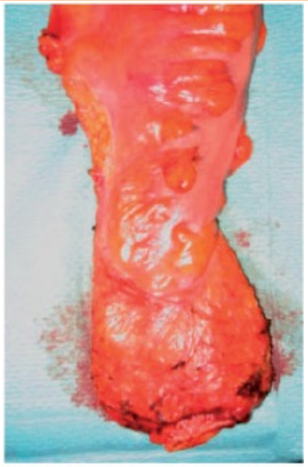
Rectal Cancer Care: an evolving paradigm



Neoadjuvant
(Chemo)-Radiotherapy

Adjuvant
Chemotherapy

SURGERY



Total
Mesorectal
Excision

↑ LOCAL CONTROL

↓ ACUTE - LATE TOXICITY
PERMANENT STOMA

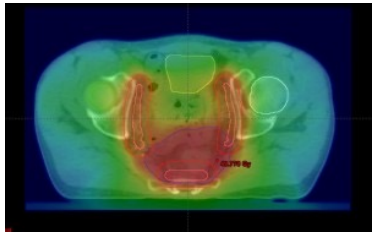
= DFS
OS

European J of cancer 2014;50:1.el-1-34
Clin Colorectal Cancer 2017;17: 1-12

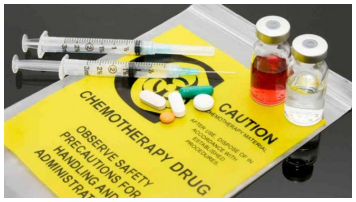
Rectal Cancer Care: an evolving paradigm

Risk stratification

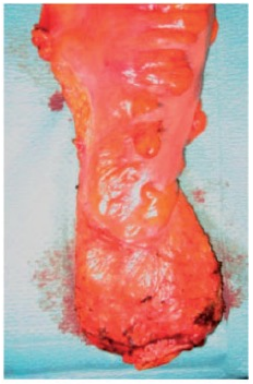
Response Prediction



Radiotherapy



Chemotherapy



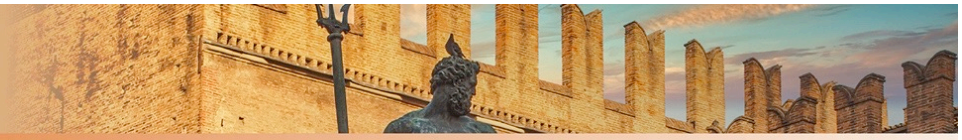
Surgery

→ Oncological outcome

→ Adverse effects

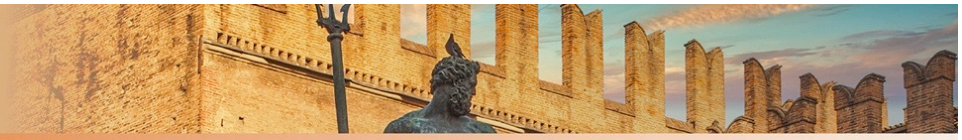
→ QoL

European J of cancer 2014;50:1.el-1-34
Clin Colorectal Cancer 2017;17: 1-12



Organ Preservation in early – low risk rectal cancer

- Rationale
- The available evidence
- How to optimize treatment



Organ Preservation in early – low risk rectal cancer

- **Rationale**
- The available evidence
- How to optimize treatment

Organ Preservation in early – low risk rectal cancer

Preoperative (Chemo)radiation

pCR 8-27%
in LARC

pCR ≥ 30%
if smaller tumors

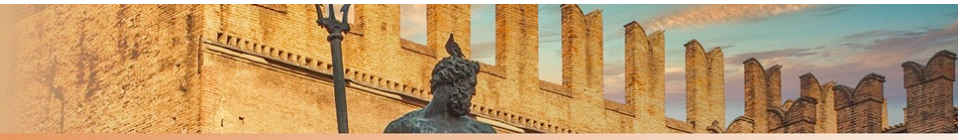
pCR ⇨ better oncological outcomes

TME

- 25-30% surgical morbidity
- 20% long term stoma
- 12% urinary disfunction
- sexual disfunction

QoL in elderly and young patients

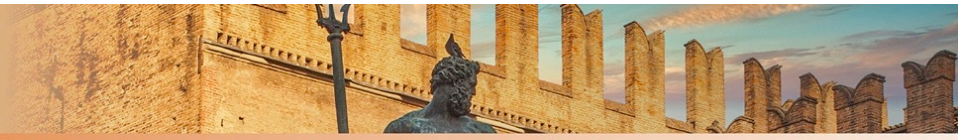
Lancet Oncol 2010;240:711-718
BJS 2022;109: 695-703



Organ Preservation in early – low risk rectal cancer

?

Integrated treatment including organ preservation:
- Is safe in terms of oncological outcomes?
- Could be beneficial for patients?

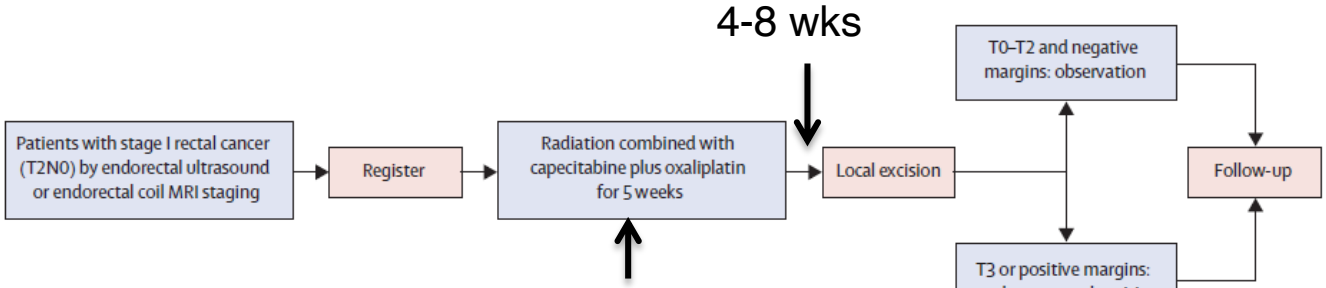


Organ Preservation in early – low risk rectal cancer

- Rationale
- **The available evidence**
- How to optimize treatment

Organ preservation for clinical T2N0 distal rectal cancer using neoadjuvant chemoradiotherapy and local excision (ACOSOG Z6041): results of an open-label, single-arm, multi-institutional, phase 2 trial

Julio Garcia-Aguilar, Lindsay A Renfro, Oliver S Chow, Qian Shi, Xiomara W Carrero, Patricio B Lynn, Charles R Thomas Jr, Emily Chan, Peter A Cataldo, Jorge E Marcet, David S Medich, Craig S Johnson, Samuel C Oommen, Bruce G Wolff, Alessio Pigazzi, Shane M McNevin, Roger K Pons, Ronald Bleday



45 Gy/25 fz
sequential boost 9 Gy/5 fz

Amended after 53 pts
45 Gy/25 fz
Sequential boost 5.4 Gy/3 fz

Primary endpoint: 3yrs DFS

Secondary: R0 resection rate, pCR, morbidity,
QoL (FISI, FACT-C)

Lancet Oncol 2015;16:1537-46

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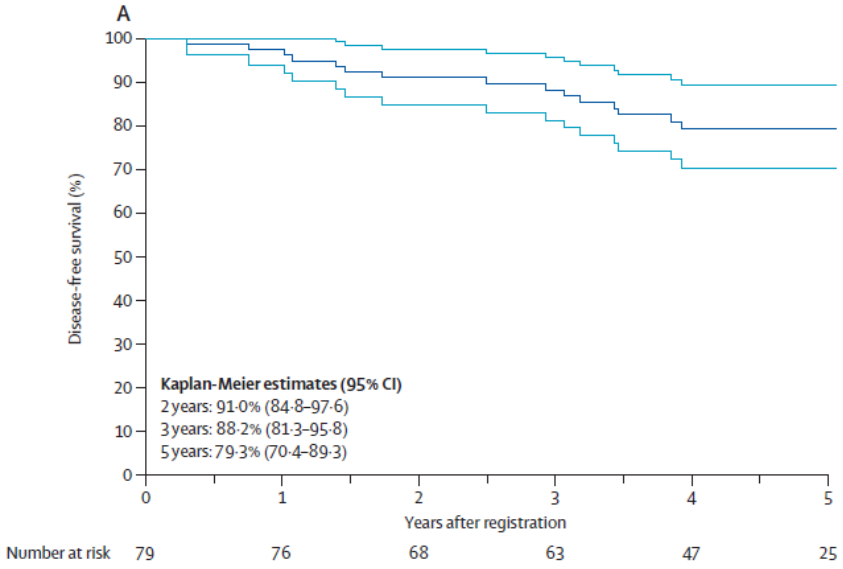
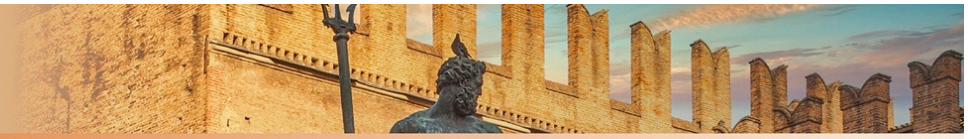


79 pts included / 77 had surgery
38(49%) ypT0/is
11(14%) ypT1
24(31%) ypT2
3 (4%) ypT3 ⟶ 2 APR no residual cancer, NED 47 months
1 refused surgery, pelvic recurrence

4% local recurrence

Median follow up 54 months **91% organ preservation**

Lancet Oncol 2015;16:1537-46



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	Original dose group (n=53)			Revised dose group (n=26)			Overall (n=79)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Gastrointestinal	4 (8%)	18 (34%)	0	18 (69%)	5 (19%)	0	22 (28%)	23 (29%)	0
Pain	2 (4%)	9 (17%)	1 (2%)	16 (62%)	2 (8%)	0	18 (23%)	11 (14%)	1 (1%)
Dermatological	2 (4%)	7 (13%)	0	7 (27%)	2 (8%)	0	9 (11%)	9 (11%)	0
Haematological	1 (2%)	4 (8%)	1 (2%)	11 (42%)	6 (23%)	1 (4%)	12 (15%)	10 (13%)	2 (3%)

	Original dose (n=52)			Revised dose (n=25)			Overall (n=77)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Haematological	0	1 (2%)	0	0	1 (4%)	0	0	2 (3%)	0
Haemorrhage	1 (2%)	1 (2%)	1 (2%)	4 (16%)	1 (4%)	0	5 (6%)	2 (3%)	1 (1%)
Infectious or febrile neutropenia	3 (6%)	1 (2%)	0	1 (4%)	1 (4%)	0	4 (5%)	2 (3%)	0
Pain	13 (25%)	5 (10%)	0	7 (28%)	1 (4%)	0	20 (26%)	6 (8%)	0
Gastrointestinal	8 (15%)	3 (6%)	0	11 (44%)	0	0	19 (25%)	3 (4%)	0
Neurological	0	0	0	2 (8%)	1 (4%)	0	2 (3%)	1 (1%)	0

Table 4: **Surgery-related adverse events for all eligible patients who underwent surgery**

QoL evaluation

Fecal Incontinence Severity Index (FISI)
Functional Assessment of Cancer Therapy-Colorectal (FACT-C)

Baseline 71 pts
12 months 62 pts

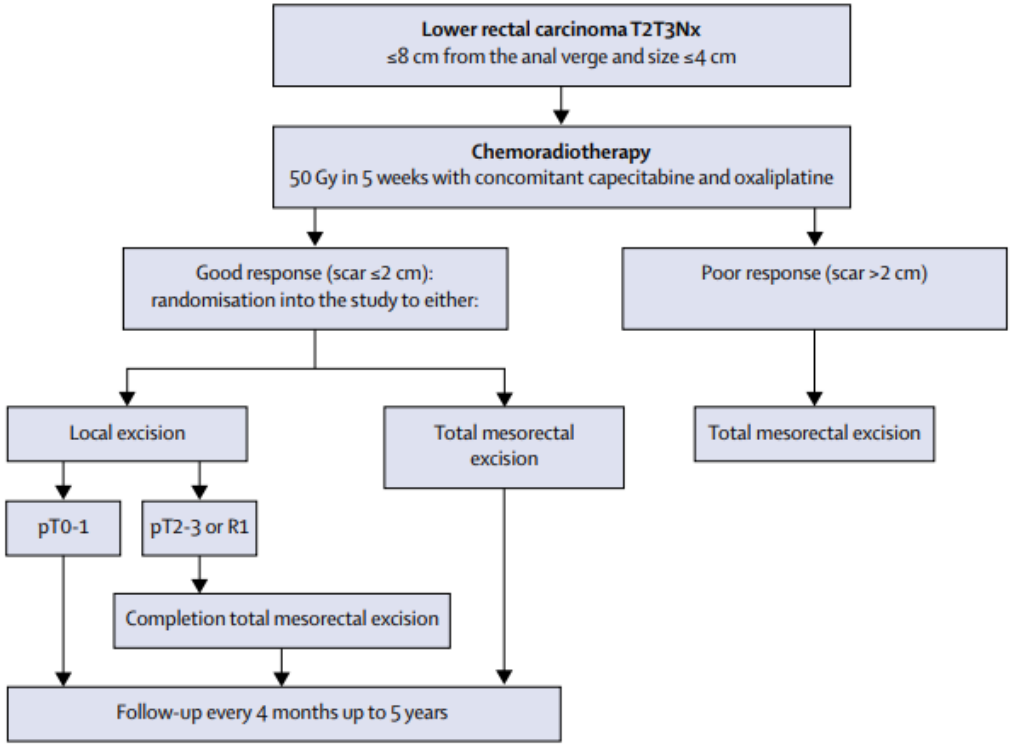
Lancet Oncol 2015;16:1537-46

Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial

Eric Rullier, Philippe Rouanet, Jean-Jacques Tuech, Alain Valverde, Bernard Lelong, Michel Rivoire, Jean-Luc Faucheron, Mehrdad Jafari, Guillaume Portier, Bernard Meunier, Igor Sieznieff, Michel Prudhomme, Frédéric Marchal, Marc Pocard, Denis Pezet, Anne Rullier, Véronique Vendrely, Quentin Denost, Julien Asselineau, Adélaïde Doussau

Organ preservation with chemoradiotherapy plus local excision for rectal cancer: 5-year results of the GRECCAR 2 randomised trial

Eric Rullier, Véronique Vendrely, Julien Asselineau, Philippe Rouanet, Jean-Jacques Tuech, Alain Valverde, Cecile de Chaisemartin, Michel Rivoire, Bertrand Trilling, Mehrdad Jafari, Guillaume Portier, Bernard Meunier, Igor Sieleznieff, Martin Bertrand, Frédéric Marchal, Anne Dubois, Marc Pocard, Anne Rullier, Denis Smith, Nora Frulio, Eric Frison, Quentin Denost



Primary endpoint: composite outcome of death-recurrence-morbidity-2yrs side effects

Secondary: 5yrs DFS OS LR DMFS

Lancet 2017;390:469-79
Lancet Gastroenterol Hepatol 2020;5:465-74

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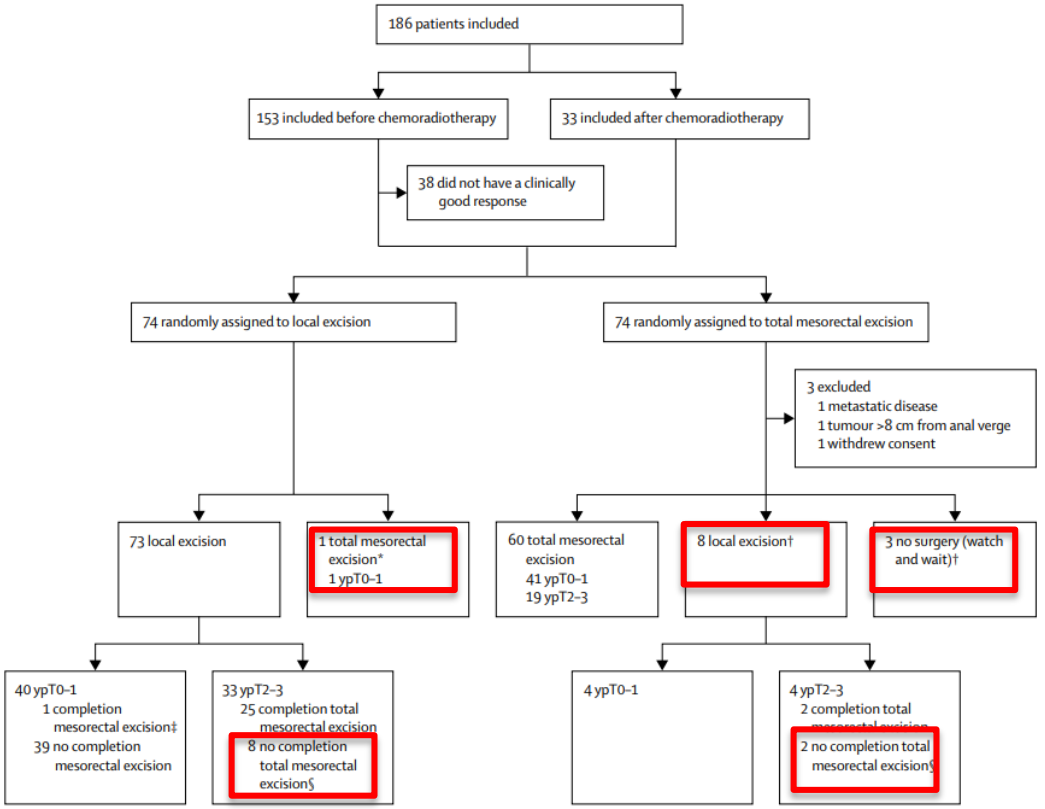
	Local excision (n=74)*	Total mesorectal excision (n=71)*	Odds ratio (95% CI)	p value†
Primary outcome: composite of death, tumour recurrence, morbidity, and side-effects at 2 years				
One or more events present	41/73 (56%)	33/69 (48%)	1·33 (0·62–2·86)	0·43
Details of composite outcome				
Death	4/74‡ (5%)	4/71‡ (6%)	0·98 (0·18–5·24)	0·98
Tumour recurrence	11/71 (16%)	14/70 (20%)	0·81 (0·32–2·03)	0·63
Major morbidity	17/70 (24%)	15/69 (22%)	1·18 (0·51–2·72)	0·68
Side-effects total	24/69 (35%)	19/65 (29%)	1·29 (0·53–3·14)	0·54
Colostomy	9/70 (13%)	5/68 (7%)	1·76 (0·61–5·02)	0·27
Faecal incontinence§	3/62 (5%)	9/65 (14%)	0·60 (0·20–1·82)	0·34
Sexual dysfunction	17/73 (23%)	12/67 (18%)	1·10 (0·46–2·64)	0·81



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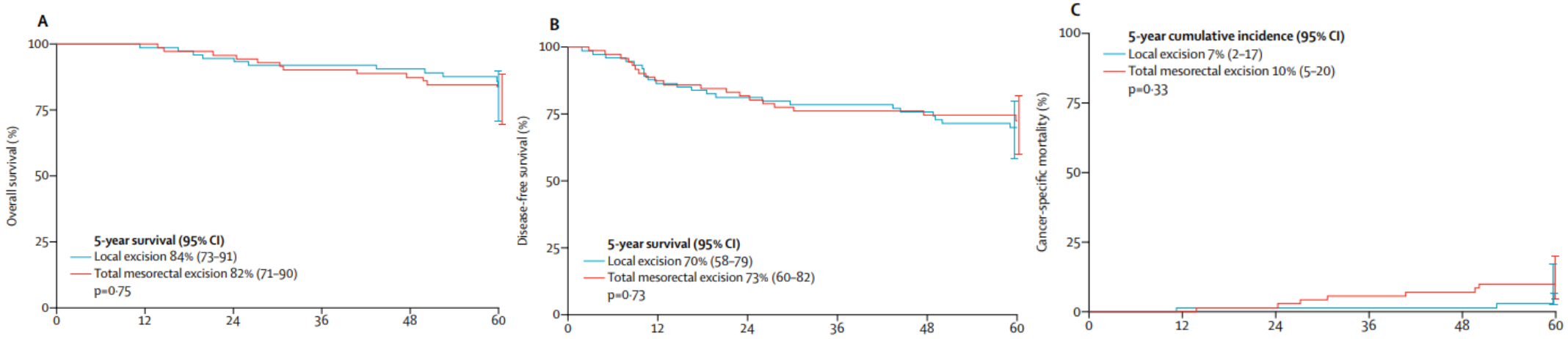

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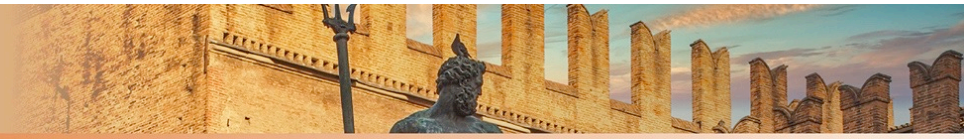

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	Local excision (n=74)	Total mesorectal excision (n=71)
Nodal stage		
N0	42 (57%)	48 (68%)
N1	32 (43%)	23 (32%)
Surgery undertaken		
Local excision	47 (64%)	6 (8%)
Local excision plus completion total mesorectal excision*	26 (35%)	2 (3%)
Total mesorectal excision†	1 (1%)	60 (85%)
No surgery	0	3 (4%)

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	Local excision	Total mesorectal excision	Unadjusted hazard ratio (95% CI)	Unadjusted p value	Adjusted hazard ratio (95% CI)	Adjusted p value
Modified intention-to-treat analysis	n=74	n=71	NA	NA	NA	NA
			–3·31)	0·95	0·71 (0·19–2·58)	0·60
			76)	0·61	0·48 (0·08–2·90)	0·42
			06)	0·90	0·86 (0·36–2·06)	0·73
			98)	0·75	0·92 (0·38–2·22)	0·85
			06)	0·73	0·87 (0·44–1·72)	0·68
			85)	0·33	0·65 (0·17–2·49)	0·53

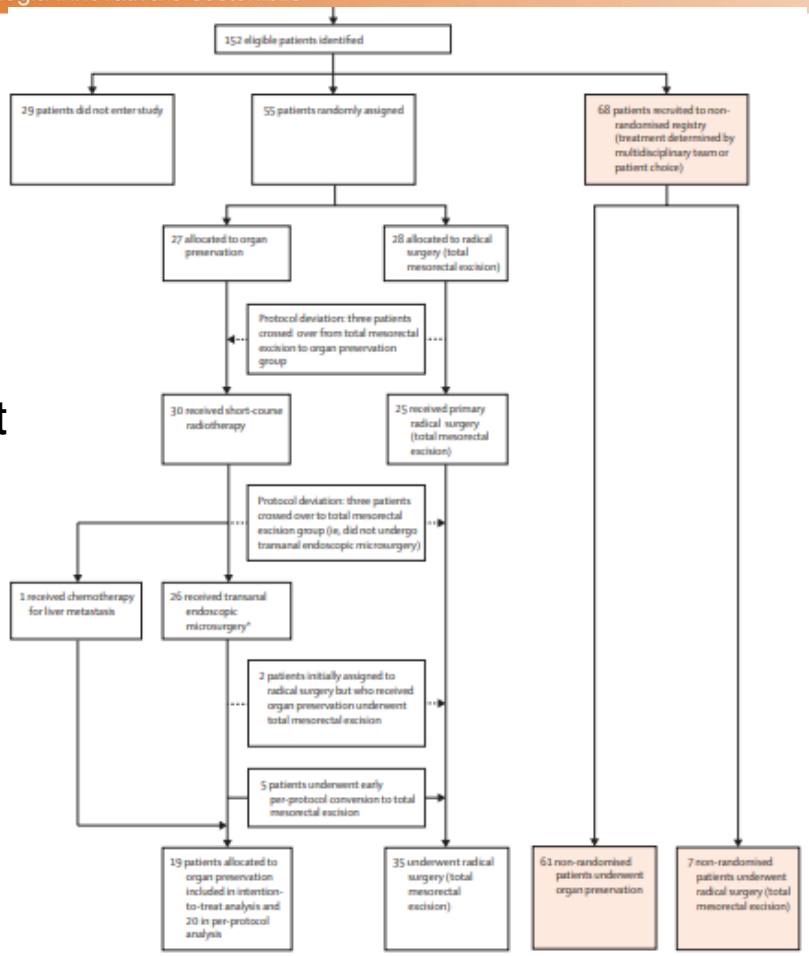
Patients Selection

QoL evaluation

Lancet 2017;390:469-79
Lancet Gastroenterol Hepatol 2020;5:465-74

Radical surgery versus organ preservation via short-course radiotherapy followed by transanal endoscopic microsurgery for early-stage rectal cancer (TREC): a randomised, open-label feasibility study

*Simon P Bach, Alexandra Gilbert, Kristian Brock, Stephan Korsgen, Ian Geh, James Hill, Talvinder Gill, Paul Hainsworth, Matthew G Tutton, Jim Khan, Jonathan Robinson, Mark Steward, Christopher Cunningham, Bruce Levy, Alan Beveridge, Kelly Handley, Manjinder Kaur, Natalie Marchevsky, Laura Magill, Ann Russell, Philip Quirke, Nicholas P West, David Sebag-Montefiore, on behalf of the TREC collaborators**



Primary endpoint: cumulative randomisation at 12, 18, and 24 months.

Secondary outcomes: safety, efficacy
health-related quality of life
EORTC QLQ C30 CR29

Lancet Gastroenterol Hepatol 2021; 6: 92–105

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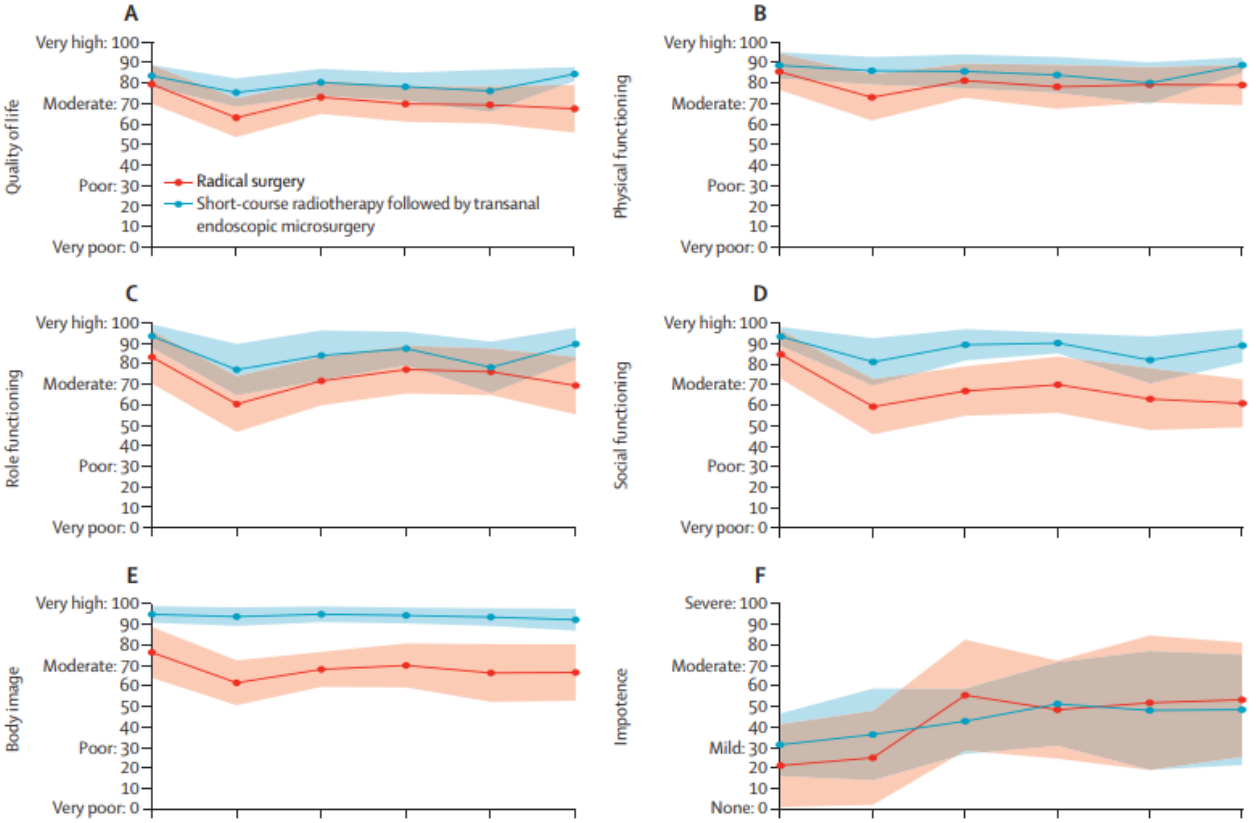


Cumulative randomization:
18 patients at 12 months,
31 at 18 months,
39 at 24 months
55 at 36 months

Good compliance to SCRT-organ preservation

No differences in Oncologic Outcomes

Lancet Gastroenterol Hepatol 2021; 6: 92–105

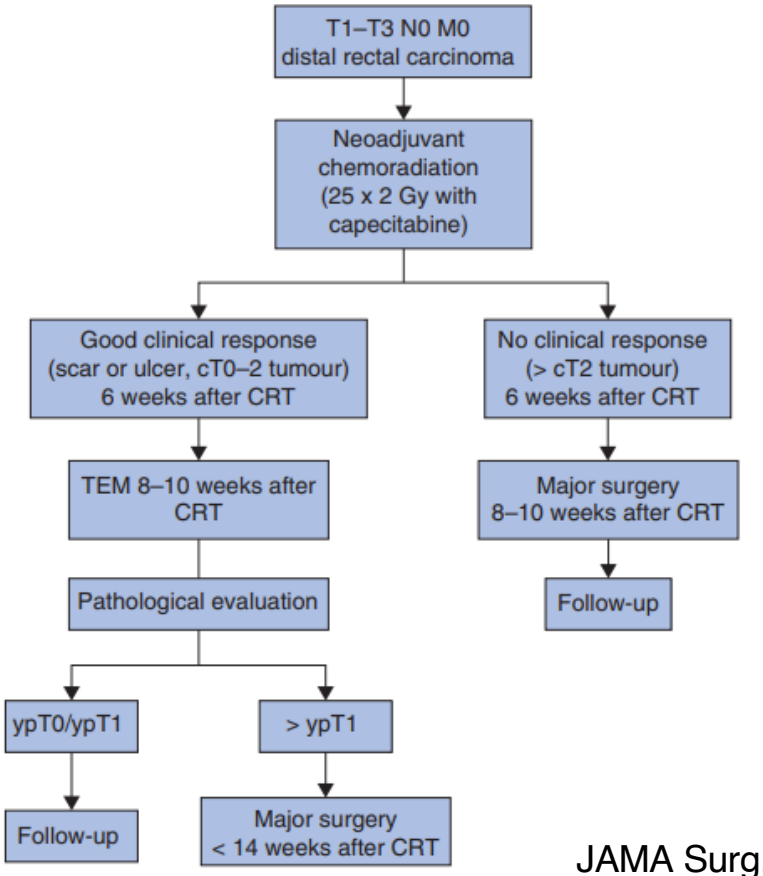
JAMA Surgery | Original Investigation

Long-term Oncological and Functional Outcomes of Chemoradiotherapy Followed by Organ-Sparing Transanal Endoscopic Microsurgery for Distal Rectal Cancer
The CARTS Study

Rutger C. H. Stijns, MD; Eelco J. R. de Graaf, MD, PhD; Cornelis J. A. Punt, MD, PhD; Iris D. Nagtegaal, MD, PhD; Joost J. M. E. Nuyttens, MD, PhD; Esther van Meerten, MD, PhD; Pieter J. Tanis, MD, PhD; Ignace H. J. T. de Hingh, MD, PhD; George P. van der Schelling, MD, PhD; Yair Acherman, MD; Jeroen W. A. Leijtens, MD; Andreas J. A. Bremers, MD, PhD; Geerard L. Beets, MD, PhD; Christiaan Hoff, MD, PhD; Cornelis Verhoef, MD, PhD; Corrie A. M. Marijnen, MD, PhD; Johannes H. W. de Wilt, MD, PhD; for the CARTS Study Group

Primary endpoint: ypT0-1 TEM
74%

Secondary:
Locoregional recurrences
HRQL



JAMA Surg. 2019;154(1):47-54

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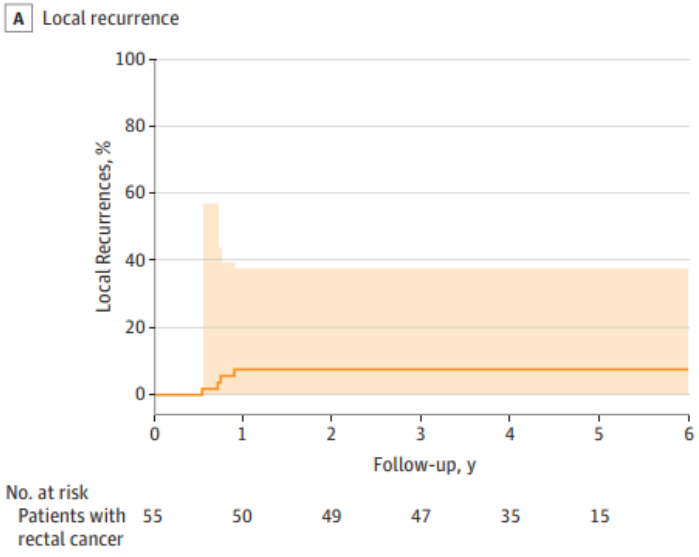
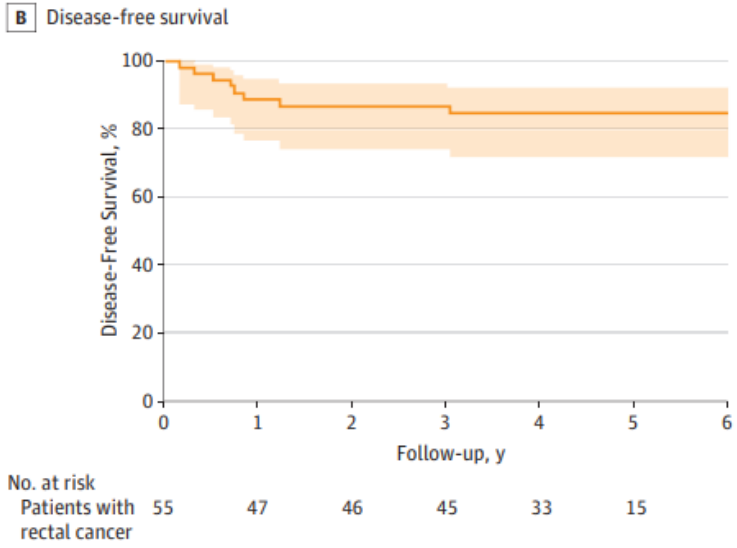
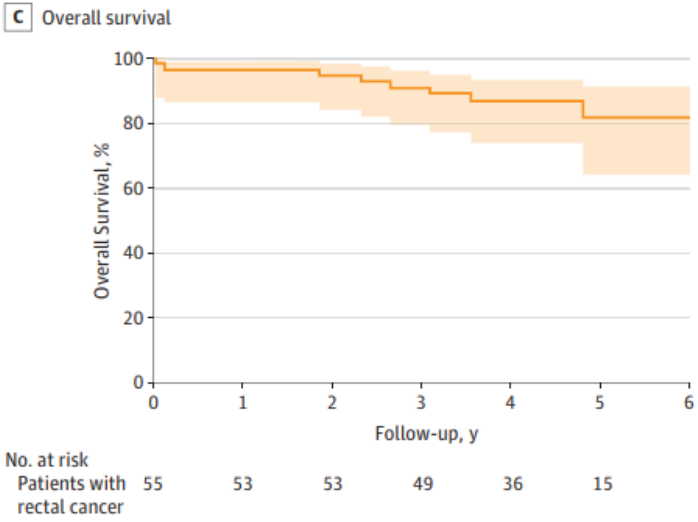
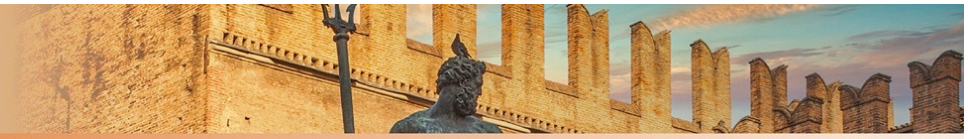






JAMA Surg. 2019;154(1):47-54



JAMA Surgery | Original Investigation

Long-term Oncological and Functional Outcomes of Chemoradiotherapy Followed by Organ-Sparing Transanal Endoscopic Microsurgery for Distal Rectal Cancer

The CARTS Study

Rutger C. H. Stijns, MD; Eelco J. R. de Graaf, MD, PhD; Cornelis J. A. Punt, MD, PhD; Iris D. Nagtegaal, MD, PhD; Joost J. M. E. Nuyttens, MD, PhD; Esther van Meerten, MD, PhD; Pieter J. Tanis, MD, PhD; Ignace H. J. T. de Hingh, MD, PhD; George P. van der Schelling, MD, PhD; Yair Acherman, MD; Jeroen W. A. Leijtens, MD; Andreas J. A. Bremers, MD, PhD; Geerard L. Beets, MD, PhD; Christiaan Hoff, MD, PhD; Cornelis Verhoef, MD, PhD; Corrie A. M. Marijnen, MD, PhD; Johannes H. W. de Wilt, MD, PhD; for the CARTS Study Group

	EORTC QLQ Score, Mean					
	TEM			TME		
EORTC QLQ Category	Baseline	Follow-up	*P* Value[a]	Baseline	Follow-up	*P* Value[a]
Global Health score	75.5	74.4	.73	81.7	73.1	.17
Physical Functioning score	89.7	83.3	.06	92.0	83.0	.03
Role Functioning score	86.7	84.4	.59	91.7	85.2	.18
Emotional Functioning score	72.0	86.9	.001	76.7	80.6	>.99
Cognitive Functioning score	88.4	88.9	.72	93.3	90.7	.71
Social Functioning score	88.4	89.4	.60	98.3	88.9	.10
Fatigue score	20.2	21.9	.60	12.2	18.7	.03
Nausea and Vomiting score	4.0	2.5	.67	5.0	24.7	.03
Pain score	8.1	12.7	.06	6.7	3.7	.16
Dyspnoe score	15.2	12.8	.48	10.0	18.5	.29
Insomnia score	22.2	14.4	.16	16.7	11.1	>.99
Appetite Loss score	5.1	17.8	.02	3.3	25.9	.04
Constipation score	8.1	5.6	.56	6.7	7.4	.66
Diarrhea score	13.1	7.8	.36	10.0	14.8	.66
Financial Difficulties score	7.1	13.3	.17	10.0	7.4	.79

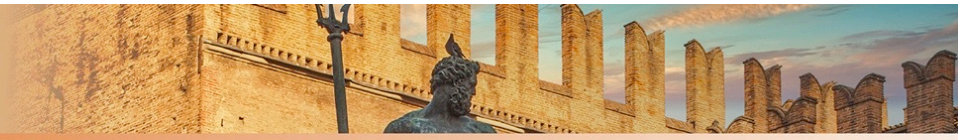
	EORTC QLQ Score, Mean					
	TEM			TME		
EORTC QLQ Category	Baseline	Follow-up	*P* Value[a]	Baseline	Follow-up	*P* Value[a]
Body Image score	95.5	88.1	.08	97.2	79.0	.11
Anxiety score	49.4	69.0	.005	58.3	74.1	.32
Weight Loss score	97.5	98.8	.32	91.7	96.3	.56
Sexual Interest score	56.9	59.0	.44	48.9	66.7	.16
Urinary Frequency score	24.1	29.2	.26	35.4	33.3	.50
Blood and Mucus in Stool score	29.5	2.7	.001	41.7	0	.32
Stool Frequency score	20.0	21.3	.72	22.2	27.8	.32
Dysuria score	1.3	8.3	.13	8.3	11.1	.56
Abdominal Pain score	11.1	13.1	.45	16.7	14.8	>.99
Buttock Pain score	13.6	22.6	.12	8.3	25.9	.20
Bloating score	11.1	15.5	.19	20.8	11.1	.08
Dry Mouth score	8.6	8.3	.32	16.7	11.1	.41
Hair Loss score	4.9	9.5	.41	0	0	>.99
Taste score	1.2	2.4	.32	0	3.7	.32
Flatulence score	34.6	38.3	.33	37.5	11.1	.23
Fecal Incontinence score	10.3	18.7	.25	16.7	33.3	.32
Painful Stools score	8.3	4.7	.16	20.8	50.0	.32
Sore Skin score	NA	16.7	NA	NA	16.7	NA
Embarrassment score	NA	16.7	NA	NA	35.2	NA
Stoma Care Problems score	NA	NA	NA	NA	66.7	NA
Impotence score	18.2	37.9	.78	20.8	63.3	.18
Dyspareunia score	4.2[b]	21.4[c]	.18	0	NA	NA

JAMA Surg. 2019;154(1):47-54

Organ Preservation in early – low risk rectal cancer

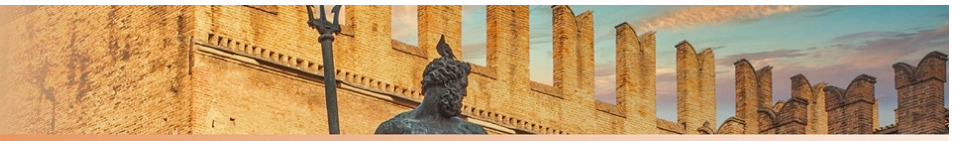
- Promising in terms of safety
- Oncological Outcomes comparable to TME
- Randomized trials are feasible

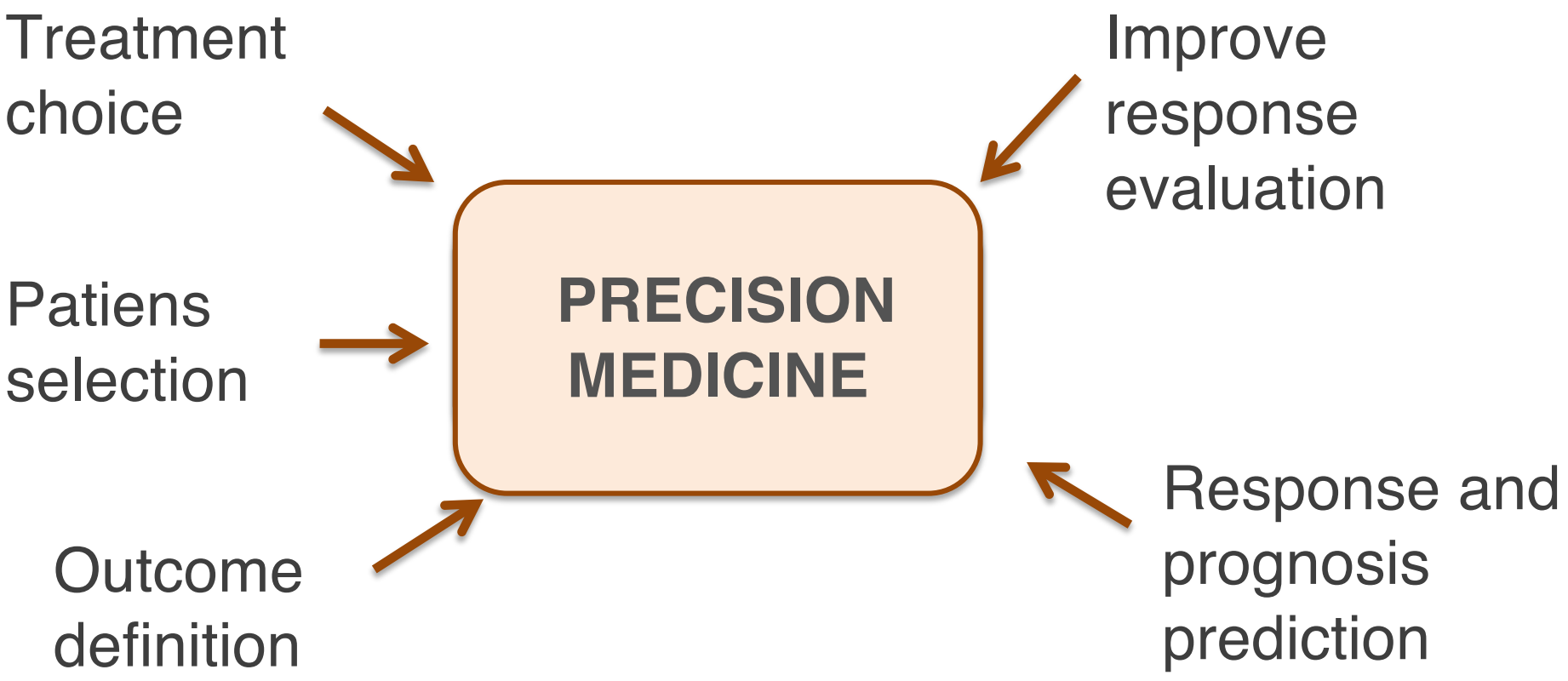
- Patients selection
- QoL crucial endpoint



Organ Preservation in early – low risk rectal cancer

- Rationale
- The available evidence
- **How to optimize treatment**




Treatment choice
Improve response evaluation
Patiens selection
PRECISION MEDICINE
Outcome definition
Response and prognosis prediction

Treatment choice

Organ Preservation in cT2N0 Rectal Cancer After Neoadjuvant Chemoradiation Therapy

The Impact of Radiation Therapy Dose-escalation and Consolidation Chemotherapy

Angelita Habr-Gama, MD, PhD,† Guilherme Pagin São Julião, MD,* Bruna Borba Vailati, MD,* Jorge Sabbaga, MD, PhD,‡ Patricia Bailão Aguilar, MD,§ Laura Melina Fernandez, MD,* Sergio Eduardo Alonso Araújo, MD, PhD,† and Rodrigo Oliva Perez, MD, PhD*†¶*

1991-2006
46 cT2N0 pts
45 Gy/25 fz
Boost 5.4 Gy/3 fz
FU-Leucovorin

→

2006-2016
35 cT2N0 pts
45 Gy/25 fz
Boost 9 Gy/5 fz
FU-Leucovorin

cCT FU-Leucovorin
3 cycles

→ cCR → WW

→ cPR → TME

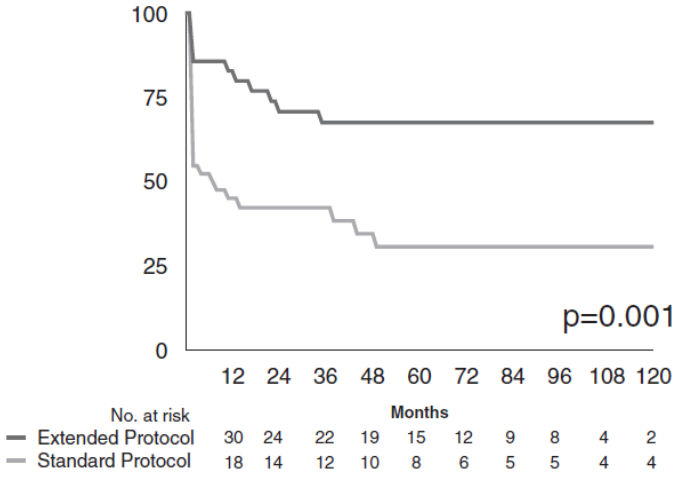
Ann Surg 2019; 269: 102-107

Treatment choice

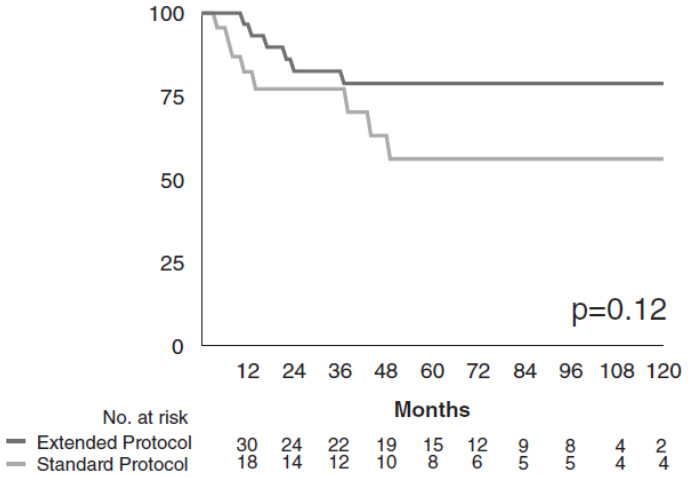
Organ Preservation in cT2N0 Rectal Cancer After Neoadjuvant Chemoradiation Therapy

The Impact of Radiation Therapy Dose-escalation and Consolidation Chemotherapy

Angelita Habr-Gama, MD, PhD,† Guilherme Pagin São Julião, MD,* Bruna Borba Vailati, MD,* Jorge Sabbaga, MD, PhD,‡ Patricia Bailão Aguilar, MD,§ Laura Melina Fernandez, MD,* Sergio Eduardo Alonso Araújo, MD, PhD,† and Rodrigo Oliva Perez, MD, PhD*†¶*



Five-year surgery-free survival for all cT2N0



Five-year surgery-free survival cT2N0 after cCR

cCR
56.6% standard CRT
85.7% after extended CRT

Ann Surg 2019; 269: 102-107

Treatment choice

Contact x-ray brachytherapy (Papillon) in addition to chemoradiotherapy to improve organ preservation in early cT2-T3 rectal adenocarcinoma: The 3-year results of OPERA randomized trial (NCT02505750).

Check for updates

Jean-Pierre Gerard, Nicolas N. Barbet, Tanguy Pacé-Loscos, Nicolas Magné, Jessica Serrand, Laurent Mineur, Melanie Deberne, Thomas Zilli, Amandeep Singh Dhadda, Arthur Sun Myint

cT2-T3ab
cN0-N1< 8mm
Staged using MRI

→ CRT 45Gy/ 5 wks / Capecitabine 825 mg / m^2
Sequential boost (9Gy/ 5 fr/ 1 wk)

→ T< 3 cm boost CXB (90 Gy/ 3 fr/ 4 wks)
sequential CRT

→ T≥ 3 cm CRT
sequential boost CXB (90 Gy/ 3 fr/ 4 wks)

144 pts
Median Follow up 34 months

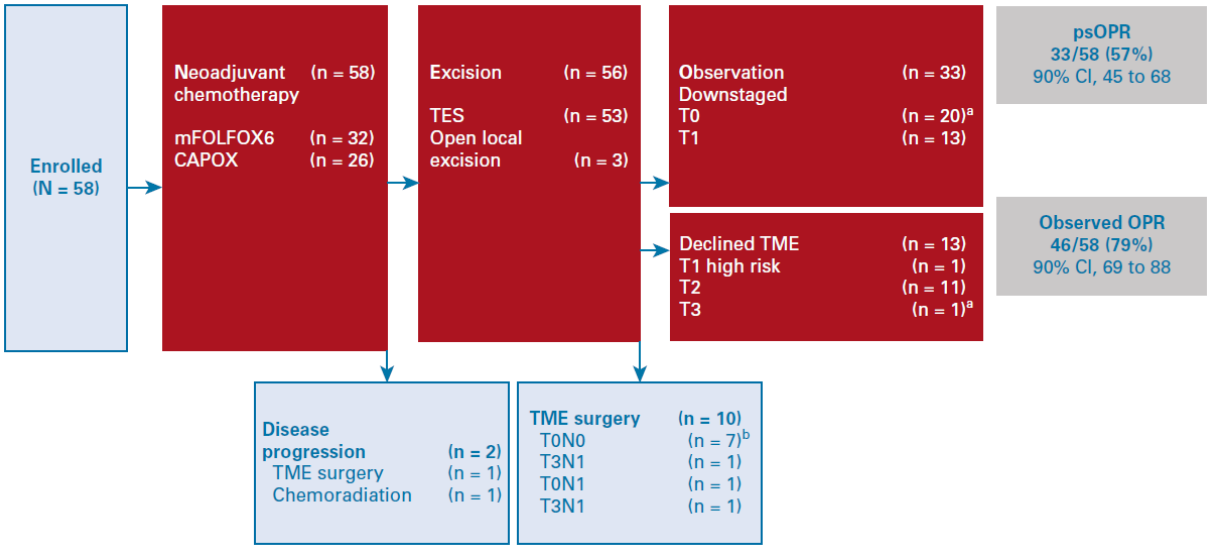
3y Organ Preservation
60% EBRT vs 81% CBX
97% CBX before CRT

J Clin Oncol 2022; 40, no. 16_suppl 3512-3512.

Treatment choice

Neoadjuvant Chemotherapy, Excision, and Observation for Early Rectal Cancer: The Phase II NEO Trial (CCTG CO.28) Primary End Point Results

Hagen F. Kennecke, MD, MHA[1]; Chris J. O'Callaghan, PhD, DVM, MSc[2]; Jonathan M. Loree, MD, MS[3]; Hussein Moloo, MD, MPH[4]; Rebecca Auer, MD, MSc[4]; Derek J. Jonker, MD[4]; Manoj Raval, MD, MSc[5]; Reilly Musselman, MD[4]; Grace Ma, MD[6]; Antonio Caycedo-Marulanda, MD[6]; Vlad V. Simianu, MD[7]; Sunil Patel, MD[2]; Lacey D. Pitre, MD[8]; Ramzi Helewa, MD, MSc[9]; Vallerie L. Gordon, MD[10]; Katerina Neumann, MSc, PhD, MD[11]; Halla Nimeiri, MD[12]; Max Sherry, MSc, MBA[2]; Dongsheng Tu, PhD[2]; and Carl J. Brown, MD, MSc[5]



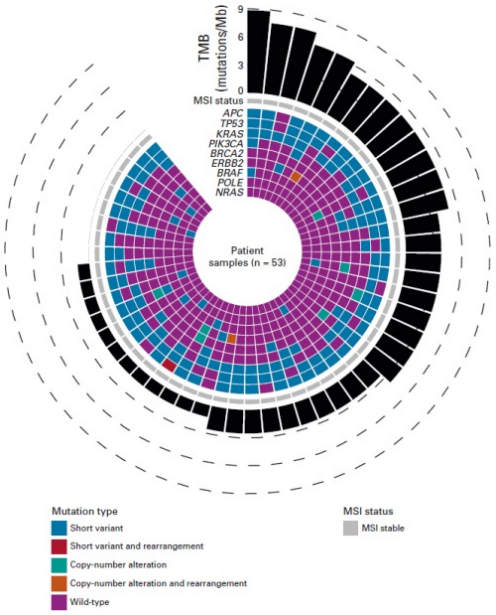
1yr / 2yr locoregional relapse free survival 98% and 90%

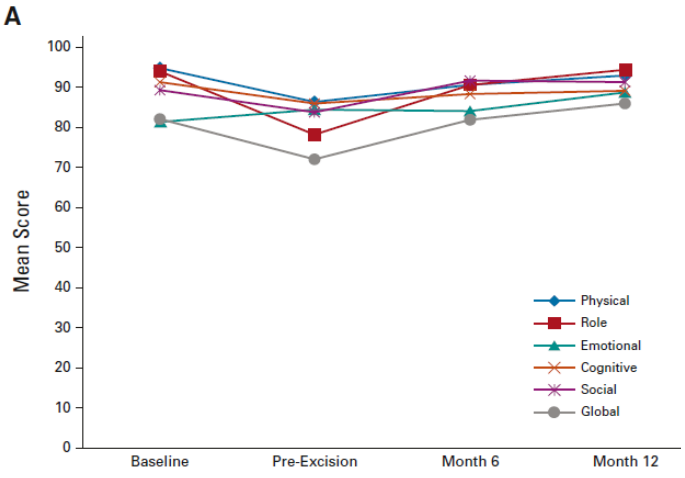
J Clin Oncol 2022 Aug 18;JCO2200184

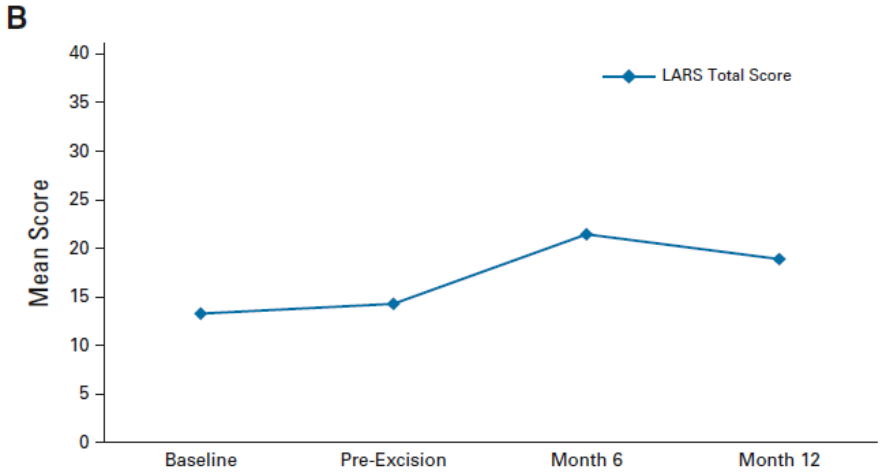
Treatment choice

Neoadjuvant Chemotherapy, Excision, and Observation for Early Rectal Cancer: The Phase II NEO Trial (CCTG CO.28) Primary End Point Results

Hagen F. Kennecke, MD, MHA[1]; Chris J. O'Callaghan, PhD, DVM, MSc[2]; Jonathan M. Loree, MD, MS[3]; Hussein Moloo, MD, MPH[4]; Rebecca Auer, MD, MSc[4]; Derek J. Jonker, MD[4]; Manoj Raval, MD, MSc[5]; Reilly Musselman, MD[4]; Grace Ma, MD[6]; Antonio Caycedo-Marulanda, MD[6]; Vlad V. Simianu, MD[7]; Sunil Patel, MD[2]; Lacey D. Pitre, MD[8]; Ramzi Helewa, MD, MSc[9]; Vallerie L. Gordon, MD[10]; Katerina Neumann, MSc, PhD, MD[11]; Halla Nimeiri, MD[12]; Max Sherry, MSc, MBA[2]; Dongsheng Tu, PhD[2]; and Carl J. Brown, MD, MSc[5]





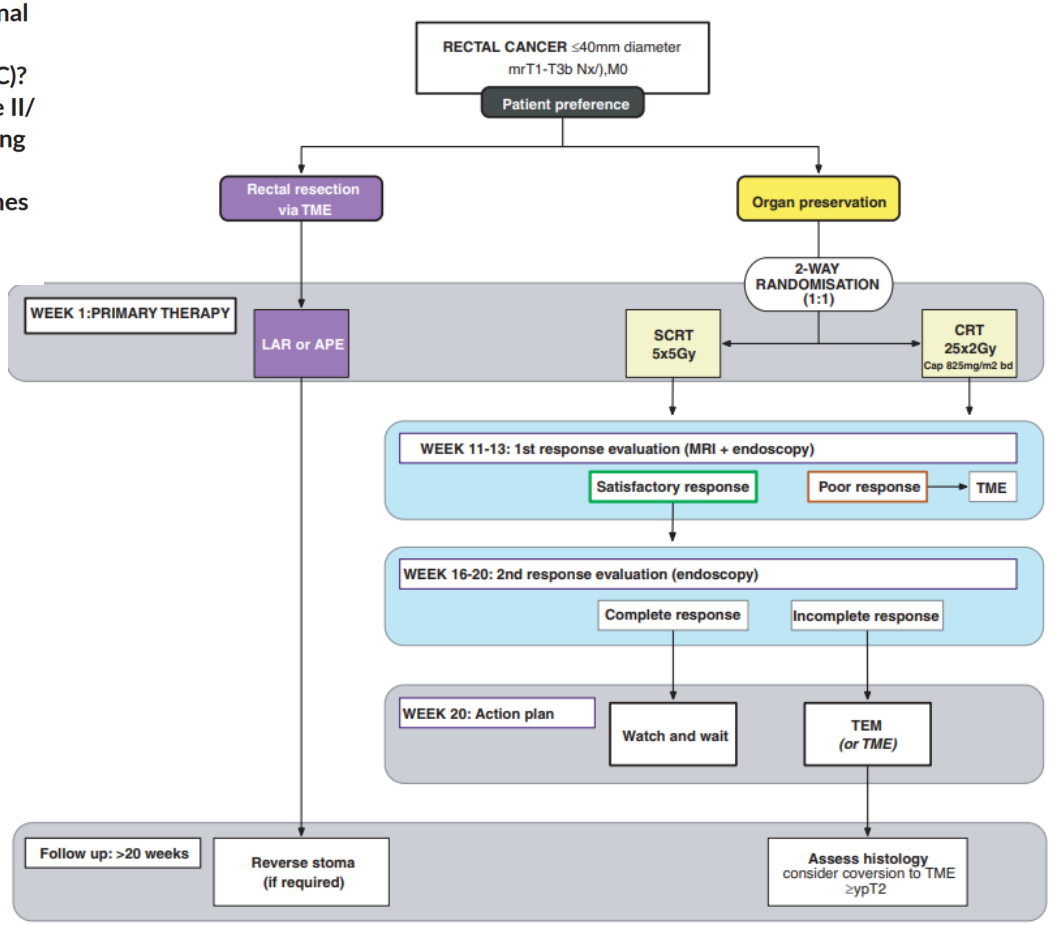


J Clin Oncol 2022 Aug 18;JCO2200184

Treatment choice/ Patients selection

Can we Save the rectum by watchful waiting or TransAnal surgery following (chemo)Radiotherapy versus Total mesorectal excision for early REctal Cancer (STAR-TREC)? Protocol for the international, multicentre, rolling phase II/III partially randomized patient preference trial evaluating long-course concurrent chemoradiotherapy versus short-course radiotherapy organ preservation approaches

Simon P. Bach | the STAR-TREC Collaborative†



Primary outcome:rate of organ preservation at 30 months.

Secondary:
Clinician-reported outcomes (acute tox)
Rate of non-operative management
Non-regrowth pelvic tumour control/DFS at 36 months,
OS 60 months
Patient-reported toxicity, health-related quality of life
Exploratory biomarker research uses circulating tumour DNA to predict response and relapse

Colorectal Disease. 2022;24:639–651

Patients selection

Watch and wait after a clinical complete response in rectal cancer patients younger than 50 years

Renu R. Bahadoer [1], Koen C. M. J. Peeters[1], Geerard L. Beets [2,3], Nuno L. Figueiredo [4,5], Esther Bastiaannet[1,6], Alexander Vahrmeijer [1], Sofieke J. D. Temmink[7], W. M. Elma Meershoek-Klein Kranenbarg[1], Annet G. H. Roodvoets[1], Angelita Habr-Gama[8], Rodrigo O. Perez [8], Cornelis J. H van de Velde[1] and Denise E. Hilling[1,9,*] and the International Watch & Wait Database Consortium (IWWD)

	< 50 years (*n* = 199)	≥ 50 years (*n* = 1353)	P§
Age at diagnosis (years)*	45 (40–48, 21–49)	66 (60–73, 50–98)	
Sex			0.145
M	123 (61.8)	907 (67.0)	
F	76 (38.2)	446 (32.0)	
Co-morbidity			<0.001
Yes	30 (16.9)	453 (47.6)	
No	148 (83.1)	499 (52.4)	
Unknown	21	401	
Clinical tumour category†			0.011
cT0–1‡	0 (0.0)	22 (1.8)	
cT2	34 (20.5)	349 (28.1)	
cT3	119 (71.7)	789 (63.5)	
cT4	13 (8)	82 (6.6)	
Unknown‡	33	111	
Clinical node category†			0.198
cN0	54 (32.1)	477 (37.8)	
cN1	68 (40.5)	471 (37.4)	
cN2	46 (27.4)	313 (24.8)	
Unknown	31	92	

	< 50 years (*n* = 199)	≥ 50 years (*n* = 1353)	P‡
Follow-up after decision to watch and wait (years)*	3.5 (2.9, 4.2)	3.1 (3.0, 3.3)	
Alive at end of registered follow-up			0.016
Yes	188 (94.5)	1203 (88.9)	
No	11 (5.5)	152 (11.2)	
Local regrowth†			0.715
Yes	44 (22.1)	315 (23.3)	
Within 6 months	21 of 44 (48)	117 of 315 (37.1)	
Within 7–12 months	12 of 44 (27)	106 of 315 (33.7)	
Within 13–24 months	7 of 44 (16)	63 of 315 (20.0)	
After 2 years	4 of 44 (9)	28 of 315 (8.9)	
Timing unknown	0 (0)	1 of 315 (0.3)	
No	155 (77.9)	1038 (76.7)	
Distant metastases†			0.754
Yes	19 (9.5)	120 (8.9)	
Within 12 months	8 of 19 (42)	43 of 120 (35.8)	
Within 13–24 months	5 of 19 (26)	32 of 120 (26.7)	
After 2 years	0 (0)	6 of 120 (5.0)	
Timing unknown	6 of 19 (32)	39 of 120 (32.5)	
No	180 (90.5)	1233 (91.1)	

BJS, 2022, 109, 114–120

Outcome definition

International consensus recommendations on key outcome measures for organ preservation after (chemo)radiotherapy in patients with rectal cancer

Emmanouil Fokas[1,2,3,4,30✉], Ane Appelt[5,30], Robert Glynne-Jones[6], Geerard Beets[7,8], Rodrigo Perez[9], Julio Garcia-Aguilar[10], Eric Rullier[11], J. Joshua Smith[10], Corrie Marijnen[12], Femke P. Peters[12], Maxine van der Valk[8], Regina Beets-Tan[7,13], Arthur S. Myint[14], Jean-Pierre Gerard[15], Simon P. Bach[16], Michael Ghadimi[17], Ralf D. Hofheinz[18], Krzysztof Bujko[19], Cihan Gani[20,21], Karin Haustermans[22], Bruce D. Minsky[23], Ethan Ludmir[23], Nicholas P. West[24], Maria A. Gambacorta[25], Vincenzo Valentini[25], Marc Buyse[26,27], Andrew G. Renehan[28,29], Alexandra Gilbert[5,30], David Sebag-Montefiore[5,30] and Claus Rödel[1,2,3,4,30]

Organ preservation assessed at 30–36 months after commencing treatment should be the primary intermediate end point for randomized phase II/III trials using either NOM or LE (for patients with a cCR or ncCR)

- Patient-reported LARS score is recommended as the best-available method of measuring anorectal function.

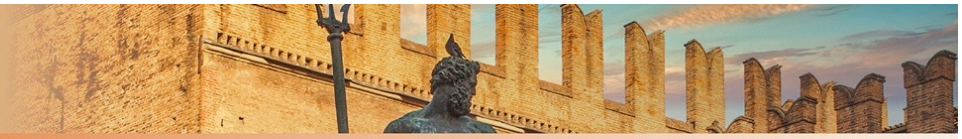
- A new organ preservation-specific score should be developed that includes the ability to measure other functional aspects, such as urinary and sexual dysfunction in addition to bowel dysfunction.

- Overall QoL, should be used to document adverse events and how they affect patients.

- Ten symptomatic toxicity items were selected as the highest priorities for evaluation, with a specific time schedule for measurement.

- A new, validated PRO scale should be developed specifically for patients undergoing treatment with organ preservation approaches.

Nat Rev Clin Oncol 2021;18(12):805-816



Response and prognosis prediction

Prediction of Poor Response to Neoadjuvant Chemoradiation in Patients With Rectal Cancer Using a DNA Repair Deregulation Score: Picking the Losers Instead of the Winners

Leandro Jimenez, M.S.[1] • Rodrigo O. Perez, M.D., Ph.D.[2]
Guilherme Pagin São Julião, M.D.[2] • Bruna Borba Vailati, M.D.[2]
Laura M. Fernandez, M.D.[2] • Joaquim Gama-Rodrigues, M.D., Ph.D.[2]
Angelita Habr-Gama, M.D., Ph.D.[2] • Jennifer DeVecchio, M.B.[3]
Matthew F. Kalady, M.D.[3,4] • Anamaria A. Camargo, Ph.D.[1]

Artificial intelligence with magnetic resonance imaging for prediction of pathological complete response to neoadjuvant chemoradiotherapy in rectal cancer: A systematic review and meta-analysis

Lu-Lu Jia[1], Qing-Yong Zheng[2], Jin-Hui Tian[3], Di-Liang He[1], Jian-Xin Zhao[1], Lian-Ping Zhao[4] and Gang Huang[4*]

[1]The First Clinical Medical College of Gansu University of Chinese Medicine, Lanzhou, China, [2]Evidence-Based Nursing Center, School of Nursing, Lanzhou University, Lanzhou, China, [3]Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou, China, [4]Department of Radiology, Gansu Provincial Hospital, Lanzhou, China

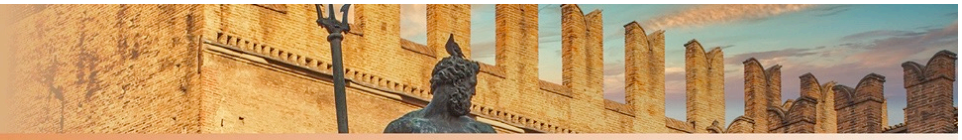
Can pretreatment platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios predict long-term oncologic outcomes after preoperative chemoradiation followed by surgery for locally advanced rectal cancer?

Sang Hyun An, Ik Yong Kim
Department of Surgery, Yonsei University Wonju College of Medicine, Wonju, Korea

A Panel of Tumor Biomarkers to Predict Complete Pathological Response to Neoadjuvant Treatment in Locally Advanced Rectal Cancer

Chiara Dalle Fratte,* Silvia Mezzalira,* Jerry Polesel,† Elena De Mattia,* Antonio Palumbo,‡ Angela Buonadonna,§ Elisa Palazzari,¶ Antonino De Paoli,¶ Claudio Belluco,# Vincenzo Canzonieri,‡** Giuseppe Toffoli,* and Erika Cecchin*

Dis Colon Rectum 2020; 63: 300–309
Front. Oncol. 12:1026216
Ann Coloproctol 2022;38(3):253-261
Oncology Research, Vol. 28, pp. 847–855



Conclusions

In early- low risk rectal cancer cT2-T3ab N0

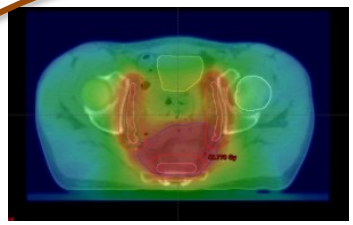
- Intergrated treatments involving organ sparing approach are safe in terms of toxicity and effective in terms Oncological Outcomes
- This approach can improve QoL of patients
- To evaluate this approach a QoL evaluation is needed
- Different integrated approaches were reported
- RT and/or CT intensification appears to be useful

Conclusions

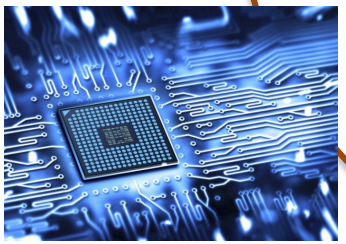
In early- low risk rectal cancer cT2-T3ab N0

- Randomised trials are feasible but should include patients preference
- Patients selection is crucial and requires refined classification of risk
- Clinical factors should be integrated with molecular, biologic and radiomic features

Conclusions



PATIENT



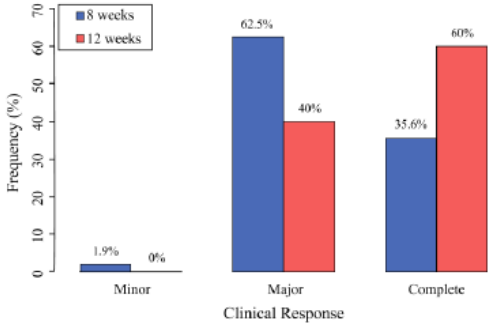
Conclusions

L'esperienza Italiana

Local Excision After Preoperative Chemoradiotherapy for Rectal Cancer: Results of a Multicenter Phase II Clinical Trial

Salvatore Pucciarelli, M.D.[1] • Antonino De Paoli, M.D.[2] • Mario Guerrieri, M.D.[3]
Giuseppe La Torre, M.D.[4] • Isacco Maretto, M.D.[1] • Francesco De Marchi, M.D.[5]
Giovanna Mantello, M.D.[6] • Maria Antonietta Gambacorta, M.D.[7]
Vincenzo Canzonieri, M.D.[8] • Donato Nitti, M.D.[1] • Vincenzo Valentini, M.D.[7]
Claudio Coco, M.D.[9]

160 patients
98 patients were managed with LE and 62 with WW.
cCR increased from 8- to 12-week restaging.
At a median 24 months follow-up, a tumor regrowth was found in 15 (24.2%) patients undergoing WW.



Rectal Sparing Approach After Neoadjuvant Therapy in Patients with Rectal Cancer: The Preliminary Results of the ReSARCh Trial

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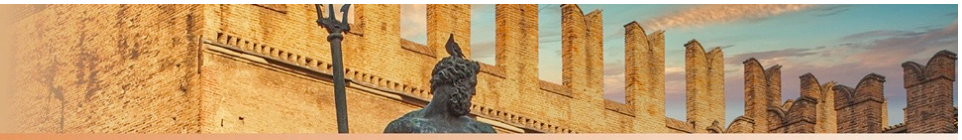
	ypT stage		
	ypT0 (n = 57)	ypT1 (n = 22)	ypT > 1 (n = 19)
Clinical response at 12 weeks			
Major (n = 63)	31 (49.2%)	15 (23.8%)	17 (27.0%)
Complete (n = 35)	26 (74.3%)	7 (20.0%)	2 (5.7%)

Dis Colon Rectum 2013; 56: 1349–1356
Ann Surg Oncol. 2022 Mar;29(3):1880-1889



Conclusion

Azienda Ospedaliera – Università di Padova.

Dipartimento di Scienze Chirurgiche, Oncologiche e Gastroenterologiche.

Università di Padova

Registro dei trattamenti conservativi dopo radio e/o chemioterapia neoadiuvante nei pazienti con carcinoma del retto

N. Registro

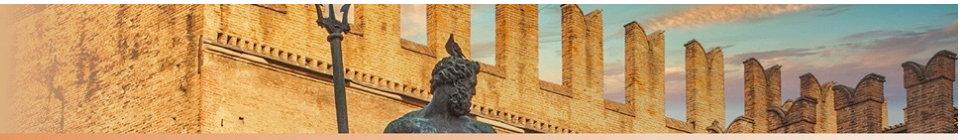
V 1.0 15/02/2022

Gruppo Coordinatore.

Chirurgia Generale 3. Dipartimento di Scienze Chirurgiche, Oncologiche e Gastroenterologiche.

Azienda Ospedaliera - Università di Padova

SICO/AIRO/AIOM



Grazie per l'attenzione